

# Quality of life in patients with soft tissue extremities sarcoma

Angéla Christie Filankembo Kava<sup>1</sup>, Noura Qarmiche<sup>1</sup>, Laila Chbani<sup>2</sup>, S.Arifi<sup>3</sup>, N.Tachfouti<sup>1</sup>, M.Berraho<sup>1</sup>, M.Maaroufi<sup>4</sup>, M.Idrissi<sup>5</sup>, A.Ibrahimi<sup>5</sup>, A.Mrini<sup>5</sup>, T.Bouhafa<sup>6</sup>, S.El Fakir<sup>1</sup>

1. Department of epidemiology and public health, Faculty of Medicine, University Sidi Mohammed Ben Abdellah, Fez, Morocco

2. Department of Pathology Hassan II University Hospital, Fez, Morocco

3. Medical oncology department, Hassan II University Hospital, Fez, Morocco

4. Department of Radiology, Hassan II University Hospital, Fez, Morocco

5. Department of Trauma-orthopedics B4, Hassan II University Hospital, Fez, Morocco

6. Department of Radiotherapy, Hassan II University Hospital, Fez, Morocco

Corresponding author: Angéla Christie Filankembo Kava

Mail: [fackava@gmail.com](mailto:fackava@gmail.com)

Telephone : +241065363369

**Abstract:** Aim: Sarcoma treatment has several side effects in addition to the symptoms related to the pathology itself. In addition to physical condition, it also concerns psychological health and socioeconomic life and can alter quality of life. The aim of this study is to evaluate quality of life and its determinants in patients suffering of sarcoma. Methodology: A prospective study in Hospital Hassan II of Fez from June 2017 to January 2020. Quality of life has been evaluated using EORTC-QLQ C30 questionnaire. Results: We included 117 patients with a male / female sex ratio of 1.4. Patients under 60 years were predominant (64.1%). Liposarcoma was found in 33.3%. Metastases and comorbidity were found in 39.5% and 78.6% of cases respectively. The mean overall health score was 51.1 (SD = 26.7). The highest functioning score was social functioning at 95.3 (SD = 14.7). Considering the symptom areas, pain and fatigue were the most graceful symptoms with scores of 38.1 (SD = 33.1) and 36.7 (SD = 34.1) respectively, while diarrhea and constipation was less common with a mean score of 5.90 (SD = 18.1) and 9.7 (SD = 26.0). In the functional domains, men had a better functional role ( $\beta = 16.23$ ) but a worse social functioning ( $\beta = -21.43$ ). Older patients had a poorer mean functioning score ( $\beta = -19.45$ ). Regarding symptoms, women had more insomnia ( $\beta = -21.43$ ) but less loss of appetite ( $\beta = 46.02$ ). Conclusion: Quality of life in patients with soft tissues sarcoma is altered.

**Keywords:** sarcoma, histology, quality of life, EORTC-QLQ C30 questionnaire

## INTRODUCTION

Sarcomas are rare malignant tumors that develop from connective and supporting tissues. Although the pathogenesis remains difficult to determine, some risk factors have been highlighted, in particular gender and bone growth rate.

The mode of discovery is most often pain or swelling next to the tumor. Once discovered, treatment is most often based on a combination of surgery and radiotherapy if the tumor is localized and chemotherapy for advanced and / or metastatic local tumors. These different therapeutic modalities have side effects that can sometimes manifest themselves several years after the initial treatment in addition to the symptoms related to the pathology itself, sometimes long-term follow-up[1]. In addition to physical condition, it also concerns psychological health and socioeconomic life and can alter quality of life. As a result, the quality of life (QoL) of patients with sarcoma may be impaired. Assessment of health-related quality of life (HRQoL) is essential for holistic care [2].

Quality of life (QoL) measurements, based on the patient's perspective, are used frequently nowadays to determine the global impact of diseases as well as medical treatments. HRQoL assesses the health status of patients, which reflects the physical, psychological, social, and emotional conditions. HRQoL has been recognized as an important measure of wellbeing in patients with chronic diseases such as cancer. HRQoL is an important outcome in itself, but also studies across disease states have demonstrated an association between lower HRQoL and mortality[3].

HRQoL could serve as an important indicator for the treatment outcomes, particularly for the patients with chronic diseases such cancer.

Indeed, many studies performed comparing the quality of life in the general population to that of patients with sarcoma have shown lower quality of life scores in subjects with sarcoma [4,5].

In Morocco, the specific incidence rate of bone sarcoma in 2012 was 0.9% and conjunctive tumor was 1.2% respectively in men and women according to the cancer registry of Grand Casablanca[6]. It is a rare cancer for which the quality of life of the subjects requested remains to be assessed (4).

The aim of the present study was to describe self-reported HRQOL in patients with sarcoma and to investigate its associations with sociodemographics and clinical variables.

## **PATIENT AND METHODS**

This was a prospective study of cases of soft tissue sarcoma of extremities realized in Hassan II hospital of Fez from January 2017 to October 2020. The eligibility criterion was a histological test for soft tissue sarcoma and Surface mass (above aponeurotic) > 5 cm or deep mass regardless of the size. The items collected were: Age at diagnosis ranged in class (<60 years and older than 60 years), sex, level of education, habitat type, histological type and FNCLCC (Fédération nationale des centres de lutte contre le cancer) Grade, tumor stage, type of habitat, marital status, the performans status of seeing (scale WHO), the existence of comorbidities, , the metastatic status, the type of treatment.

### *COLLECTION DATA PROCEDURE*

Quality of life was measured using the Moroccan Arabic version of EORTC QLQ-C30 [7]. The EORTC QLQ-C30 is a well-known instrument for measuring quality of life in cancer patients. It is composed of nine multi-item scales: 5 functional scales, a global QOL scale (GQOL), and three symptom scales (fatigue, pain, nausea / vomiting). In addition, there are five single item symptom scales (dyspnea, sleep disturbance, appetite loss, constipation and diarrhea); and a final item evaluates the perceived financial impact of the disease. The QLQ-C30 is a self-reporting questionnaire; however it was administered to illiterate patients by trained interviewers.

All socio-demographic, economic and therapeutic data were extracted for sarcoma: age, gender, geographic origin, marital status, profession, income, histological type and Grade, tumor stage, type of habitat, marital status, the performans status of seeing (scale WHO), the existence of comorbidities, , the metastatic status, the type of treatment.

### *STATISTICAL ANALYSIS*

Scores of the items were linearly transformed to a scale from 0 to 100. A high score for a functional scale represents a healthy level of functioning, a high score for the global health status represents a high quality of life, but a high score for a symptom item represents a high

level of symptomatology [8].

Descriptive analysis was performed for sociodemographics and clinical features. To describe the quality of life scores, we calculated the means and standard deviations.

We analyzed the association of scale scores with socio-demographic and clinical variables, by t-tests and one-way ANOVA. Variables with  $P \leq 0.20$  on univariate analysis were taken in account in the multivariate linear regression model to assess the predictors of the scales of the EORTC QLQ – C30. Results of the multivariate analyses are presented as  $\beta$  with a P value. The significance level was set at 0.05. Data analysis was performed using the statistical software package SPSS 17.0.

### *ETHICAL APPROVAL*

Ethical approval was obtained from the ethics committees in the University Hospital Center Hassan II in Fez- Morocco and all the subjects were informed of the conditions related to the study and gave their written, informed consent number 34/16.

### *CONFLICT OF INTEREST AND FUNDING*

The authors declare no conflict of interest. This research did not receive any funding from a public, commercial or not-for-profit funding agency.

## **RESULTS**

A total of 117 subjects were included in the study. The male–female sex ratio was 1.4. Patients under 60 years ago were predominant; they represented 64.1% of the sample. Majority of patients came from urban areas (60.6 %), a significant number were illiterate (56.4 %), and only 4.5 % had a high level of education.

Clinically, liposarcoma was found in 33.3%. Patients were most frequently in grade 1 according to WHO performans status (68.0%). Metastasis was found in 39.5% and comorbities in 78.6% of cases. Only 33.3% of patients received an association of chemotherapy-radiotherapy and surgery, neo-adjuvant chemotherapy in 29.2%, neo-adjuvant radiotherapy in 14.6% and firstly surgery in 16.7%. Table 1 displays the demographic and clinical characteristics of participants.

Tableau 1: Patient’s baseline characteristics (N=117)

Characteristics	Effective (%)
Gender (N=116)	
Female	48 (41.0)
Male	68 (58.1)
Age range (N=117)	
<60 years	75 (64.1)
>60 years	42 (35.9)
Level of studies (N=112)	
None	66 (56.4)
Primary	19 (17.0)
Secondary	17 (15.2)
Universitary	5 (4.5)
Other	5 (4.5)
Habitat (N=109)	
Urban	66 (60.6)
Rural	43 (39.4)
Histology (N=108)	
Leiomyosarcoma	13 (12.0)
Liposarcoma	36(33.3)
EWING sarcoma	8(7.4)
Other	51 (47.2)
Treatment (N=16)	
None	3 (6.3)
Chemotherapy	14 (29.2)
Radiotherapy	7 (14.6)
Surgery	8 (16.7)
Association	16 (33.3)
Scale WHO (N=50)	
0	6 (12.0)
1	34 (68.0)
2	10 (20.0)
Comorbidity (N=40)	
Yes	33 (78.6)
No	9 (21.4)
Metastasis (N=43)	
Yes	17 (39.5)
No	26 (60.5)

HEALTH RELATED QUALITY OF LIFE  
EORTC QLQ-C30

Of the QLQ – C30 scales, table 2 presents the mean scores of the functional and the symptom scales. The mean score for the global health status for breast cancer patients was 51.1 (SD = 26.7). The best functional outcomes were found for the social and cognitive functioning subscales (the respective mean scores were 95.3 (SD = 14.7) and 82.1 (SD=22.2)). In the symptom scale, Pain and Fatigue were the most pronounced symptoms (the mean scores were 38.0 (SD =33.1) and 36.7 (SD = 34.1) respectively), diarrhea and constipation were the less frequent symptoms (the respective mean scores were5.90 (SD=18.1) and 9.7 (SD = 26.0)).

Tableau 2: Scores of EORTC QLQ-C30 among sarcoma Patients, Morocco

Domain	Mean	Standard deviation
<i>Global health score and functioning</i>		
Global Health Status	51.1	26.7
Physical Functioning	61.4	33.1
Role Functioning	55.6	38.2
Emotional Functioning	71.9	27.7
Cognitive Functioning	82.2	22.2
Social Functioning	95.3	14.7
<i>Symptoms Domains</i>		
Fatigue	36.7	34.1
Nausea and Vomiting	11.6	24.7
Pain	38.0	33.1
Dyspnea	26.0	32.5
Insomnia	21.4	31.1
Appetite Loss	24.7	36.6
Constipation	9.7	26.0
Diarrhea	5.90	18.1
Financial difficulty	21.5	31.3

FACTORS ASSOCIATED WITH HRQOL SCALE SCORES

- UNIVARIATE ANALYSIS

Considering global health, there have not significant difference among sociodemographics and clinical variables. Regarding functioning domain, female reported a worse physical functioning score than male (53.1 vs 48.29; p=0.048). They also reported a worse functioning score than male (43.6 vs 63.7; p=0.010). Older patients presented a worse physical functioning score than patient less than 60 years ago (52.7 vs 65.9; p=0.048). They also presented a smallest role functioning score than younger patient (42.9 vs 62.2; p=0.018). In symptoms domains, female presented most frequently fatigue than male (45.02 vs 31.0; p=0.047). Female described also more frequently insomnia and appetite loss than male (35.9 vs 11.3; p<0.001 and 34.2 vs 18.1; p=0.034). Patient with an university level presented a better cognitive functioning score than other (p=0.004) and a better social functioning score (p=0.034). Subjects with a university level reported a better functioning cognitive score and a better social functioning score (p=0.004 and p=0.034 respectively). Patients with primary instruction level reported most frequently diarrhea (p=0.018). These results are reported in table 3.

Tableau 3: Factors associated with HRQOL scale scores

Characteristics	QL	PF	RF	CF	SF	FA	NV	PA	SL	AP	DI
	β	β	β	β	β	β	β	β	β	β	β
Gender(versus Female) Male		9.33	2.60			-12.58	-8.67		-21.23*	-14.59	
Age range (versus <60 years) >60 years	-2.10	-7.01			3.22	11.59					

Level of studies (versus None)										
Primary	4.27	5.06	-	-	-		16.75	-6.07		14.11*
Secondary	19.55	21.0	13.79*	17.28*	10.6		*	-15.55		*
Universitary	*	8	*	*	6		6.15	-16.72		-4.40
Other	0.11	23.7	-3.99	9.20	-		-7.04	-24.29		-4.40
	9.28	5	2.28	12.81	3.29		-			-4.40
		6.45	2.05	3.65	2.95		10.08			
Histology (versus Leiomyosarcoma)										
Liposarcoma		11.3	4.26			-		0.25	-5.03	-
EWING sarcoma		8	6.72			3.08		16.1	8.50	25.1
Autre		-	-1.83			0		3	7.13	9
		5.56				18.2		-		-
		-				0		22.4		5/50
		10.1				26.8		8		-
		7				8				0.54

Global health status(QL), Physical functioning(PF), Role functioning(RF), Emotional functioning (EF), Cognitive functioning (CF), Social functioning(SF), Fatigue(FA), Nausea and vomiting(NV), Pain(PA), Dyspnoea(DY),Insomnia(SL), Appetite loss(AP), Constipation(CO),Diarrhoea(DI), Financial difficulties(FI).

\*:P<0.05

\*\* :P<0.01

- MULTIVARIATE ANALYSIS BETWEEN SOCIO-DEMOGRAPHICS AND CLINICAL VARIABLES AND QUALITY OF LIFE EORTC QLQ C-30

In functioning domains, we reported that man had better functioning role than female ( $\beta=16.23$ ) but worse social functioning ( $\beta= -21.43$ ). Older patients presented a worse mean role functioning score than patients under 60 years ( $\beta=-19.45$ ). Patient with instruction reported a better functioning physical mean score than patient without instruction. Patient without instruction presented a worse mean functioning physical score than patient without instruction. Patient with histological diagnosis of liposarcoma described a better functioning role mean score than patient with histological diagnosis of leiomyosarcoma.

Regarding symptoms domains, female presented more frequently insomnia than male ( $\beta= -21.43$ ) but less appetite loss than male ( $\beta=46.02$ ). There was no difference considering other symptoms domains between male and female. Patient with histological diagnosis of leiomyosarcoma described less pain than patient with liposarcoma, Ewing Sarcoma and other sarcoma (table 4).

**Tableau 4:** Multivariate analysis between socio-demographics and clinical variables and quality of life EORTC QLQ C-30

Characteristics	PF $\beta$	RF $\beta$	FA $\beta$	SL $\beta$	AP $\beta$	PA $\beta$
Gender Male versus Female	-	16.23*	-	-21.43**	46.02*	-
Age range >60 years versus <60 years	-	-19.45*	-	-	-	-
Study level (versus none)						
Primary	6.27					
Secondary	25.60**	-	-	-	-	-
Universitary	25.16					
Other	9.16					
Histology (versus leiomyosarcoma)						
Liposarcoma	-	12.99	-3.08	-	-	2.19
EWING sarcoma		-5.373	18.20			15.75
Other		-21.85	26.87			27.15

---

--	--	--	--	--	--	--

Global health status(QL), Physical functioning(PF), Role functioning(RF), Emotional functioning (EF), Cognitive functioning (CF), Social functioning(SF), Fatigue(FA), Nausea and vomiting(NV), Pain(PA), Dyspnoea(DY),Insomnia(SL), Appetite loss(AP), Constipation(CO),Diarrhoea(DI), Financial difficulties(FI).

\*:P<0.05

\*\* :P<0.01

## DISCUSSION

The study reported that global mean health score of patient with sarcoma is altered. This result is in according with those published by Poveda et al before treatment but they reported a global health score higher during treatment at 6-12 months and >12 months[9]. So all these results are smallest that those reported by Saebye et al and Coens et al[10,11].These difference can be explained by the various methodologies used. Indeed Poveda et al. and Coens et al recruited only patients participating in a clinical trial. Our study is a prospective study and recruited patients in daily clinical practice.

Overall patients had worse score symptoms domains compared to functioning domains. Social functioning score was better compared to other functioning score domains. Hudgens et al[12] reported better score cognitive functioning. Considering symptoms domains, fatigue and pain were most decsirbed . As with other studies, pain, fatigue, and insomnia are suggested to be part of a group of symptoms where each may cause or influence the outcome of the other[13].

Our study revealed significant differences in functioning and emotional scale scores among patients with soft tissues sarcoma and bone sarcoma in terms of age, gender, level of studies and histological diagnosis.

Older patients had a significantly lower role function score than younger patients. Role functioning involves the ability to perform all forms of work and leisure activity. Paredes et al suggested that older patients felt more socially isolated in addition to functional impairment occurring with age. [14]. In more functional impairment occurs with increasing age. It has been described as being associated with reduced quality of life[11].

Male patients reported higher functioning mean score than female. Heaver et al explained than female have less muscle mass and strength which can have an effect on the rehabilitation process due to difficulties in compensating[15]. Additionally, patients reported more insomnia but less loss of appetite than men. This can be explained by the fact that women are more receptive to receiving psychosocial support than men therefore are more apt to be part of their psychological distress. Given the cultural context, men prefer to manage their illness individually and hide their emotions from their families.[14].

.Low levels of health education among patients are linked to inadequate use of health care services, higher mortality, poor self-rated health, lower physical functioning over time in older people and weaker skills to interpret health information, manage and understand treatments[16].

Liposarcoma was associated with a better physical functioning score and patients reported less fatigue and pain. This may be the result of a different initial tumor grade between different histological profiles.

None association has been found between quality of life domains and habitat type, presence of comorbidity or metastasis and treatment. Presence of comorbidities and metastasis has been previously described as influent quality of life factor in other malignancies. In fact, comorbidities occurs with increasing age and has been described as being associated with reduced quality of life[11]. These associations had not been found in our study.

Radiotherapy has been significantly associated with reduced functional outcome in the study conducted by Saebye and al. Radiotherapy is general given to patients with subfascial tumors and tumors located near vital structures such as vessels or nerves, where the surgical procedure itself may have a negative effect impact on functional outcome[10] but these results have not previously been found in other studies as in our study[17].

Our study has limitations, especially the non-comparative character. As is often done in studies on quality of life, a study design could have been carried out before and after in order to highlight the impact of the different socio-demographic variables on the evolution before, during and after the treatment. Therefore, the results of this study reinforce and support the need for a prospective study examining quality of life before and after treatment at 3, 6, and 12 months. In addition, we did not explore treatment side effects. that can influence the quality of life.

However, this study is one of the first to examine the quality of life of patients with soft tissue and bone sarcoma on a large sample of subjects with sarcoma in the Moroccan population. The assessment of the quality of life was carried out using a specific questionnaire that has undergone cross-cultural validation.

Therefore, the findings from this study reinforce and support the need for a prospective study examining pre- and post-treatment QOL at 3, 6 and 12 months, which is currently.

## CONCLUSION

Quality of life in patients with soft tissues and bone sarcoma is altered.

Some socio-demographic and clinical variables have been described as influencing factors and suggest leads for better treatment decisions in the future for patients with soft tissues and bone sarcoma.

CONFLICT OF INTEREST: none

## REFERENCES

1. Les sarcomes osseux | Fondation ARC pour la recherche sur le cancer. <https://www.fondation-arc.org/cancer/sarcomes-osseux>. Accessed 18 September 2020.
2. Jones RL, Cesne AL. Quality of life and patients' expectations in soft tissue sarcoma. *Future Oncol*. 2018;14(10s):51–62.
3. Dorr DA, Jones SS, Burns L, Donnelly SM, Bruncker CP, Wilcox A, et al. Use of health-related, quality-of-life metrics to predict mortality and hospitalizations in community-dwelling seniors. *J Am Geriatr Soc*. 2006;54(4):667–673.
4. Une étude longitudinale sur l'ajustement émotionnel des patients atteints de sarcome: le rôle déterminant des variables démographiques, cliniques et d'adaptation - PAREDES - 2012 - European Journal of Cancer Care - Wiley Online Library. <https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1365-2354.2011.01269.x>. Accessed 18 September 2020.
5. Maggi G, Terrenato I, Giacomelli L, Zoccali C, Condoleo MF, Falcicchio C, et al. Sarcoma patients' quality of life from diagnosis to yearly follow-up: experience from an Italian tertiary care center. *Future Oncol*. 2019;15(27):3125–3134.
6. Registre des cancers du grand Casablanca. [https://www.contrelecancer.ma/site\\_media/uploaded\\_files/RCRGC.pdf](https://www.contrelecancer.ma/site_media/uploaded_files/RCRGC.pdf). Accessed 18 September 2020.
7. El Fakir S, Abda N, Bendahhou K, Zidouh A, Bennani M, Errihani H, et al. The european organization for research and treatment of cancer quality of life questionnaire-BR 23 breast cancer-specific quality of life questionnaire: psychometric properties in a Moroccan sample of breast cancer patients. *BMC Res Notes*. 2014;7:53.
8. Fayers P, Aaronson NK, Bjordal K, Sullivan M. *EORTC QLQ-C30 Scoring Manual*. 1995. European Organisation for Research and Treatment of Cancer <https://abdn.pure.elsevier.com/en/publications/eortc-qlqc30-scoring-manual-2>. Accessed 20 October 2020.
9. Poveda A, López-Pousa A, Martín J, Del Muro JG, Bernabé R, Casado A, et al. Phase II Clinical Trial With Pegylated Liposomal Doxorubicin (CAELYX®/Doxil®) and Quality of Life Evaluation (EORTC QLQ-C30) in Adult Patients With Advanced Soft Tissue Sarcomas: A study of the Spanish Group for Research in Sarcomas (GEIS). *Sarcoma*. 2005;9(3–4):127–132.
10. Saebye C, Fugløe HM, Nymark T, Safwat A, Petersen MM, Baad-Hansen T, et al. Factors associated with reduced functional outcome and quality of life in patients having limb-sparing surgery for soft tissue sarcomas – a national multicenter study of 128 patients. *Acta Oncol*. 2017;56(2):239–244.
11. Coens C, van der Graaf WTA, Blay J-Y, Chawla SP, Judson I, Sanfilippo R, et al. Health-related quality-of-life results from PALETTE: A randomized, double-blind, phase 3 trial of pazopanib versus placebo in patients with soft tissue sarcoma whose disease has progressed during or after prior chemotherapy-a European Organization for research and treatment of cancer soft tissue and bone sarcoma group global network study (EORTC 62072). *Cancer*. 2015;121(17):2933–2941.

12. Hudgens S, Forsythe A, Kontoudis I, D'Adamo D, Bird A, Gelderblom H. Evaluation of Quality of Life at Progression in Patients with Soft Tissue Sarcoma. *Sarcoma*. 2017;2017. doi:10.1155/2017/2372135.
13. Aktas A, Walsh D, Rybicki L. Symptom clusters: myth or reality? *Palliat Med*. 2010;24(4):373–385.
14. Paredes T, Pereira M, Moreira H, Simões MR, Canavarro MC. Quality of life of sarcoma patients from diagnosis to treatments: predictors and longitudinal trajectories. *Eur J Oncol Nurs Off J Eur Oncol Nurs Soc*. 2011;15(5):492–499.
15. Heaver C, Isaacson A, Gregory JJ, Cribb G, Cool P. Patient factors affecting the Toronto extremity salvage score following limb salvage surgery for bone and soft tissue tumors. *J Surg Oncol*. 2016;113(7):804–810.
16. Halverson JL, Martinez-Donate AP, Palta M, Leal T, Lubner S, Walsh MC, et al. Health Literacy and Health-Related Quality of Life Among a Population-Based Sample of Cancer Patients. *J Health Commun*. 2015;20(11):1320–1329.
17. Davis AM, Sennik S, Griffin AM, Wunder JS, O'Sullivan B, Catton CN, et al. Predictors of functional outcomes following limb salvage surgery for lower-extremity soft tissue sarcoma. *J Surg Oncol*. 2000;73(4):206–211.