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**Quality of Life, Anxiety and Depression in Soft Tissue Sarcomas as Compared to More Common Tumours: An Observational Study**

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## **ABSTRACT**

The aim of this study is to compare the quality of life and the levels of anxiety and depression in a relatively large group of subjects undergoing chemotherapy for soft tissue sarcoma and a control group of subjects undergoing chemotherapy for the most common types of cancer. 56 soft tissue sarcoma affected patients and 56 patients with common tumours, homogeneous in regards to stages of disease and sociodemographic characteristics, were enrolled in two oncological centres in Turin, Italy. Quality of life was assessed by Functional Assessment of Cancer Therapy-General and anxiety and depression by Hospital Anxiety and Depression Scale. All patients had ongoing chemotherapy. The comparison between the two groups shows no difference in either quality of life or in anxiety and depression. There are instead gender differences, since females in the group of common tumours show higher levels of anxiety in comparison to those affected by sarcomas, while males show, at a lower degree, the opposite trend. This study suggest that levels of Quality of Life, anxiety and depression are similar in rare and common tumours. The majority of patients are able to cope with the disease in an adaptive manner. However, for some patients the disease poses a threat to their physical and mental integrity; psychological support of these patients may reduce the development of significant morbidity and help patients to better manage the course of the disease and the effects of the treatment.

**Keywords:** sarcoma; rare tumours; quality of life; anxiety; depression; chemotherapy.

## **INTRODUCTION**

The diagnosis and treatment of cancer may have a severe impact on individuals, affecting their Quality of Life (QoL) and increasing anxiety and depression (Saevardottir et al., 2010). QoL in cancer patients is affected both by the mounting physical debility due to the pathology and the treatment related side effects and by patients' concerns and expectations about the disease (Siddiqi et al., 2009).

Differences in gender and age might influence the emotional interpretation of this condition, affecting the perception of QoL (Parker et al., 2003).

Anxiety and depression have been found to negatively affect the quality of life of cancer patients, and psychological distress may differ depending on age and gender (Saevardottir et al., 2010).

These concerns can be also influenced by the information about their disease and the social representations of the "metaphor" of that rare type of cancer like Soft Tissues Sarcomas (STS). STS are rare malignant tumours (1% of all cancers) originating from mesenchymal tissue, which can arise anywhere in the body (Clark et al., 2005; Jemal et al., 2004). The majority of STS are located in the limb or limb girdle. Retroperitoneal, visceral and gynaecological sarcomas are even less common. A large series of studies have identified as important determinants of survival the following prognostic factors: volume of the disease; depth of anatomic site of origin; and grade and presence of metastasis (Jemal et al., 2004; Fletcher et al., 2002). Five-year survival rate, following AJCC and UICC staging, strictly correlates with the stage: in stage I, 5 year survival is 90%, 70% for stage II, 50% for stage III and 0-15% for stage IV.

This kind of pathology can differ from the more common one because in patients suffering from rare tumours there are usually limited observations on the efficacy of treatments and low-level grades of recommendation in clinical guidelines on therapy (Karavasilis et al., 2008; Minchom et al., 2010; Leahy et al., 2012).

This aspect, together with the difficult management of disease symptoms, may represent a significant burden to daily life and can have important effects on patients' quality of life (Paredes et al., 2011).

Most of the studies on patients affected by STS focus on the follow-up of bone tumours (Felder-Puig et al., 1998; Eiser and Grimer, 1999; Aknes et al., 2007) but very little data come from the literature on quality of life and the degree of anxiety and depression (Paredes et al., 2011; Paredes et al., 2012). As far as we know, there are no data available on the comparison of emotional distress between patients with rare malignancies and those with more common tumours.

Patients affected by STS frequently undergo a difficult and sometimes a not correct diagnostic process, mostly due to the scarce knowledge of a rare pathology, especially in peripheral hospital institutions, and when the definitive diagnosis is performed, it is at the end of a long time-consuming and weary course for the patient. Moreover sometimes patients bearing STS begin wrong treatments.

On the contrary patients affected by common cancers usually benefit from standardized diagnostic processes, shared by almost all institutions, which leads to diagnosis in a short time, allowing a prompt start of the appropriate treatment.

Furthermore patients with STS need frequently much more demolishing surgical interventions, including limb amputations, than those performed in the case of common tumours.

These differences from patients with STS, compared with those affected by common tumours could account for different psychological reactions and attitudes to the treatment, with potential differences in impact on quality of life and on emotional status.

Psychological features have been studied on tumours with relatively high frequency, while there are very few data on the QoL and emotional reactions of patients suffering for rare tumours.

The aim of this exploratory study is to compare the quality of life and the levels of anxiety and

depression in the early stages of treatment between a relatively large group of subjects undergoing chemotherapy for sarcomas and a comparison group of subjects undergoing chemotherapy for most common types of cancer (breast, lung, colon-rectum, prostate carcinomas).

## **PATIENTS AND METHODS**

### **Study population**

In the Piedmont Region, Italy, a network for the multidisciplinary management of cancer patients has been instituted since 2000. In each approved centre of this network, patients suffering from common cancers are treated and followed with shared protocols and the same guidelines. This methodological approach assures homogeneity of treatment and similar results. Rare tumours should be addressed in specialized centres specifically devoted to the management of these diseases.

From June 2008 to February 2010 consecutive patients with STS within the first three months of their chemotherapy were enrolled at the Medical Oncology Department of “Gradenigo” Hospital, Turin, which is the reference centre for the treatment of such neoplasms in Piedmont. Control patients were consecutively enrolled within the first three months of chemotherapy at the Medical Oncology Department of San Luigi Hospital, Orbassano (Turin), during November 2009.

Inclusion criteria for patients with sarcomas were: histological confirmed diagnosis of sarcoma, began chemotherapy in the last three months, ongoing chemotherapy, awareness of diagnosis of neoplastic disease, ability to do the physical and psychological tests, age between 18 and 75 years, and written informed consent.

The comparison group consists of consecutive patients affected by breast cancer, colon-rectum cancer, lung cancer and prostate cancer - so-called “big killers” - with the same inclusion criteria of the sarcoma group.

Exclusion criteria from the study for both groups were: illiteracy, pre-existing major psychiatric

history, concomitant therapy with psychotropic drugs, poor performance status ( $\geq 3$  of ECOG scale), other major illness, drug addiction, and prison detention.

### **Assessment instruments**

Assessment questionnaires were self-administered during the patients' stay in the day hospital. The questionnaires were given to the patients by a physician (A. B. for the STS group and A.S. for the control group) who were also available for answering questions about compiling the questionnaire. The same physicians have previously assessed the eligibility of each patient.

In the first section of data collection, personal relevant characteristics and cancer history variables including gender, age, education level and marital status were gathered.

The second section consisted of the following instruments:

Health Related QoL was evaluated using the general version of Functional Assessment of Cancer Therapy General (FACT-G) (Cella et al., 1993; Smith et al., 2007), developed and validated for use in clinical trials in its validated Italian version (Bonomi et al., 1996). FACT-G is a 29-item self-report questionnaire evaluated by means of a five-point Likert scale rated from 0 (not at all) to 4 (very much). It is composed of five subscales: physical well-being, functional well-being, social/family well-being, emotional well-being, and relationship with doctor. The range of scores on the FACT-G is 0 to 116, a higher value signalling a better quality of life. Patients were asked to rate how they feel today and omit the previous 7 days.

The levels of anxiety and depression were assessed by means of the Hospital Anxiety and Depression Scale (HADS); a simple but effective tool to evaluate the presence of a mood disorder in hospital populations and hospital outpatients (Zigmond and Snaith, 1983) in its validated Italian version (Costantini et al., 1999).

It consists of two subscales, one to determine anxiety status and one to determine depression status. Each subscale contains 7 items, which are evaluated by the patient on a four-point Likert scale (0–

3), so that the possible scores range from 0 to 21 for both anxiety and depression. For each subscale, a result of 0 to 7 represents the normal condition; of 8 to 10 identify mild cases; of 11 to 15 moderate cases; and of 16 or above indicates the presence of severe cases (Snaith and Zigmond, 1994; Crawford et al., 2001; Quelhas and Costa, 2009). The patient was asked to indicate for each item how he felt in the previous two weeks.

### **Statistical analysis**

Analyses were performed using the Statistical Package for Social Sciences (SPSS version 14.0; Chicago, IL, USA).

Student's *t*-test and  $\chi^2$  test were used to calculate demographic differences and clinical variables in the two groups.

As a secondary aim of the study, we examined the role of gender and age as predictors - together with the group type - of QoL and anxiety and depression symptomatology. For this purpose a factorial analysis of variance was used, including gender and group as independent variables, the scores of FACT-G and HADS as dependent variables and age as a covariate. Test F were calculated for the main effect of every independent variable as well as for the interactions. To perform the factorial analysis of variance a GLM procedure of the statistical SPSS package vers. 17 was used. All tests were two sided. A  $p < 0.05$  was considered statistically significant.

## **RESULTS**

### **General characteristics**

A total of 56 patients were enrolled in the sarcoma group and 56 in the control group. In the sarcoma group no refusal or drop out was recorded, while in the control group 6 patients after the screening refused to consent.

The characteristics of the two groups of patients are shown in Table 1.



There were no differences in demographics or in cancer history between the two groups.

In regards to QoL there are no statistically significant differences between the group of patients with sarcomas and the other with more common tumours (Tab. 2).

Furthermore there are no significant differences between the two oncological groups as a whole either in anxiety mean scores. On the contrary there is a significant difference in depression mean scores (Tab. 2).

Analysis of frequencies reveals that there are some significant differences between the two groups, considering a cut-off of 11 as indicating a possible presence of a moderate or severe anxiety or depression symptomatology: anxiety is more frequent in the common tumours group than in the sarcoma group (35.7% vs. 12.5%). Instead depression is more frequent in the sarcoma group than in the comparison group (23.2% vs. 10.7%) (Tab. 3).

Concerning the interaction analyses emerges that the interaction between age and group is a significant predictor of Social Well-Being ( $p=.010$ ;  $\eta^2=.06$ ), showing two different trends in the STS group and in the comparison group. In particular among STS patients a worse Social Well-Being is associated with the increase of age; on the contrary, among control group patients, an older age correlates with a better Social Well-Being.

Furthermore we find a significant interaction between gender and patient group ( $p=.032$ ;  $\eta^2=.04$ ): females with sarcomas show significantly lower scores in the anxiety subscale ( $7.64\pm 2.68$ ) in comparison to females with common tumours ( $10.32\pm 4.99$ ). Males affected by sarcomas show a slight opposite trend, with higher scores in anxiety ( $6.14\pm 3.98$  vs.  $6.89\pm 3.47$ ).

## **DISCUSSION**

Most data about anxiety, depression, and QoL come from studies on relatively common tumours, and there is a lack of studies comparing these issues in rare versus common tumours.

This exploratory study was designed to compare QoL, anxiety and depression in patients with Soft Tissue Sarcomas and more common tumours.

The diagnosis of a rare tumour doesn't seem to affect the aspects of QoL differently from common cancers. The two groups showed similar average levels of anxiety and depression, although moderate levels of anxiety were more usual in the common tumours group and moderate levels of depression and depressive symptoms were more frequent in the sarcoma group.

In this study, we also found different trends in Social Well-Being - depending on the interaction between age and group - and in anxiety symptomatology - depending on the interaction between gender and group. At this point in time, no clear explanation for this finding exists, and we think any speculation is not feasible even taking into account the lack of studies available in literature on this topic. Thereby future studies should better explore such issues.

It is important to emphasize, as already evidenced by other studies (Aknes et al., 2007; Paredes et al., 2011), that only a small percentage of patients exhibit severe levels of anxiety and depression symptoms. This result shows that the majority of patients, regardless of whether they are suffering from rare or common tumours, are able to cope with the disease in an adaptive manner.

However, for some patients the disease poses a threat to their physical and mental integrity and this might lead to the development of psychopathological symptoms, which must be adequately evaluated and addressed to specific mental health services.

Limitations of our study include its relatively small size (even if it is very hard to enroll more patients in the case of a rare tumour) and the fact that patients were treated in two different institutions (Soft Tissue Sarcomas patients in Gradenigo Hospital and the other patients in San Luigi Hospital). However both the institutions belong to the same oncological regional network, sharing training programs and organisation of care. Moreover, the interviews were performed in the same manner for both groups of patients.

Another limitation of our study is that we evaluated anxiety and depression symptomatology with the self administered HADS, without a more extensively diagnostic procedure (e.g. a clinical interview according to DSM-IV-TR).

Furthermore we recognise that a single evaluation in the initial part of the disease history cannot disclose the complexity of coping with the development of a chronic and long lasting disease such as cancer. Further studies are needed to perform a prospective evaluation by means of multiple assessments in different phases of the disease.

In conclusion, this comparative study suggest that levels of QoL and anxiety and depression are similar in rare and common tumours. Psychological support of patients exhibiting emotional distress at specific time periods of their cancer treatment may reduce the development of significant morbidity and help patients to better manage the course of the disease and the effects of the treatment.

#### CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

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TABLES

Table 1. General characteristics of the two groups.

	Common tumour (N=56)	STS (N=56)	<i>p</i>
Gender	F 28 (50%) M 28 (50%)	F 28 (50%) M 28 (50%)	1.000 <sup>a</sup>
Age (mean±SD)	54.02±14.31	53.45±14.08	.832 <sup>b</sup>
Education			
Primary school:	15 (26.8%)	9 (16.1%)	.162 <sup>c</sup>
Low secondary school:	16 (28.6%)	21 (37.5%)	
High secondary school:	23 (41.1%)	19 (33.9%)	
University:	2 (3.6%)	7 (12.5%)	
Marital status			
Married:	40 (71.4%)	42 (75.0%)	.950 <sup>d</sup>
Widowed:	4 (7.1%)	4 (7.1%)	
Single:	7 (12.5%)	7 (12.5%)	
Divorced:	5 (8.9%)	3 (5.4%)	
Primary tumours site	breast: 25 (44.6%) lung: 17 (30.4%) colon-rectum: 8 (14.3%) prostate: 6 (10.7%)	trunk: 22 (39.3%) limbs: 24 (42.8%) head and neck: 6 (10.7%) retroperitoneum: 4 (7.2%)	-
Stage of disease	Localized: 34 (60.7%) Metastatic: 22 (39.3%)	Localized: 29 (51.8%) Locally advanced: 18 (32.1%) Metastatic: 9 (16.1%)	-

<sup>a</sup> Chi square test

<sup>b</sup> T test

<sup>c</sup> Chi square test

<sup>d</sup> Chi square test

Table 2. Comparison between STS group and common tumour group concerning QoL and anxiety and depression levels.

	Group		95%CI for the Difference Between Means		<i>p</i>
	Common tumour	STS	Lower Limit	Upper Limit	
	(N=56)	(N=56)			
HADS anxiety	8.23 (4.94)	7.27 (3.10)	-.580	2.509	.219
HADS depression	6.48 (4.00)	7.96 (3.46)	-2.882	-.083	.038
Physical well-being	19.78 (7.12)	18.84 (6.65)	-1.641	3.520	.472
Social well-being	18.42 (3.35)	19.04 (3.93)	-1.979	.754	.376
Relationship with doctor	6.14 (2.00)	6.57 (1.23)	-1.052	.195	.176
Emotional well-being	15.94 (4.44)	16.18 (5.07)	-2.021	1.546	.792
Functional well-being	15.20 (5.31)	13.64 (6.38)	-.640	3.756	.163
FACT-G total score	75.49 (14.37)	74.27 (17.60)	-4.798	7.257	.689



Table 3. Prevalence of anxiety and depression symptomatology.

	Group		$\chi^2$	<i>p</i>
	Common tumour (N=56)	STS (N=56)		
HADS-Anxiety score				
Normal	28 (50%)	29 (51.8%)	11.506	0.009
Mild	8 (14.3%)	20 (35.7%)		
Moderate	16 (28.6%)	6 (10.7%)		
Severe	4 (7.1%)	1 (1.8%)		
HADS-Depression score				
Normal	33 (58.9%)	21 (37.5%)	10.072	0.018
Mild	17 (30.4%)	22 (39.3%)		
Moderate	4 (7.1%)	13 (23.2%)		
Severe	2 (3.6%)	0 (0%)		