Psychological Distress among Patients with Suspected Sarcoma Requiring Biopsy Confirmation

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Abstract: _**Objectives**: Cancer journeys differ for every patient. It's a process that starts from early suspicion of cancer. There are emerging studies focusing on the psychological impact of patients who had been diagnosed with cancer. In fact, psychological distress is common among patients with sarcoma. The purpose of this study is to assess psychological distress in patients with suspected sarcoma and to identify risk factors. At the orthopaedic clinic of a sole sarcoma referral tertiary center in the southern region of Peninsular Malaysia._ _**Material and Methods**: Prior to the biopsy, the patient had to complete a set of questionnaires, including social demographics and a 21-item Depression Anxiety Stress Scale (DASS-21) self-assessment for psychological distress evaluation. The investigators would follow up with the histopathological results after biopsy was taken. Logistic regression was used to determine the significant association between each subsection of psychological distress and other risk factors._ _**Results**: A total of 79 patients with suspected sarcoma were recruited within 12-months period. The prevalence of stress, anxiety and depression was 15.2%, 21.5%, and 15.2%, respectively. The majority reported feeling normal or mild anxiety and depression, but a significant minority experienced clinically significant levels of moderate or higher anxiety and depression. Univariate analysis showed a significant connection between ambulatory status and stress/depression (p value = 0.015 and 0.003) as well as between Indian ethnicity and anxiety level (p value = 0.009). Ambulatory status was linked to higher depression (p value = 0.021) and Indian ethnicity was linked to higher anxiety (p value = 0.009)._ _**Conclusion**: Proper attention should be paid to the psychological needs of sarcoma patients._

Keywords: Psychological distress, DASS-21, biopsy, sarcoma

1. Introduction

The Malaysia National Cancer Registry report 2012 - 2016 stated that the lifetime risk for males to get cancer was 1 in 10 and the ratio among females was 1 in 9[1]. The top five most common cancers in males were colorectal, lung, prostate, nasopharynx, and liver cancer. As for females, the top five most common cancers were breast, colorectal, cervix, uteri, lung, and ovary cancer [1]. Musculoskeletal cancer can either be a primary sarcoma or secondary metastasis from other cancers. Sarcomas is rare and only accounts for less than 1% of adult malignancy, with soft tissue sarcoma being more common than bone sarcoma [2].

Cancer journeys differ for every patient. It's a process that starts from early suspicion of cancer; diagnosis of cancer; staging of cancer; cancer treatment either surgery, chemotherapy, or radiotherapy; recovery and rehabilitation; surveillance; recurrence; cured or succumbed [3]. Most patients experience grief when they are diagnosed with cancer. Cancer survival rates have risen, but the process of diagnosis and treatment has a large impact on patients' physical and mental health. It includes fatigue, discomfort, stress, distress, anxiety, and depression [4–6].

There were emerging studies focusing on the psychological impact of the patients who had been diagnosed with cancer. There were 50 to 64% of patients who were being investigated or treated for early prostate cancer and experienced anxiety symptoms [7]. Ise et al. found that 32% of those with soft tissue or bone cancer had psychological distress prior to surgery. Melissa et al. also reported that the prevalence of moderate to severe DASS-21 scores for all three subscales was noted in up to 28.9% in two groups of sarcoma patients, namely those who were recently diagnosed

and those who were pre-operative patients [9]. Younger age, female gender, malignant tumour, lower functional score, patients with more pain, previous psychiatric problems, and lower social economic status were at higher risk of developing psychological distress[3, 4, 8–13].

The staging of tumours can be divided into local staging and systemic staging. Local staging involved history taking, physical examination, imaging studies, and finally histology confirmation of the diagnosis via biopsy. Systemic staging involved screening to rule out metastasis. After a series of investigations, patients with suspected sarcoma will be informed regarding the need for a biopsy to confirm the diagnosis. To the best of the author's knowledge, there is no data at present from a study about psychological distress among patients with suspected sarcoma prior to biopsy. In fact, it is a common outpatient procedure in an orthopaedic clinic, and yet the psychological distress of patients is overlooked.

In view of the scarcity of the data available at the moment, this study aims to determine the prevalence of stress, anxiety and depression among patients with suspected sarcoma requiring biopsy confirmation and its significant risk factors.

2. Materials and Methods/ Methodology

This was a cross-sectional study with universal sampling. The study was carried out in the orthopaedic clinic of Hospital Sultan Ismail (HSI), Johor Bahru, Malaysia. The orthopaedic oncology team in the orthopaedic department of HSI was established in 2008. It is the sole sarcoma referral tertiary center in the southern region of Peninsular Malaysia.

A biopsy will be done after an imaging study of the lesion to confirm the diagnosis and decide on further treatment. The data collection was carried out from 1 January 2022 until 31 December 2022, for a duration of 12-months. The study was registered under the National Medical Research Registry (NMRR) and approved by the Medical Research and Ethic Committee (MREC).

All patients 18 and older seen in the orthopaedic clinic were screened for inclusion and exclusion criteria.Participants must be 18 or older, have a suspicious lesion requiring a biopsy, and be able to read and write English or Malay. The patient who has a pre-existing psychiatric illness would be excluded from the study. Those who fulfil the study criteria would be recruited into the study.

Before a biopsy was taken, patients were given a set of questionnaires to answer, which takes about five to 10 minutes. Investigators would keep track of patients' histopathological results. Those who could not complete the questionnaire would be excluded from the study's analysis.

Social demographic questionnaire
The first part of the questionnaire is to obtain patients' general information. The demographic variables include age, gender, ethnicity, marital status, education, occupation, economic status, and economic burden. Economic status is defined according to the household income classification in Malaysia, namely B40, M40, and T20[14]. B40 refers to the bottom 40% of the income earners, M40 represents the middle 40%, and T20 refers to the top 20% of the Malaysian household income. Investigators must provide patient's ambulation status, provisional and final diagnoses in the second questionnaire.Gathering the patient's past information and medical record will give a premorbid ambulatory status, initial diagnosis, and ultimate diagnosis.

Depression Anxiety Stress Scales-21 (DASS-21)
Depression Anxiety Stress Scales (DASS-21) is a 21-item self-report questionnaire in the public domain[15]. DASS-21 measures psychological distress levels of depression, anxiety, and stress. Each item is rated on a four-point Likert scale ranging from 0 (did not apply to me at all over the last week) to 3 (applied to me very much or most of the time over the past week). It is available in both English and Malay languages. Both English and Malay versions of the questionnaire would be used in the study. The Malay version of the DASS-21 is well validated [16]. It has good Cronbach's alpha values of 0.84, 0.74, and 0.79, respectively, for depression, anxiety, and stress [16].

Patients who fulfilled study criteria would be approached to fill up the DASS-21 questionnaire before a biopsy is taken. Patients with moderate or higher severity will be referred to a psychiatric clinic. Based on the DASS-21 scoring template, the scores for each of the subjects over each of the domains were then evaluated as per the severity-rating index. Its cut-off scores will measure the levels of psychological distress in the present study. The study will use its composite scores for depression, anxiety, and stress for its inferential analyses.

3. Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics 26. Descriptive statistics were used for the basic social demographic data of the subjects, as well as the DASS-21scores and their levels of severity. Simple logistic regression was used to compare each domain (stress, anxiety, and depression) in DASS-21 categories of normal and abnormal (mild, moderate, severe, and extremely severe) to determine the significance of all variables on the levels of stress, anxiety, and depression (measured by the DASS-21) among the patients. Multivariate logistic regression was used to analyze variables with p values of <0.25. The significant level for this study was set at $p <0.05$.

4. Results

Table 1 showed the social demographic information of patients who have undergone biopsies. The mean age was 44.92 ± 19.71, with the youngest patients being 18 years old, and the oldest patients being 89 years old. 69.6% of the patient population was Malay (69.6%), followed by Chinese (22.8%) and Indian (7.6%). Majority of the patients were male (60.8%), younger than 55 years old (64.6%), completed secondary education (51.9%), married (59.5%), and pre-morbidly ambulatory (93.7%). More than half of the patients were unemployed (55.7%), which consists mainly of patients who were students and housewives. In terms of socioeconomic background, 75.9% of the patients were in low-income group B40, which accounts for 75.9% of the total, followed by M40, which accounts for 24.1% of the total. Lower limb involvements were more common (72.2%) than upper limb involvement (24.0%) followed by pelvis involvements (3.8%). Biopsy results found that 67.1% of the samples were malignant or intermediate malignant tumours.

The prevalence of stress, anxiety, and depression among our patients was 15.2%, 21.5%, and 15.2%, respectively, with 5.1% of patients experiencing anxiety at the extremely severe level (Table 2). In simple logistic regression, it was found that patients' ambulatory status, particularly being unable to ambulate pre-morbidly, was significantly associated with higher stress (p=0.015; OR: 10.83; 95% CI: 1.59-73.91) and depressive (p=0.003; OR: 33.0; 95% CI: 3.27-332.75) levels. Indian ethnicity (p=0.009; OR: 34.0; 95% CI: 2.45-474.55) was significantly associated with a higher anxiety level. Indian patients were 51 times more likely to have an abnormal anxiety level.There was a 20-fold increase in risk of depression for those not ambulating normally (Table 3). As there was only one variable (ambulatory status) with a p value <0.25 in the domain of stress, hence multivariate logistic regression was not performed.

Table 1: Social demographic information of patients who have undergone biopsies

Variable		Frequency (n)	Percentage (%)
Age	<55 yeas old	51	64.6
	55 and above	28	35.4
Gender	Male	48	60.8
	Female	31	39.2
Race	Malay	55	69.6
	Chinese	18	22.8

	India	6	7.6
Education	Primary	19	24.1
	Secondary	41	51.9
	Degree	19	24.1
Marital status	Single	25	31.6
	Married	47	59.5
	widow/widower	7	8.9
Employment status	Unemployed	44	55.7
	Employed	35	44.3
Occupation	Labourer	14	17.7
	Administrative personnel	9	11.4
	Half skilled worker	7	8.9
	Professional	5	6.3
Economic status	B40	60	75.9
	M40	19	24.1
	T20	0	0
Number of economic burden	0	42	53.2
	1	4	5.1
	2	16	20.3
	3	10	12.7
	4 or more	7	8.9
Ambulatory status	Ambulate normally	74	93.7
	Required assistance	5	6.3
Location of lesion	Upper limbs	19	24
	Lower limbs	57	72.2
	Others (pelvis)	3	3.8
Histopathological diagnosis	Benign	26	32.9
	Intermediate malignant	11	13.9
	Malignant	42	53.2

Table 2: DASS-21 score according to domains for patients undergoing biopsy

Domain	Level of severity	Frequency (n)	Percentage (%)
Stress	Normal	67	84.8
	Mild	5	6.3
	Moderate	6	7.6
	Severe	1	1.3
	Extremely severe	0	0
Anxiety	Normal	62	78.5
	Mild	5	6.3
	Moderate	5	6.3
	Severe	3	3.8
	Extremely severe	4	5.1
Depressed	Normal	67	84.8
	Mild	3	3.8
	Moderate	4	5.1
	Severe	2	2.5
	Extremely severe	3	3.8

Table 3: Factors associated with stress, anxiety, and depression in patients

Variable	Simple logistic regression		Multivariate logistic regression	
	Odd ratio (95% CI[†])	P value	Adjusted odd (95% CI[†])	P value
Stress				
Ambulatory status				
Required assistance to ambulate (‡ref: ambulate normally)	10.83 (91.59, 73.91)	0.015*	-	-
Anxiety				
Race				
Malay	4.74 (0.57, 39.36)	0.149	8.08 (0.71, 92.52)	0.093
Chinese (‡ref)	-	-	-	-
India	34.00 (2.44, 474.55)	0.009*	50.92 (2.67, 970.35)	0.009*
Gender				
Female (‡ref: Male)	2.05 (0.69, 6.06)	0.196	1.67 (0.49, 5.72)	0.412
Ambulatory status				
Required assistance to ambulate (‡ref: ambulate normally)	6.43 (0.98, 42.19)	0.053	10.06 (0.75, 135.54)	0.082
Depression				
Economic status				
B40 (‡ref: M40)	4.04 (0.49, 33.57)	0.196	2.314 (0.23, 23.41)	0.477
Educational level				
Primary	6.43 (0.67, 61.47)	0.106	2.60 (0.17, 39.93)	0.494
Secondary	3.09 (0.35, 27.03)	0.314	2.71 (0.24, 30.88)	0.421
Tertiary (‡ref)	-	-	-	-
Types of lesion				
Benign	-	-	-	-
Intermediate	5.56 (0.45, 68.94)	0.182	8.38 (0.60, 116.45)	0.113
Malignant (‡ref: benign)	6.818 (0.81, 57.40)	0.077	3.58 (0.39, 33.02)	0.261
Ambulatory status				
Required assistance to ambulate (‡ref: ambulate normally)	33.00 (3.27, 332.75)	0.003*	20.81(1.59, 274.56)	0.021*

* p value <0.005
†CI= Confidence interval ‡ref= reference group

5. Discussion

Sarcomas are rare cancers that are mostly unpreventable and occur spontaneously, except for a few with cancer related syndromes. Some patients might not have heard about sarcoma and its related information. Psychological distress was prevalence among patients who undergo biopsy for suspected breast or prostate lesion[5, 7, 12, 13, 15].

However, the results of psychological distress from other types of cancer cannot simply be extrapolated to represent extremity sarcoma patients[9]. The prevalence of depression and anxiety in sarcoma specific cohorts were up to 33.3% and 47.2% respectively[9]. Paredes et alassessed the patients in three different phases (diagnosis phase, treatment phase, follow up phase); anxiety were highest in the diagnosis phase (29.3%) and depression were highest in the treatment phase (19.4%)[3]. The prevalence among our patients were lower than other authors; the prevalence of stress, anxiety and depression were 15.2%, 21.5%, and 15.2%. However, the patients reported with anxiety were highest as compared to other authors. These might be because our study only take the psychological assessment at very early stage of the disease. As diagnosis confirmed and treatment started, patient might experience increase in psychological disturbance due to treatment outcome, prolonged rehabilitation as well as change in life role and body image [9]. Disease recurrence during follow up were also associated with significant increase in anxiety and depression [3].

Sarcomas are rare and heterogeneous in terms of anatomical location and histological diagnosis. It primarily involves the extremities and is associated with more physical disabilities. Sarcoma can happen in any age group, and up to two third of sarcomas occur in patients younger than 55 years old,which was in the pre-retirement productive age group with socioeconomic burden[17]. Neoadjuvant treatment, adjuvant treatment, surgery, wound care, and rehabilitation could take from weeks to months or even longer if complications arise[18]. It reflected an absence from the workplace and a loss of income for the patients. This explained why younger age group were associated with more psychological distress[8, 9]. The older age group (>55 years old) experienced less stress; perhaps they were in a relatively stable phase of life in terms of family, financial responsibility, and career[9]. 64.6% of our patients were from the age group younger than 55 years old, with a mean age of 44.92 ± 19.71. However, there was no statistically significant difference in psychological distress between our patients under the age of 55 and those over the age of 55. These might be due to good social security, as healthcare is heavily subsidised and patients do not need to worry about the cost of treatments in our country.

Low income, a lower education level, and being an ethnic minority were important risk factors for psychological distress in cancer patients [9–11]. Low education level was associated with lower income and quality of life, which lead to more distress [9]. There was no correlation between low income and low educational level with psychological distress in our study. However, ethnic minority (Indian) indeed reported odds of having abnormal anxiety level that was about 51 times higher as compared to other ethnicities. Sarcomas, which mainly involved the limbs, required treatment that might cause permanent restriction in the function of the limbs after wide resection and even worse if amputation was unavoidable. Poor performance status and physical impairment were strongly correlated with psychological distress[3, 8, 9, 19–22]. Patients with poor physical function pre-morbidly were associated with more stress and depression in our study, which was similar to the finding by other authors. Female gender, which was reported as one of the important risk factors for psychological distress, was not seen in our patients. Cancer induced inflammation was implicated in causing depression in patients with malignant cancer [23]. The inflammation can induce changes in the central nervous system via neurotransmitter systems and neuropathways [24]. However, our patients with histologically confirmed malignancy did not show more psychological distress than patients with benign lesions.

6. Conclusion

Patients with psychological distress were associated with poorer outcomes in terms of physical function, pain, quality of life, and survival [3, 9–11, 18–20, 22, 23, 25]. Psychological distress that presents since the early course of disease is associated with persistent distress even one year after the surgery[9]. Hence, it is imperative to identify patients with psychological distress in an early state and intervene as necessary; at the same time, monitor their psychological wellbeing throughout the treatment.

Conflicts of Interest
No conflict of interest related to this article.

Authors' Contribution
Ng YH and SI draft the study design. Ng YH performed data collection and manuscript preparation. Chai YC performed statistical analysis. Ng YH and Chai YC wrote the manuscript with input from all authors. SI involved in editing the manuscript critically. All authors read and approved the final manuscript.

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