Quality of Life in Pre- and Post-Treatment among Head and Neck Cancer Survivors at A Tertiary Centre, Malaysia

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Abstract

Background: Treatment for head and neck cancer (HNC) may result in a variety of long term consequences that impair their health and quality of life (QoL). HNC patients often are prone to have a poor health related QoL due to significant changes in vital functions. Despite researches being done in the area cancer survivors' QoL internationally, those done locally were relatively scare and not clear. The study aimed to determine and compares the pre and post treatments QoL in HNC patients.

Methods: A cohort study was carried out to recruit 81 newly diagnosed HNC patients purposively; pre and six months post treatment using QoL Cancer Survivor and Questionnaire-Head & Neck 35 questionnaires. Data was analyzed for descriptive and inferential analysis.

Results: A total of 40 (50%) patients participated and the result shows that QoL of HNC patients were at medium level (6.22 ± 1.8) pre-treatment, and however reduced (4.84 ± 1.16) at 6 months post treatment), despite the symptoms or problems that occur reduced post treatment compared (1.58 ± 1.25). The Pearson coefficient correlation test result shows that QoL of HNC patients pre and post treatment were strong but negatively correlated (r = -0.447, p = 0.002).

Conclusion: Understanding of QoL and affecting factors in HNC patients' QoL is very crucial as it may potentially assist in designing interventions that lessen the adverse impact of this disease process and more accurately support those in active treatment, survivors, and caregivers.

Keywords: head and neck cancer, quality of life, treatment

Introduction

Head and neck cancer (HNC) accounts for about 3% of all cancers in the United States and this year, an estimated 59,340 people (43,390 men and 15,950 women) will develop HNC. Most patients are between 50 and 70 years old, although younger people also can develop HNC. The Malaysian National Cancer Registry Report 2007-2011 showed HNC was the fifth most common cancer in Malaysia, and 2,884 cases were reported in the peninsula with the highest number after breast cancer in women (3,525) and higher than colorectal (2,866) and lung (2,048) cancer cases. The incidence of HNC increases with age, especially in those over 50 years. Most patients are between 50 and 70 years old, although younger people also can develop HNC.

A study was done on an outcome of surgically HNC in one of the tertiary referral centre in the East Coast of Malaysia concluded that surgical management of HNC at the centre had a satisfactory outcome in view of a relatively low percentage of recurrence and rate of wound breakdown. However, further study on the quality of life (QoL) as well as survival analysis of these patients is necessary to thoroughly evaluate the approach and strategy in managing HNC. Hence, the QoL of HNC patients need to be measured to assist multidisciplinary providing care and support to them. HNC patients are prone to have a poor health related QoL due to significant changes in vital functions related to food, communication, and social interaction. In addition, the function and appearance of head and neck region are crucial to self-image and QoL as patient’s physical, psychological and social well-being are heavily influenced by deformity and dysfunction resulting from the tumour.

QoL measures the effects of chronic illness, treatments, and short and long-term disabilities and its assessment is an important aspect of the current care for cancer patient. Most studies of the outcomes of cancer treatment have
included disease-free survival, tumor response, and overall survival. However, clinicians and researchers have come to realize these outcomes are inadequate for assessing the impact of cancer and its treatment on the patient’s daily life, as well as for identifying interventions to improve or maintain the patient’s QoL. Many vital functions such as mastication, swallowing, speaking, taste, smell, and appearance can be affected, both pre and post treatment. Even minor disturbance of the anatomy by surgery may lead to significant dysfunction and disfigurement, and hence to psychosocial complaints. For this reason, HNC has been described as a psychologically highly traumatic cancer type.5

According to Ferrell model,6 the concept of QoL (Figure 1) have four domains which are physical well-being is the control or relief of symptoms and the maintenance of function and independence, psychological well-being is the attempt to maintain a sense of control in the face of life-threatening illness characterized by emotional distress, altered life priorities, and fear of the unknown, as well as positive life changes, social well-being is the effort to deal with the impact of cancer on individuals, their roles, and relationships and spiritual well-being is the ability to maintain hope and derive meaning from the cancer experience, which is characterized by uncertainty. These important domains are very crucial to cancer or HNC patients and understanding and ability to ensure that they meet the domains will assist them in going through their illness. In a study of QoL HNC patient on cancer survivors at 1 year after treatment,7 it was found that the final path model showed that optimism, educational level, any coexisting disease, number of somatic symptoms, household income, eating ability, support from others, whether the cancer is under control or not and travelling time from home to hospital have direct or indirect effects, or both, on the QoL of HNC survivors. In addition, another study shown that clinical significant improvements in health related QoL were not found between 1 and 5 years and the problems with teeth, opening of the mouth, dryness in the mouth, and sticky saliva were persistent or worsening.8 Therefore, QoL HNC patient need to be measured to improved their QoL or has a peaceful death.

A study on the QoL of HNC patients after tumour therapy and subsequent rehabilitation conducted9 using University of Washington QoL (UWQOL) and QoL - H&N 35 questionnaire found that after tumour treatment but before rehabilitation, swallowing scored the highest, followed by dry mouth, social contacts, sticky saliva, mouth opening and pain, but the result only yield both physical and psychological aspect and not covered the spiritual well-being of the HNC patients’ QoL. The author of this study concluded that significant post-rehabilitation enhancement on almost all scales of both instruments and they proposed that QoL in HNC patients and its enhancement through rehabilitation deserves more attention than it is currently paid in the literature. However, the study only focused on QoL in HNC patients after the treatment and the rehabilitation only. The QoL aspect measured on physical symptoms and psychosocial well-being. For patients and their carer, QoL following head and neck cancer is a crucially important issue. The treatment of head and neck cancer is more than cure and survival. The cancer and its treatment affect functions that are integral to human existence for example, communication, eating, socialization, and interpersonal contacts.10 Evidence also shown that stage III and IV advanced disease stages were associated with reduce QOL while stage I and II at diagnosis had better QOL at 1 year.7 More than half of the head and neck cancer patients develop dysphagia with the commonest site of head and neck cancer at the tongue.11 Consistently, other study also stated that impairment from disease and treatment of head and neck cancer patients can interfere with basic functions, including eating and speech, and can have profound effect on social interactions and psychological state.12

Religion and spirituality can help cancer patients find meaning in their illness and provide comfort in the face of fear.13 A study of African-American Cancer Survivors’ Use of Religious Beliefs to Positively Influence the Utilization of Cancer Care found,14 suggested that religious beliefs and practices positively influenced attitudes toward their illness and ability to endure treatment. Study shown that people who received less spiritual care than they desired were at significantly greater risk of depressive symptoms and lower sense of spiritual well-being, defined as poorer sense of purpose in life, meaning and peace.15 Spiritual well-being will contribute to cancer patients’ QoL and their ability to cope with terminal illness. In addition, when cancer

![Figure 1. Quality-of-life Model Applied to Cancer Survivors (Ferrell, 1997)](image-url)
threatens the meaning of an individual life, religion and spirituality are often important coping strategies.\textsuperscript{16}

Those statements is consistent with the finding of a study on cancer patients that found many of them talked about their acceptance with the illness that Allah has given to them and the calamity with total acceptance (redha).\textsuperscript{17} Some said in the beginning of the diagnosis, they felt sad and find difficulties in accepting the illness. The question of “Why me?” were also raised. However, they said that a few days later they felt calmer when the concept of redha sunk in and they were able to accept the illness as a trial from God. The acceptance will somehow will affect how they determine their QoL following cancer.

Understanding of QoL and the effects may potentially assist healthcare professional in designing interventions that lessen the adverse impact of this disease process and more accurately support those in active treatment, survivors, and caregivers. Despite researches that have been done in the areas of cancer survivors’ QoL internationally, those done locally were relatively scares and not clear. Due to that, this aim was to explore the association between the QoL of HNC survivors that were managed with different approaches before treatments started and after 6 months post (first) treatments.

Methods

A cohort study design was conducted to determine the QoL of HNC patients in two tertiary hospitals in Malaysia between the year of 2013 to 2015, using two questionnaires distributed to the HNC patients pre-treatment and 6 months post-treatment. The study population included were those newly diagnosed HNC patients (carcinomas in the oral cavity, pharynx, nose, larynx, sinuses and salivary glands) and undergoing treatment (surgery, radiotherapy, chemotherapy, or combination), aged 18 years old and older: and able to understand Malay or English. The non-Malaysian, recurrent or metastasized cancer, and refused treatment and 6 months post-treatment. The study's purpose, research procedures, assurance of confidentiality, and their right to withdraw at any time. Respondents were provided with information regarding the study’s purpose, research procedures, assurance of confidentiality, and their right to withdraw at any time. The return of the completed questionnaire was treated as their consent to participate.

Approval for the study was obtained from the International Islamic University Malaysia and the National Medical Research Ethics Committee of Malaysia. Respondents were provided with information regarding the study’s purpose, research procedures, assurance of confidentiality, and their right to withdraw at any time. The return of the completed questionnaire was treated as their consent to participate.

Results

A total of 60 newly diagnosed HNC patients we listed, however 20 of the patients were uncontactable and leaving to 40 patients only included from the study. Out of 40 patients, 26 were men (65%) and 14 were women (35%). The mean age of the patients was 53 years and 34 patients (85%) were married. Majority of patients were Malay 31 (77.5%) and followed by Chinese 7 (17.5%). Seventeen (42.5%) patients were smokers, 1 (2.5%) used alcohol, 4 (10%) of patients had family cancer history.

The squamous cell carcinoma was the most common type and was seen in 32 (80%) cases. There were 20 (50%) patients with pharyngeal/laryngeal cancer, 15 (37.5%) patient. The scoring should be based on a scale of 0 = worst outcome to 10 = best outcome. The QoL instrument is based on previous versions of the QoL instrument. This instrument was revised in cancer survivorship studies and includes 41 items representing the four domains of QoL including physical well-being, psychological well-being, social well-being and spiritual well-being. Overall test re-test reliability was 0.89 with subscales of physical r = 0.88, psychological r = 0.88, social r = 0.81, spiritual r = 0.90 and overall analysis using Cronbach’s alpha so-efficient was r = 0.93 with subscales alphas of spiritual r = 0.71, physical r = 0.77, social r = 0.81 and r = 0.89 for psychological.\textsuperscript{19}

The second questionnaire was the QLQ-H&N35 comprises of 35 questions incorporating 7 multi-item scales and 11 single items which is specific tool for HNC survivors. The multi-item scales are pain, swallowing, senses, speech, social eating, social contact, and sexuality. The single items are teeth, opening mouth, dry mouth, sticky saliva, coughing, felt ill, pain killers, nutritional supplements, feeding tube, weight loss, and weight gain. For all items and scales, high scores indicate more problems. The alpha coefficient is >0.70.

Data were analysed for descriptive (mean and SD) and inferential analysis (Pearson coefficient correlation) with p value was set at p <0.05; using the Statistical Package for Social Science version 20 software. For this research, the researchers were using a reversed cut-off point for mean scores analysis. The cut-off point concept above was adopted from a social science study.\textsuperscript{20} Lowest mean score ranked indicated most problem or low/poor QoL and vice versa.

 approve for the study was obtained from the International Islamic University Malaysia and the National Medical Research Ethics Committee of Malaysia. Respondents were provided with information regarding the study’s purpose, research procedures, assurance of confidentiality, and their right to withdraw at any time. The return of the completed questionnaire was treated as their consent to participate.
patients with a cancer of the oral cavity, and 5 (12.5%) patients with other site of HNC. The distribution of patients according to treatment modalities was: 27 (67.5%) had undergone surgery, 8 (20%) treated by combination either radiotherapy with chemotherapy or surgery with chemotherapy, 4 (10%) had undergone chemotherapy alone and 1 (2.5%) treated by radiotherapy alone.

**Pre-treatments QOL assessment** Descriptive analyses were done and the mean and SD score of each item and overall QoL domains pre-treatment (6.22 ± 1.8) (medium level) and post treatments (4.84 ± 1.16). The mean score of the psychological well-being was 5.54 (SD = 1.83) seen as lowest ranked among all domains. The mean score of physical well-being (6.75 ± 1.66), social well-being (6.54 ± 1.89) and spiritual well-being (7.03 ± 1.88) (Table 1).

In terms of each individual domain, the physical well-being measured using subscale that contains eight items. The total means score for physical well-being was 6.76. Physically, most of the survivors experienced serious problems with ‘sleep changes’ (2.95 ± 2.14), fatigue (5.12 ± 2.09) and pain (5.53 ± 2.06). The total means score for psychological well-being was 5.54 and among the psychological general items, the lower scores were observed for items like ‘fear of metastasis cancer’ (3.22 ± 2.34), ‘fear with future diagnostic test’ (3.45 ± 2.06) and ‘distress /anxiety with disease and treatments’ (3.63 ± 2.61). As for the social concerns domains, the total mean score was 6.54 and the lower outcomes were observed in items ‘family distress’ (3.90 ± 1.84), employment interference (5.18 ± 2.29), and financial burden (5.65 ± 1.79). While, the total mean score for spiritual well-being was 7.03. The score were seen as low in the items, ‘future uncertainty’ (5.25 ± 1.81), spiritual activities (5.65 ± 2.06). The survivors highly involved with religious activities, besides they have high life mission and hopeful.

### Table 1. Participants’ Response to QoL Domains (subscale) Pre and Post Treatment

<table>
<thead>
<tr>
<th>QOL DOMAIN (SUBSCALE)</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean  SD</td>
<td>Mean  SD</td>
</tr>
<tr>
<td>Physical well-being</td>
<td>6.75 1.66</td>
<td>1.78 1.08</td>
</tr>
<tr>
<td>Psychological well-being</td>
<td>5.54 1.83</td>
<td>5.89 1.62</td>
</tr>
<tr>
<td>Social well-being</td>
<td>6.54 1.89</td>
<td>3.61 1.53</td>
</tr>
<tr>
<td>Spiritual well-being</td>
<td>7.03 1.88</td>
<td>7.05 1.58</td>
</tr>
<tr>
<td>Overall mean QoL</td>
<td>6.22 1.8</td>
<td>4.84 1.16</td>
</tr>
</tbody>
</table>

### Table 2. Distribution of HNC Patients’ Symptoms or Problem Pre and Post Treatment

<table>
<thead>
<tr>
<th>Domain/single-item</th>
<th>Pre-treatments</th>
<th>Post-treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean  SD</td>
<td>Mean  SD</td>
</tr>
<tr>
<td>Symptoms / problems</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>1.84 0.97</td>
<td>1.24 0.57</td>
</tr>
<tr>
<td>Swallowing</td>
<td>1.64 0.71</td>
<td>1.25 0.54</td>
</tr>
<tr>
<td>Senses</td>
<td>1.29 0.63</td>
<td>1.09 0.35</td>
</tr>
<tr>
<td>Speech</td>
<td>1.48 0.83</td>
<td>1.11 0.69</td>
</tr>
<tr>
<td>Social eating</td>
<td>1.71 0.78</td>
<td>1.16 0.41</td>
</tr>
<tr>
<td>Social contact</td>
<td>1.28 0.42</td>
<td>1.23 0.24</td>
</tr>
<tr>
<td>Sexuality</td>
<td>1.24 0.57</td>
<td>1.17 0.13</td>
</tr>
<tr>
<td>Teeth</td>
<td>1.23 0.69</td>
<td>1.10 0.50</td>
</tr>
<tr>
<td>Opening mouth</td>
<td>1.90 0.81</td>
<td>1.30 0.52</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>1.73 0.82</td>
<td>1.38 0.57</td>
</tr>
<tr>
<td>Sticky saliva</td>
<td>1.33 0.66</td>
<td>1.15 0.48</td>
</tr>
<tr>
<td>Coughing</td>
<td>2.03 0.62</td>
<td>1.70 0.61</td>
</tr>
<tr>
<td>Felt ill</td>
<td>2.63 0.93</td>
<td>1.93 0.57</td>
</tr>
<tr>
<td>Total mean score</td>
<td>1.64 0.73</td>
<td>1.29 0.48</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Experience /condition</th>
<th>Pre-treatments</th>
<th>Post-treatments</th>
</tr>
</thead>
</table>

|                        | N (%)         | N (%)          |
| Pain killer           | 12 (30)       | 1 (2.5)        |
| Nutritional supplement | 5 (12.5)    | 4 (10)         |
| Feeding tube          | 2 (5)         | 4 (10)         |
| Weight loss           | 23 (57.5)     | 9 (22.5)       |
| Weight gain           | 1 (2.5)       | 8 (20)         |
Symptoms or problems pre ad post treatment. The cut-off point used: low (1.00–1.86), medium (1.87–2.93) and high (2.94 – 4.00) mean scores. For all items and scales, lower scores indicate more problems or poor symptoms outcome and vice versa. As presented in Table 3, the mean score for overall symptoms or problem scales pre-treatments was 1.64. The mean score of the sexuality was 1.24 and was the lowest among all the 7 multi-item scales. The mean score of pain was 1.83, swallowing was 1.64, senses was 1.29, speech was 1.48, social eating was 1.71 and social contact was 1.28. The lowest score for single items was ‘sticky saliva’ (1.33) and highest score for item ‘felt ill’ (2.63). Thirty per cents of subjects used pain killer, 12.5% used nutritional supplement and 57.5% of subjects had loss weight during the pre-treatment (Table 2). Whereas, the mean score of overall QoL symptoms scales after 6 month posts treatments was 1.29 and 0.35 lower than pre-treatments. The mean score of the sense was 1.09 and was the lowest among all the 7 multi-item scales. The mean score of pain was 1.24, swallowing was 1.25, speech was 1.11, social eating was 1.16, social contact was 1.23 and sexuality was 1.17. The lowest score for single items was ‘teeth problem’ (1.10) and highest score for item ‘felt ill’ (1.93). With regard to HNC patients’ experience/condition (Table 3), only 2.5% subjects used pain killer, 10% used nutritional supplement and 22.5% of subjects had loss weight during the pre-treatment, these numbers reduce compared than pre-treatments. Overall symptoms experience showed significant drop after treatments with mean score reducing from 1.64 to 1.29 indicating improves in health. Item felt ill, pain, problems in opening mouth and social eating were ranked as the most distressing symptoms.

Association of HNC patients’ QoL and symptoms or problems to pre and post treatment period. Pearson coefficient correlation test was employed to explore the associations. The results shows (Table 3) that the QOL of HNC patients pre and post treatment was strong but negatively correlated ($r = -0.447, p = 0.002$). While with regards to symptom or problems, the result suggested that there is no significant relationship between symptom or problem of HNC patients pre ad post treatment.

Discussion

Our study is the first to compare the pre and 6 months post treatments QoL in HNC patients. The study QoL cancer was already established as important study for HNC patient or survivor and toward another kind of cancer, but it was still unclear how contrast between QoL of HNC patient pre and post treatment. Most published studies that compare pre and post QoL in patients with head and neck cancer are too small to allow comparison analyses. Therefore, comparisons between studies may be difficult.

In current study, the more prevalent was seen in older age HNC patients. HNC occurs mainly between the fifth and sixth age decade, being the number of elderly HNC rising as the result of demographic changes. Aged patients are predisposed to spontaneous mutations and hypo methylation of the DNA, important predisposition factors for tumour cell transformation and oncogene activation and thus favouring tumour development. Actually, it is observed an increase of HNC in geriatric population.21

Mostly HNC patients were male. Such gender difference seems to be associated with cumulative risk factors exposure (oral hygiene, dental status, oral mucosal lesions, alcohol and tobacco use, virus infection and lifestyle). The male participants are predominantly ex-smokers and smokers and female HNC patient are mainly non-smokers. This corroborates other findings showing that men are more likely than women to be current smokers.22

Overall mean score symptoms experience of HNC patients showed significant increase after 6 months of treatments indicating improvements in health compared...
to baseline. As compared to another study found during and at the end the radiotherapy and 1 month after the treatment, all symptom scales were impaired significantly. However, six months after the end of the radiotherapy, except for dry mouth, sticky saliva, dental problems and sensory problems, all symptom scores returned to normal. In fact, symptoms such as pain, swallowing difficulties, feeling sick, difficulties with eating in a social environment, difficulties with social interaction and weight loss showed improvement from baseline, and the patients have even gained weight.

Overall mean score QoL for HNC patients showed significant decrease after 6 months of treatments indicating deteriorating in QoL compared to baseline. But in our study, categorized based on domain only physical and social well-being deteriorate, whereas psychological and spiritual well-being slightly improve after treatment. HNC treatments including radiotherapy and chemotherapy are physically demanding, and the invisible nature of the treatment along with its delivery in a highly technical environment can cause a great deal of concern for patients. This reflects the physical impact experience by the HNC patients, which is not only the impact of the disease itself on their physical wellbeing, but also the impact that is derived from the treatment employed to cure the disease. Previous study explore the meanings of being in the physical environment of an oncology clinic by collecting narratives from staff, patients, and significant others. Patients reported that being at the oncology center meant being forced into a world of cancer and impending death, which required them to surrender their bodies to medicine and rely on the ‘paradox’ of radiotherapy.

In the current study ‘felt ill, pain, problems in opening mouth and social eating’ were ranked as the most distressing symptoms and deteriorate most as compared pre and post treatment. This is similar to the finding found ‘poor values for pain, problems with consuming food in a social environment, loss of taste, the problem of opening the mouth’ in the EORTC-QLQ-C30 and QLQ H&N 35 questionnaires applied to 102 patients with HNC. However, the findings from the study which identified that problems related to nutrition such as dry mouth, trouble swallowing, and loss of taste, as well as physical problems, were the most bothersome to patients towards the end of treatment, with only minimal improvement in reported problems one month later. Similar finding found in a study in China on QOL and the impacts and the result emphasize on the importance of ear and oral nursing and psychological care to the patients.

In current study, there was several patients ‘lost weight during pre and post treatment, but greater number lost weight during pre-treatment as besides malnutrition, treatment with radiotherapy, dry mouth and trouble with social eating’ were shown to be related as well. Unfortunately, dry mouth and trouble with social eating was direct and usually long lasting sequel of head and neck cancer treatment and are difficult to treat. Concurrent attention should be given to both delivering good quality treatment options that save lives and focusing on ways to minimize therapy specific impact on the structure of the head and neck. Clearly, identification of disease implies smaller malignancy and a single modality treatment that ensure less organ tissue removal or smaller radiation field.

Among all the domains spiritual well-being (item of ‘hopeful’) score was highest for pre and post treatment. Means, spiritual aspect was less affected and HNC patient still gain their hopeful for survival. In a study on Muslim patients conducted by Proceedings OC results showed that many patients talked about their acceptance of the illness based upon their religious teachings. Many stated they had come to terms with their diagnosis with total acceptance and resignation (redha). Some said that in the early days following their diagnosis, they felt sad and had difficulty in accepting the illness. The question of “why me?” was also raised. However, they said that a few days later they felt calmer when the concept of redha sunk in and they were able to accept the illness as a trial from God.

Patients who received less spiritual care than they desired were at significantly greater risk of depressive symptoms and lower sense of spiritual wellbeing, defined as poorer sense of purpose in life, meaning, and peace. Spiritual wellbeing can contribute to cancer patients’ QoL and their ability to cope with terminal illness. In addition, when cancer threatens the meaning of an individual life, religion and spirituality are important coping strategies for some individuals. The current study however, different from other study that followed the survivors in a longer period of time, where their HRQL was assessed 1,2,3,6 and 12 months during post their first modality of cancer treatment.

There were several limitations encountered in this current study. The retrospective study may somehow affect the patients to remember the difference between QoL pre and post treatment. Most of the patients had reported maximum toxicity 2 months post treatment. Therefore, it is important that, patients must be followed until they have recovered from the acute and sub-acute toxicity. Although the results of this current study manage to show evidence that treatment has an impact (negatively) onto the QoL pre and post treatment, however some domains in QoL scale did show some improvement after treatments. The finding also shows that a combination of treatments may have some influence to the seriousness of the effect and complaints. The researchers hope that the findings of the study will facilitate
multidisciplinary team to enhance the symptoms control, psychological and spiritual support in which would improve patients’ QoL.

Conclusions

In conclusion, understanding of the HNC survivors’ QoL and related issues is very crucial and should be considered while providing care and assisting them through their rehabilitation period. Baseline and regular assessments on the impact of HNC to patients’ QoL should be carried out to monitor these problems. A further high quality research is required to develop appropriate and effective interventions for this population and advance programs that will aim at maximizing rehabilitation outcomes.

Acknowledgement

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Conflict of Interest Statement

We confirm that none of the authors have any competing interests in the manuscript. The research data is stored in the external hard drive and kept safely in the university storage. It can be accessed from the principal researcher.

References