



QOL of the Patients with Lymph Edema: Evaluation of Japanese Patients using SF-36

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Abstract

Purpose: This cross-sectional study aimed at evaluating the health-related quality of life (QOL) of Japanese patients with lymphedema.

Methods: A cross-sectional, descriptive study was conducted. Twenty-seven patients with lymphedema of the upper or lower limb(s) who presented to the two institutions between January and December 2010 completed the Short Form 36 (SF-36: a generic health-related QOL measure).

Results: All components and summary scores of the generic health-related QOL reported by the patients were statistically worse than that of the Japanese norms. The patients with symptom duration of longer than 1 year, who underwent radiation therapy, or those undergoing chemotherapy reported significantly lower QOL.

Conclusion: Lymphedema significantly deteriorates the QOL of the patients. Further evaluation with longitudinal design, increased number of cases and disease-specific QOL scale is warranted to better understand the QOL of the patients.

Keywords

Quality of life, Lymphedema, Symptom assessment

Introduction

Lymphedema is a chronic condition in which extremities become edematous due to the inadequate lymphatic circulation followed by the accumulation of protein-rich fluids in the interstitial tissues [1]. The leading cause of lymphedema is filariasis in developing countries, whereas in developed countries, it often occurs following treatment of cancer (secondary lymphedema) or due to congenital hypoplasia of lymphatic system (primary lymphedema) [2]. Primary lymphedema accounts for 6-12% of the entire patients and the majority of the patients are classified as secondary lymphedema [1].

Lymphedema is reported to severely affect patient's quality of life (QOL), and there are extensive reports regarding the issue [3,4]. In summary, the patients with lymphedema experience physical, psychological as well as social concerns. But there are few studies which evaluated the QOL of Japanese patients in a statistically reliable way [5,6]. In a report published in 2009, the efficacy of complex physical therapy on 40 Japanese patients with lymphedema was evaluated using Short Form-36 (SF-36, a generic health-related QOL scale) and Skindex29 (disease-specific health-related QOL scale for skin-related problems). This was a preliminary report and the actual scores of the QOL scales were not stated, although the authors reported a statistically significant improvement in some of the Skindex29 scores after treatment [5]. A more recent study investigated QOL of 83 Japanese patients with primary lymphedema using SF-36, EuroQol 5-dimension (EQ-5D, a generic health-related QOL scale), and Brief-COPE (a tool to assess coping styles of the patients) [6]. In this study, the patients reported significantly lower scores in general health perception subscale of SF-36 compared to Japanese norms, but all the other subscales were maintained at national average.

The studies described above either lacked description of QOL scores in detail or was focused on patients with primary lymphedema, which is a minority of the entire lymphedema population, and QOL of Japanese patients with lymphedema is yet to be explored. In the present study, we evaluated the generic health-related QOL of 27 Japanese patients with lymphedema using Japanese version of SF-36, and clarified some of the factors related to the patients' QOL.

Materials and Methods

The QOL of the patients with lymphedema who consulted the department of plastic and reconstructive surgery of two institutions (Hiratsuka City Hospital and Tochigi Cancer Center) between January

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and December 2010 were evaluated. Hiratsuka City Hospital is a general hospital and covers approximately 200-thousand populations residing in the city. Tochigi Cancer Center is a cancer-specialized center and covers approximately 500-thousand populations in the area. The diagnosis was made by 2 plastic surgeons experienced in lymphedema care, based on patient's history and physical examination. The locations of the edema were upper or lower limb(s). The patients with medical history other than lymphedema that may cause edema of the limbs, such as liver dysfunction or venous insufficiency, were excluded. The study was approved by the Institutional Review Boards (IRB) of the two institutions, and written informed consent was established from all the participants after explanation of the study.

Japanese version of SF-36 version 2 was used to evaluate generic health-related QOL. SF-36 is a questionnaire type of tool to assess generic health-related QOL, and its reliability and validity have been established [7]. Japanese version was introduced in use in 1998, and the values of Japanese norms (average scores) have been established in the study targeting 4500 individuals [8-10]. It consists of 36 questions and expresses 8 categories of subscales and 2 summary scores to describe HRQOL (Table 1). The lower scores represent the worse QOL.

The free responses were collected as well to investigate the underlying issues. The paper questionnaires with return envelope with postage stamp were sent to the patients. The patients were asked to fill in the forms for themselves at home and call the authors of the present study if any difficulty was met in filling the questionnaire. Because the sample size was relatively small (n=27), the numerical data concerning the patients were expressed in median and range.

The evaluation consisted of two parts. First, the QOL of the entire patients was compared to that of the Japanese norms. Then, the patients were divided into two groups according to the following criteria, and inter-group comparison within the patient group was performed:

- Age (younger than 60 years versus 60 years or older)
- Etiology (primary versus secondary)
- Number of affected sides (unilateral versus bilateral)
- Affected limb (upper versus lower limb)
- Stage according to the International Society of Lymphology, in which stage 0 is preclinical stage, stage 1 is edema reversible with elevation, stage 2 is edema irreversible with elevation, and stage 3 is elephantiasis [11]. (Stage 1 versus 2 and 3)
- Duration of symptom (shorter than 1 year versus equal to or longer than 1 year)
- History of radiation therapy
- Whether currently undergoing chemotherapy or not
- Whether experiencing cellulitis in the past or not
- Difference in the circumference of the affected and non-affected limb (less than 5% versus equal to or greater than 5%)
- Past history affecting motor functions of the limb (such as fracture)

-Treatment of lymphedema (currently undergoing versus cessation or no history of treatment)

The scores were standardized according to the age and sex-matched Japanese norms and converted to the deviation value (z score: the score of 50 equals the average age and sex-matched Japanese score, and the difference of 10 points equals one standard deviation). The 8 subscales and 2 summary scores were analyzed. In the comparison of the entire patients and the Japanese norms, the QOL scores were expressed in average and 95% confidence interval, and statistical significance was regarded as present if the 95% confidence interval of the patients' score did not overlap the point of 50 (Japanese average). In the comparison between the two subgroups within the patients, the QOL scores were expressed in median and range, and statistical analysis was done with Mann-Whitney U test (non-parametric test). Non-parametric test was utilized because of the small sample size and the uneven distribution of the patients' QOL scores to the lower side. The difference was regarded as statistically significant if $p < 0.05$. Statistical software SPSS 11.0 for Windows (SPSS Inc., Illinois) was used in the analyses.

Results

Patient characteristics

Thirty-three patients were recruited in the study. Two patients did not respond, 4 patients denied participating, and total of 27 patients (81.8%) were included in the study. The patients were relatively high-aged (median 60 years old) and all were female. Majority of the patients were diagnosed as secondary lymphedema due to treatment of cancer (n=22). Lower limbs were more frequently involved (n=23), and majority of the patients were at stage II (n=21) (Table 2).

Patients - Japanese norms

In all of the 8 subscales and 2 summary scores of QOL scores, the patients' scores were significantly lower than the Japanese average (Table 3) (Figure 1).

Inter-subgroup comparison within the patient group

Duration of symptoms: The patients suffering from lymphedema for equal to or longer than 1 year (n=7) reported significantly worse PF (Physical Functioning) score compared to those with symptom duration of less than 1 year (n=20) (median 40.3 (range 14.0-60.0) versus median 56.3 (range 40-58.1), $p=0.041$).

Radiation therapy: The patients with history of radiation therapy (n=5) reported significantly lower scores compared to those without it (n=22) in SF (social functioning: 31.5 (19.1-32.1) versus 39.8 (23.1-57.9), $p=0.014$) and MH (mental health: 34.7 (25.5-57.9) versus 42.5 (32.3 - 65.2), $p=0.046$).

Current chemotherapy: The patients currently undergoing chemotherapy (n=2) reported significantly lower scores compared to those without it (n=25) in GH (general health perceptions: 22.7 (20.3-25.1) versus 45.4 (32.3-55.8), $p=0.021$) and SF (social functioning: 24.3 (23.1-25.5) versus 38.6 (19.1-57.9), $p=0.034$).

Table 1: Eight Subscales and Two Summary Scores of SF-36

Subscales	Descriptions
PF (physical functioning)	reflects ability on activities of daily living to vigorous exercises.
RP (role physical)	reflects presence of physical problems on executing daily works.
BP (bodily pain)	reflects presence of troubles on executing daily works due to pain.
GH (general health perceptions)	reflects general feelings of being "not healthy" or "healthy".
VT (vitality)	reflects feelings of being "exhausted" or "energetic".
SF (social functioning)	reflects presence of physical and mental problems on meeting with others.
RE (role emotional)	reflects presence of mental problems on executing daily works.
MH (mental health)	reflects feelings of being "nervous and anxious" or "calm and joyful".
PCS (physical component summary)	reflects overall physical quality of life, derived from the 8 subscales.
MCS (mental componentsummary)	reflects overall mental quality of life, derived from the 8 subscales.

Table 2: Patient Characteristics (N=27)

Characteristics	n (range)
Age (years) (median, range)	60 (25-80)
Sex (n)	
Male	0
Female	27
Etiology (n)	
Primary	4
Secondary (post-surgery)	22
Secondary (post-trauma)	1
Affected limb (n)	
Upper	4
Lower	23
Affected side (n)	
Unilateral	17
Bilateral	10
Stage (n)	
Stage I	6
Stage II	21
Duration of symptoms (years) (median, range)	4 (0-30)
History of radiation therapy (n)	
Yes	5
No	22
Current Chemotherapy (n)	
Yes	2
No	25
History of cellulitis (n)	
Yes	11
Never	16
Difference of circumference between affected and non-affected limbs	
<5%	9
>=5%	8
(bilateral involvement)	10
Past history affecting motor functions	
Present	2
Absent	25
Treatment of lymphedema	
Currently undergoing	5
Cessation / never performed	22

Table 3: QOL Scores of the Patients

Subscale	Average	95% confidence interval
PF: physical functioning	44.3	40.0 - 48.7
RP: role functioning	42.0	37.5 - 46.5
BP: bodily pain	45.1	41.9 - 48.3
GH: general health perceptions	43.4	40.1 - 46.8
VT: vitality	43.4	40.1 - 46.8
SF: social functioning	39.6	35.4 - 43.8
RE: role emotional	42.6	37.8 - 47.4
MH: mental health	43.5	39.7 - 47.3
PCS: physical component score	43.5	38.7 - 48.2
MCS: mental component score	39.7	36.1 - 43.3

No significant difference or tendency was found in the other comparisons:

- Age: younger than 60 y (n=13) versus 60 y or older (n=14)
- Etiology: idiopathic (n=23) versus secondary (n=4)
- Number of affected sides: unilateral (n=17) versus bilateral (n=10)
- Affected limb: upper (n=4) versus lower limb (n=23)
- Stage: stage 1 (n=6) versus 2 and 3 (n=21)
- History of cellulitis: experienced in the past (n=11) versus never experienced (n=16)
- Difference in the circumference of the affected and non-affected

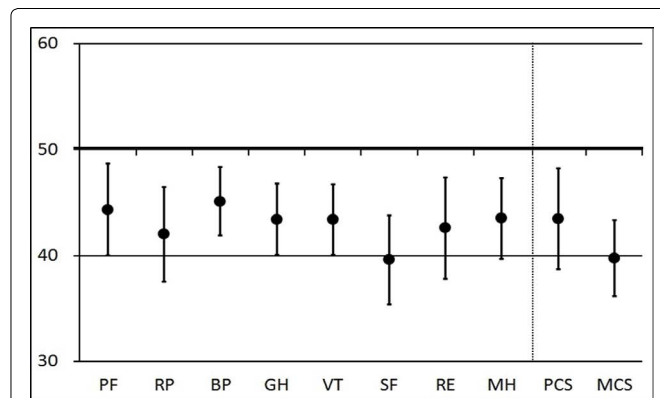


Figure 1: QOL of the Patients

The circle indicates the average and the error bar indicates the 95% confidence interval of the QOL score of the patients in deviation value. The score of 50 means the Japanese average, and the difference of 10 points equals one standard deviation. Note that the 95% confidence interval of the QOL scores do not overlap the score of 50, indicating statistical difference in the QOL between the patients and the Japanese norms. See Table 1 for the abbreviation of the subscales and summary scores.

limb: less than 5% (n=9) versus equal to or greater than 5% (n=8) (in 10 patients with bilateral lymphedema, comparison was not performed)

-Past history affecting motor functions of the limb: present (n=2) versus none (n=25)

-Treatment of lymph edema: currently undergoing (n=5) versus cessation or no history of treatment (n=22)

Free responses: The complaints of the patients were categorized into 3 groups. The representative comments are presented below:

-Physical: “difficulty in going up the stairs or executing fine movements”

-Psychological: “the impact of lymphedema on QOL is underestimated by peers and family members”, “continuing treatment is depressive”

-Social: “limitation in choosing clothes”, “difficulty in continuing jobs because unable to keep standing for long time”

Discussion

Lymphedema has a profound effect on patient’s QOL [3,4]. But there are few studies which evaluated the QOL of Japanese patients in an objective and statistical method [5,6]. In the present study, we evaluated the generic health-related QOL of Japanese patients with lymphedema with a validated tool.

QOL is a subjective evaluation reported by the patients themselves, and it is becoming increasingly important as an outcome measure of the treatment [3]. Because of the subjective nature of QOL, the method of evaluation must be tested by psychometry to establish validity and reliability, thus enabling objective and statistical analysis. Therefore, free responses are generally regarded as not appropriate for objective assessment. However, free responses were collected in the present study, not to directly measure the QOL of the patients, but to help understanding the underlying causes of the change in QOL.

Because the concept of QOL embraces the broad spectrum of elements, QOL is generally evaluated by dividing it into several components. Health-related QOL is a part of QOL concept that is affected by one’s health status. When assessing health-related QOL, it is important to evaluate both the generic health-related QOL, which is affected by one’s general health status, and the disease-specific health-related QOL, which is affected by the specific disease the person is experiencing. This is because the generic health-related QOL may miss or underestimate some of the specific symptoms caused by the disease [12]. In the present study, SF-36, a generic HRQOL scale, was

used to assess the generic HRQOL. SF-36 has been used in a wide range of health issues [13-15], and its reliability and validity are well-established in many languages including Japanese [8]. On the other hand, there was no validated health-related QOL scale specific to lymphedema in Japan at the time of this study, and we conducted our study without such scale.

There was response from 27 patients out of the 33 recruited (response rate: 81.8%). This high rate of response suggests that the results represent the entire group. It also shows the high interest the patients show toward their QOL.

In the comparison of the patients with Japanese norms, the QOL of the patients was significantly impaired in all of the 8 categories and 2 summary scores. Although data of the Japanese patients from other disease states are scarce, some of the QOL subscales are usually spared from debasement in many of the other disease conditions, such as head and neck surgery [13], breast reconstruction [14], or severe burns [15], and the total impairment of QOL is rather rare. The same tendency has been pointed out in a study using newly-developed QOL scale, in which 392 German patients with lymphedema showed markedly lower QOL scores in all fields compared to patients with venous insufficiency [16]. The result of the present study is not in consent with recently reported study on 83 Japanese patients with primary lymphedema, in which only the general health perception subscale of SF-36 was significantly decreased compared to Japanese norms [6]. This difference may be due to the difference in the study population (Okajima reported on primary lymphedema patients whereas majority of the patients in the present study had secondary lymphedema), and availability and accessibility to lymphedema-specific treatment (Okajima's study took place in Tokyo and 90% of the patients wore compression garments and nearly 60% performed self-lymphatic massage, whereas 22 out of 27 patients in the present study received no specific treatment at the time of presentation to the hospital).

The attempts to understand the causes of the severe deterioration in QOL were made. The complaints collected in the free responses could be categorized into physical (ie. difficulty with going up the stairs), psychological (ie. depressed by the need to continue treatment) and social domains (ie. inability to go to work) and covered the wide range of QOL. Many responders complained that the lymphedema is not regarded as "disease" and the severity of lymphedema is underestimated by the surrounding people after overcoming potentially life-threatening cancer. Many patients also complained the difficulty in accepting the long-lasting problems caused by the lymphedema after dramatic recovery from cancer. This gap between the expectations (survival from cancer) and reality (lymphedema) was thought to be the cause of the severe and extensive depressions in the QOL.

In the comparison within the entire patient group, the patients suffering lymphedema for more than 1 year presented statistically worse physical functioning compared to those with shorter duration. The severity of lymphedema is reported to worsen with time without treatment [17]. The decrease in physical domain of QOL observed in the present study could be due to the progressing fibrosis of the extremities, making physical activities more difficult as time passes.

The patients with the history of radiation therapy reported statistically worse mental health and social functioning. The reason for this is not clear, but the fibrosis and other complications caused by radiation might have caused some depressive effects on patients, making self-perception of health status worse and social intercourse more difficult.

The patients currently undergoing chemotherapy reported significantly lower scores in general health perception and social functioning. It is quite reasonable considering the complications caused by the therapy.

There are some limitations in this study. This is a cross-sectional study, and continual observation is mandatory to gain higher

level of evidence. Number of patients is still small, and expansion of the database will clarify more accurate view of the patients. We are currently collecting the prospective data of the patients who are undergoing treatment. These attempts will lead to better understanding of the current status of the patients with lymphedema.

Conclusion

The QOL of Japanese patients with lymphedema was investigated using SF-36, a generic health-related QOL measure. The QOL of the patients were debased in all fields compared to the Japanese norms, and the difference was statistically significant. Statistically lower QOL was observed in the patients with duration of lymphedema for longer than 1 year, those with the history of radiation therapy, and those currently undergoing chemotherapy. Further investigation with QOL scales more specific to lymphedema and more number of patients with longitudinal study design is warranted to establish higher level of evidence.

Ethical Statement

This study was approved by the institutional review boards (IRB) of the two institutions where the study took place, and all the participants submitted written consent after the explanation of the study.

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