Development of a head and neck lymphoedema specific quality of life tool: The Comprehensive Assessment of Lymphoedema Impact in the Head and Neck (CALI-HaN)

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Abstract:

Purpose: To develop a head and neck lymphoedema (HNL) specific quality of life (QoL) instrument to assess physical, functional, and social/emotional impacts of HNL.

Methods: Instrument candidate items were reviewed by HNL patients and clinicians and rated for importance, clarity, and invasiveness. The Content Validity Ratio was applied for item reduction. Three-step cognitive interviews were conducted with HNL patients to validate the items, survey format, and instructions.

Results: Initially, 130 candidate questions were developed. Following item reduction, 52 items progressed to three-step cognitive interviews. Following cognitive interviews, the Comprehensive Assessment of Lymphoedema Impact in Head and Neck (CALI-HaN) included 33 items; one global, ten physical, seven functional, and fifteen emotional.

Conclusions: Physical, functional, and socioemotional effects need to be considered when measuring QoL in patients with HNL. This study describes initial development of the CALI-HaN, an instrument that shows promise for clinical and research applications following future validation.

1. Background:

Head and neck lymphoedema (HNL) is a common, unintended consequence of head and neck cancer (HNC) and its treatments, with prevalence rates up to 90% following HNC treatment [1-2]. HNL occurs when the lymphatic system is injured, leading to accumulation of lymph fluid in the interstitial spaces. Physical and anatomic changes due to inflammation, compression, reduced mobility, and fibrosis resulting from HNL may lead to functional impairment, such as dysphagia and dysphonia [3-4]. As a result of these functional impairments, individuals with HNL may have reduced satisfaction in their quality of life (QoL) [5-6].

Health related quality of life (HRQoL) refers to “a state of complete physical, mental, and social well-being and not merely the absence of disease” [7]. Assessment of HRQoL therefore needs to encompass not only physical functioning, but also emotional and social well-being. A recent systematic review of patient reported outcomes measures (PROMs) used for patients with lymphoedema identified 17 lymphoedema-specific QoL measures, the majority of which were developed for patients with limb lymphoedema [8]. Only one scale was developed for those with HNL. The overall methodologic quality for instrument development was low to moderate, citing a lack of patient involvement as a major shortcoming of most of the instruments reviewed, including the instrument designed for HNL. Based on their review, they advocated for the development of PROMs for patients with lymphedema, using a more patient-centric approach.

It is well established that individuals diagnosed with HNC are at risk for both short and long-term decrements to QoL [9-10]. Further, there appears to be a relationship between poorer QoL and higher rates of depression and anxiety [11-13].It has been shown that patients with more severe HNL have more functional impairment and poorer QoL [3].It is important then that clinicians and researchers interested in the impact HNL treatments are able to assess not just the physical and functional effects of treatment, but also the socioemotional impacts of treatment. PROMs are considered to be the gold standard for assessing subjective patient perspectives [14]. To date, there is no tool developed specifically to encompass all aspects of QoL related to HNL.

The Patient Reported Outcomes Measurement Information System (PROMIS) recommends a 5-step process for development of PROMs [15]. Following a systematic review of existing measures, qualitative interviews and/or focus groups should be completed to identify concepts important to patients with a specific condition. Thematic analysis is then performed to identify themes common to individuals with the condition to guide development of the initial item bank. Once this item bank is developed, additional cognitive interviews should be performed with individuals with the target condition to validate the item bank prior to psychometric field testing. The COSMIN study design checklistprovides additional guidance for designing a study regarding measurement tools such as PROMs [16].

Given the unique functions of the head and neck region in respect to appearance, communication, intimacy, and consumption of food and liquid, it is imperative that these issues are addressed in any specific PROM used to measure QoL in patients with HNL. The 64-item Lymphedema Symptom Intensity and Distress Survey – Head & Neck (LSIDS-HN) was initially designed to characterize the symptom burden specific to those with HNL and fibrosis [17-18]. Patients are asked to indicate the level of “intensity” as well as “distress” associated with each symptom, using two separate 5- point Likert scales. During validation testing, the test length was raised as a concern by ~60% of those studied. Further, they reported a high level of agreement between intensity and distress ratings, suggesting that patients did not consider these to be separate constructs. Thus, the authors removed the “distress” response option and shortened the symptom list to 33 items, renaming the instrument the Head and Neck Lymphedema and Fibrosis Symptom Inventory (HN-LEF Symptom Inventory) [19]. Of the 33 items retained, most (28) refer to physical and functional symptoms with few items related to emotional well-being.

While the HN-LEF Symptom Inventory is a valuable tool for understanding symptom burden, there remains a need for a QoL instrument that will also capture the social and emotional consequences of HNL. As a result, the purpose of this study was to develop an HNL-specific QoL instrument to assess physical, functional, and social/emotional domains. We have previously reported the results of our systematic review and qualitative interviews conducted in early stages of scale development [20-21]. This paper outlines the development process from item generation through cognitive interviewing for the creation of the Comprehensive Assessment of Lymphoedema Impact in the Head and Neck (CALI-HaN).

1. Methods:

Phase 1: Item generation

Item generation for a patient-reported QoL instrument includes consideration of extant scales and interrogation of the patient perspective. A systematic reviewwas performed to identify extant tools which were examined to identify possible constructs and relevant items for consideration [20]. Qualitative interviews were conducted with 22 HNC patients from the UK and US with lymphoedema [21]. As previously published, the average age of participants was 60 years, 50% were male, and 77% were white. 50% of participants had oral cavity primaries and the overwhelming majority (95%) had a combination of surgery and radiation (demographics of this sample can be found in Table 1). Based on these interviews, candidate items were generated to reflect key themes. Items were generated by the first author and reviewed by the study team to ensure concordance with the findings of the qualitative interviews. Binning and winnowing were conducted by the study team once the initial items were generated. Binning refers to a systematic process of grouping items according to meaning to identify redundancy and completeness of encapsulating the construct(s) of interest. Winnowing is the process of eliminating those items judged to be redundant or inadequate for the purpose of the instrument being developed [15].

Phase 2: Initial validation and item reduction

Patients with HNL and HNC practitioners (n=18) were invited to participate in a study to examine the clarity, importance, and intrusiveness of the candidate items. Inclusion criteria for patients were; a prior diagnosis of HNC and HNL, age>18, English proficiency, and ability to access an online survey instrument. Clinicians were experienced in working with patients with HNC and HNL. Specialties invited to participate included surgical, radiation, and medical oncologists, nurses, physiotherapists, occupational therapists, and speech-language therapists. Ethics board approval was granted for all phases of this study.

A Qualtrics survey (Qualtrics, Provo UT) was developed and included each candidate item. Patient and clinician participants were asked “How important is this item?” using a 4-point Likert scale (1= not important and 4=very important). Additionally, they were asked “How easy is the question to understand/interpret?” using a 4-point Likert scale (1=very easy and 4=very difficult). Finally, participants were asked “Is this question upsetting or intrusive” with a simple yes/no response. At the conclusion of the survey, participants had the opportunity to add any additional questions that they felt were important to include.

The Content Validity Ratio (CVR) described by Lawshe[22] was used to assess which items were judged to be most important. The formula utilized was:

Number of raters rating an item 3 or 4 – (number of raters/2)

Number of raters/2

CVR values range from -1.0 to 1.0 with lower numbers indicating less importance and higher numbers indicating greater importance. The cutoff for initial item inclusion was 0.44 based on recommendations by Ayre and Scally [23] based upon the number of raters completing the survey. Given that the patients’ perspective should be weighted more heavily in this process to avoid potential content under-representation [24], items not reaching the cutoff of 0.44 were examined to see how many patients rated the items at a 3-4. Items with >50% of patients rating 3-4 were also included in the initial instrument draft.

Phase 3: Cognitive interviews

Following the initial item reduction process, three-step cognitive interviews were conducted to further validate the items, survey format, and instructions. Participants previously diagnosed with HNC and HNL who did not participate in the initial qualitative interviews or Phase 2 surveys were invited to participate. Potential participants were referred by HNC practitioners and were invited to participate in person, by flyer, or through email correspondence. Cancer and demographic variables were ascertained from the medical record. The Social Deprivation Index[25] was used to characterize socioeconomic status. This index is a composite measure of seven demographic characteristics reported at a zip code level where lower values represent lower community-level disadvantage.

Three-step cognitive interviews were conducted in person or via Zoom video platform by the first author. Three-step cognitive interviews combine the “think aloud” method with probing methods to determine if the participants understand the questions as the researcher intended[26]. During these interviews, participants were first asked to complete the survey, verbally stating what their interpretation of each question was and why they were answering in a particular way. Probing was then conducted to provide additional clarification about item interpretation, response options, and to compare different items. There was intentional exploration of items that were identified as potentially upsetting/intrusive on the Qualtrics survey. Participants were also asked about the instructions and definitions provided. Detailed notes were taken during the interviews and each interview was recorded. The scale was further adapted based on these interviews.

1. Results:

Phase 1:

Based upon thematic analysis of qualitative interviews, 130 unique candidate questions were developed. The binning process identified two major categories: emotional/social and physical/functional. Additionally, there was one global QoL item. Within the category of emotional/social impacts, 5 major bins were identified: appearance, cancer survivor, relationships, worry/vulnerability, and trying to cope. Within the category of physical/functional impacts, 3 bins were established: changes in life participation, discomfort, and functional impairments. Table 2 provides the initial item count for each bin as well as example questions. The winnowing process led to exclusion of 57 items due to redundancy and inclusion of 73 candidate items for further testing.

Phase 2:

A convenience sample of 18 participants completed the Qualtrics survey regarding the candidate questions, 9 clinicians and 9 patients. Most participants were between 31-50 years of age, female, white, and residing in the United States. Demographic information regarding participants is available in Table 1.

Of the 73 candidate items, 41 met the pre-set criteria using the CVR (Table 3). Of the 32 items that did not meet criteria, 11 were selected by >50% of patients as being “somewhat important” or “very important” and were thus retained. This yielded a total of 52 items to be considered for inclusion on the final scale and 21 items to be discarded. All of the initial 73 candidate items had >50% of participants rating them as “very easy” to understand. Thirteen of the candidate items (25%) had >1 participant indicating it was either “somewhat difficult” or “very difficult” to understand. Of the 52 candidate items, 12 (23%) had more than one participant indicate it was “intrusive/upsetting”. Of the 52 items, 18 reflected physical domains, 10 reflected functional domains, 23 reflected emotional domains, and one was a global item. Response options for the QoL survey were considered, and a 5-point Likert scale was selected.

Phase 3:

Three step cognitive interviews were performed with 5 individuals. Four of the interviews were conducted on Zoom and one was in person. Participants ranged in age from 29-84 years. Most were female (80%) and white (60%). SDI scores ranged from 4-71 indicating a broad range of population-level disadvantage. HNC diagnoses included tongue (2), oropharynx (1), parotid (1), and carotid sarcoma (1). All participants underwent surgical resection, two had additional radiotherapy, and two had additional chemoradiotherapy. All participants had a history of treatment for HNL within the prior 12-months.

*Feedback on instructions*: All participants indicated the provided definitions of “lymphoedema” and “quality of life” were helpful in determining how to approach the survey. They similarly reported that the instructions were helpful and necessary. All agreed that the timeline for reflection (past 7 days) would allow for some variation from day to day but not require excessive recall. They all indicated that it was important to include a statement acknowledging the possible presence of other issues, but the need to focus only on the impact of lymphoedema for the purpose of this survey.

*Feedback on response options and formatting*: The initial format of response options included a 5-point Likert scale ranging from “Strongly Agree” to “Strongly Disagree”. Several participants indicated a preference for a scale that referred more to the frequency of occurrence. Based on this feedback, response options were altered to range from “never” to “always”. All participants preferred a 5-point scale versus a scale with fewer or more options, and landscape rather than portrait layout. Participants indicated that while the survey was slightly long, it was not overly burdensome, and they would be willing to complete this survey in conjunction with clinical visits.

*Feedback on items:* Based on participant feedback, 20 items were removed. Reasons for item removal included redundancy, difficulty differentiating from other possible causes (e.g. xerostomia), wording judged as too negative, preference to avoid items that would require inverse scoring, vagueness, and irrelevance (Figure 1). Of the remaining items, slight adjustments in wording were conducted to increase clarity. Two additional items were added based on participant feedback. Participants were not concerned about items identified as potentially intrusive/upsetting on the Qualtrics survey. Items indicating “worry” about a concept were changed to “concern” based on feedback. A total of 33 items were retained for the final version of the CALI-HaN. Of the items retained, one item was a global item, 10 reflected physical issues, 7 reflected functional issues, and 15 reflected emotional issues.

1. Discussion:

Applying recommendations for PROM development previously published by the PROMIS and COSMIN groups, particularly in respect to content validity, we have initiated development of an HNL-specific QoL instrument, the Comprehensive Assessment of Lymphoedema Impact in the Head and Neck (CALI-HaN). Methods employed included a systematic review of the literature and extant scales, qualitative interviews of patients with HNL to identify important concepts and concerns, qualitative analysis to guide item bank development, refinement of the item bank based on patient and practitioner input, and additional, qualitative cognitive interviews to further validate and refine the scale. This instrument is the first of its kind to holistically assess the impact of HNL on physical, functional, and socioemotional outcomes. Inclusion of patient and expert opinions at multiple stages of development contribute to strong content validity.

HRQoL is increasingly accepted as a primary or secondary endpoint in many treatment trials [27-29]. PROMs provide clinicians and researchers the opportunity to understand the patient perspective of the impact of a disease and treatments employed to treat it. Although several tools have been designed for limb lymphoedema, there has been limited focus on measuring QoL in patients with HNL, despite the unique functional consequences experienced in the head and neck region, such as difficulties with voice and swallowing [21]. The HN-LEF Symptom Inventory [19] provides important information about the presence and severity of symptoms in patients with HNL, however focuses predominantly on physical and functional symptoms rather than emotional consequences. Thus, the CALI-HaN may fill an important gap in the available methods to assess and measure the impact of HNL on QoL.

As with most studies, there are limitations to acknowledge. While purposive sampling was utilized in recruiting patient and expert input at all points of development, those participating in phases 2 and 3 were largely white, female, and from the United States. While the sample in phase 1 was more reflective of the typical HNC demographics in the US and UK, there was overrepresentation of females in phases 2-3 which may limit the degree to which these results can be generalized. It is possible there are missing perspectives based on our use of convenience sampling for the cognitive interviews. Convenience sampling itself may indeed lead to selection bias where participants opting to participate had higher degrees of concern about their lymphoedema. In order to maximize the generalizability of the final instrument, additional validation studies will be conducted using a large, diverse population.

Future work is needed to further assess the validity, reliability, and utility of the CALI-HaN in a large validation cohort of individuals with HNL. Further, psychometric work will be necessary to ensure proper ceiling and floor effects and to establish clinically meaningful change values for this instrument. We are optimistic based on patient and expert feedback that the CALI-HaN will provide valuable insight into the holistic impact of HNL on individual patients.

1. Conclusions:

This study aimed to initiate the development process of a PROM specific to individuals with HNL to assess the impact of HNL on QoL. Data from qualitative interviews demonstrated that physical, functional, and socioemotional effects all need to be considered when measuring QoL in this population. Using methodology recommended by PROMIS and COSMIN, we initiated development of the CALI-HaN, an instrument that shows promise for both clinical and research applications. Future studies of the CALI-HaN’s measurement properties will be needed in a large, diverse cross-sectional sample.

Statement of data availability: The data that support the findings of this study are not openly available for patient privacy reasons but may be made available by the corresponding author upon reasonable request.

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Figure Legend

Figure 1: Reasons why items were removed following cognitive interviews

Table 1: Participant characteristics at each phase of development

|  |  |  |  |
| --- | --- | --- | --- |
|  | Phase 1 | Phase 2 | Phase 3 |
| Medical provider  Patient | 0  22 (100%) | 9 (50%)  9 (50%) | 0  5 (100%) |
| **Age**  18-30 years  31-50 years  51-70 years  >70 years | 0  4 (18%)  15 (68%)  3 (14%) | 0  11 (61%)  6 (33%)  1 (6%) | 1 (20%)  1 (20%)  2 (40%)  1 (20%) |
| **Sex**  Male  Female | 11 (50%)  11 (50%) | 6 (33%)  12 (66%) | 1(20%)  4 (80%) |
| **Ethnicity/race**  White  Black  Asian  Hispanic | 17 (77%)  1 (5%)  2 (9%)  2 (9%) | 13 (72%)  1 (6%)  3 (17%)  1 (6%) | 3 (60%)  0  2 (40%)  0 |
| **Country**  USA  UK  Australia | 15 (68%)  7 (32%)  0 | 15 (83%)  2 (11%)  1 (6%) | 5 (100%)  0  0 |

Table 2: Initial candidate items for QoL survey by bin

|  |  |  |
| --- | --- | --- |
|  | **Number of items** | **Example** |
| **Emotional/social**  Appearance items  Cancer survivor  Relationships  Worry/vulnerability  Trying to cope | 16  8  8  16  31 | “It bothered me how visible my lymphoedema is”  “Because of lymphoedema, I was concerned that my cancer would come back”  “Because of my lymphoedema, I felt less comfortable in social situations”  “I was concerned that lymphedema would cause other health issues in the future”  “I felt like I needed to hide my lymphoedema from others” |
| **Physical/functional**  Changes in life participation  Discomfort  Functional impairments | 16  14  21 | “Because of lymphoedema, I tended to avoid social activities”  “Because of lymphoedema, moving my head and neck was painful”  “Because of lymphoedema it was difficult to drive” |

Table 3: Qualtrics ratings of candidate items

|  |  |  |
| --- | --- | --- |
| Item | CVR value | # of patients rating as 3 or 4 |
| Lymphedema has an impact on my quality of life. | 0.89 | 8/9 |
| I feel like people are staring at me because of my lymphedema. | 0.18 | 4/9 |
| Moving my head and neck is painful because of the swelling. | 0.53 | 6/9 |
| My swallowing is difficult because of the lymphedema. | 0.65 | 7/9 |
| My voice doesn't sound normal because of the lymphedema. | 0.65 | 6/9 |
| My speech is unclear when I am swollen. | 0.65 | 6/9 |
| People have difficulty understanding me when I am swollen. | 0.65 | 7/9 |
| I cannot hug friends and family in the same way because of the lymphedema. | -0.18 | 3/9 |
| It bothers me how visible my lymphedema is. | 0.53 | 6/9 |
| It is difficult to drive because of my lymphedema. | 0.29 | 3/9 |
| My lymphedema impacts my sleep. | 0.65 | 7/9 |
| I don't feel well-rested because of the lymphedema. | 0.41 | 6/9 |
| I avoid sexual activities due to the lymphedema. | 0.41 | 5/9 |
| I cannot kiss as well because of the lymphedema. | 0.41 | 4/9 |
| When I wake up in the morning it is hard to move because of the lymphedema. | 0.29 | 5/9 |
| It is hard to breathe when I am swollen. | 0.53 | 5/9 |
| I lack self-confidence because of my lymphedema. | 0.41 | 4/9 |
| It is difficult to see clearly when I am swollen. | 0.53 | 5/9 |
| I clear my throat a lot because of the swelling. | 0.29 | 6/9 |
| It is difficult to open my mouth when I am swollen. | 0.53 | 6/9 |
| My hearing is worse when I am swollen. | 0.53 | 5/9 |
| It is physically difficult for me to manage my lymphedema. | 0.41 | 4/9 |
| I no longer like the way I look because of the lymphedema. | 0.76 | 6/9 |
| I find it difficult to chew certain foods because of the lymphedema. | 0.65 | 7/9 |
| I worry about the financial impact of my lymphedema. | 0.18 | 4/9 |
| I am not concerned with my lymphedema. | 0.41 | 4/9 |
| Sometimes I stop talking because my speech changes with the swelling. | 0.53 | 5/9 |
| I go to bed early because I am tired of dealing with my lymphedema. | -0.18 | 2/9 |
| I avoid routine chores outside the house when I am swollen. | 0.18 | 3/9 |
| I look older because of my lymphedema. | 0.29 | 6/9 |
| My lymphedema forces me to disclose to others that I had cancer. | 0.41 | 5/9 |
| My life is not normal because of the lymphedema. | 0.76 | 7/9 |
| My lymphedema makes me worry that my cancer will come back. | 0.65 | 7/9 |
| When I am more swollen, I worry that something else is wrong with my body. | 0.53 | 6/9 |
| I feel isolated from my loved ones because of my lymphedema. | 0.29 | 4/9 |
| I avoid seeing friends and family because of the change in my appearance. | 0.53 | 4/9 |
| I feel like a burden to others due to my lymphedema. | 0.18 | 3/9 |
| I feel like I need to hide my lymphedema from others. | 0.78 | 7/9 |
| I don't like having to talk about my lymphedema to others. | 0.29 | 4/9 |
| I wish that people around me understood my lymphedema better. | 0.29 | 4/9 |
| I am not comfortable with dating or intimacy because of my lymphedema. | 0.41 | 3/9 |
| I feel uncomfortable when people mention my lymphedema. | 0.29 | 2/9 |
| I worry about the impact my lymphedema has on my job or daily activities. | 0.53 | 4/9 |
| There are social activities that I don't participate in due to my lymphedema. | 0.53 | 4/9 |
| My ability to work or do my daily activities has been impacted by my lymphedema. | 0.65 | 5/9 |
| I can't do some activities as long as I would like because of my lymphedema. | 0.29 | 3/9 |
| Because of my lymphedema I choose not to engage in social activities. | 0.53 | 5/9 |
| I cannot enjoy meals with others because of my lymphedema. | 0.53 | 5/9 |
| I avoid looking at myself because of my lymphedema. | 0.53 | 4/9 |
| I never know how my lymphedema will be from day to day. | 0.41 | 5/9 |
| I worry about the lymphedema getting worse in the future. | 0.76 | 7/9 |
| My lymphedema makes me anxious. | 0.76 | 6/9 |
| I am worried that lymphedema may cause other health issues in the future. | 0.65 | 7/9 |
| I worry that if I don't manage the lymphedema now, it will be there forever. | 0.76 | 9/9 |
| I get angry when I am swollen. | 0.06 | 3/9 |
| I hate my lymphedema. | 0.41 | 6/9 |
| I am frustrated by my lymphedema | 0.65 | 7/9 |
| I feel sad when I think about my lymphedema. | 0.41 | 5/9 |
| I am unhappy because of my lymphedema. | 0.29 | 5/9 |
| I am constantly thinking about my lymphedema. | 0.29 | 3/9 |
| I worry about how the lymphedema impacts things like eating, talking, and breathing. | 0.65 | 6/9 |
| Being bothered by my lymphedema makes me feel vain. | -0.18 | 2/9 |
| I feel like I have no control over my lymphedema. | 0.76 | 7/9 |
| I have accepted that this is the new me. | 0.65 | 7/9 |
| I am hopeful that my lymphedema will improve over time. | 0.65 | 7/9 |
| I am always aware of the lymphedema. | 0.53 | 5/9 |
| I am uncomfortable throughout the day due to the lymphedema. | 0.18 | 3/9 |
| I'm embarrassed by my lymphedema. | 0.65 | 5/9 |
| My lymphedema makes me feel like I'm being strangled. | 0.53 | 5/9 |
| Tightness in my skin makes the lymphedema uncomfortable. | 0.29 | 5/9 |
| My swallowing feels restricted when I am swollen. | 0.78 | 8/9 |
| The swelling feels very stiff and solid. | 0.65 | 8/9 |
| I am unable to turn my head comfortably because of the lymphedema. | 0.65 | 7/9 |