Background:

Head and neck lymphoedema (HNL) is a common consequence of head and neck cancer (HNC) and its treatments, with prevalence rates up to 90% following HNC treatment. (Deng et al 2012; Ridner et al, 2016) HNL occurs when the lymphatic system is injured, leading to accumulation of lymph fluid in the interstitial spaces. HNL may lead to functional impairments such as dysphagia and dysphonia as a result of physical changes due to compressive symptoms, inflammation, reduced mobility, and fibrosis. (Deng et al, 2013; Murphy & Ridner, 2010). As a result of these functional impairments, individuals with HNL may have reduced satisfaction in their quality of life (QoL). (Nixon 2018, Deng 2016)

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.” (WHO, 1948). Measurements of HRQoL, therefore need to consider not only physical functioning, but also emotional and social well-being. A recent systematic review of patient reported outcomes measures (PROMs) used in lymphoedema identified 17 lymphoedema-specific QoL measures, the majority of which were developed for limb lymphoedema. (Beelen 2020) Only three instruments were developed for all types of lymphoedema and only one was developed for those with HNL. The authors of this systematic review found that 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.

The Patient Reported Outcomes Measurement Information System (PROMIS) describes a 5-step process for development of PROMs. (DeWalt 2007) Step one includes the completion of a comprehensive literature review of existing measures. Following the systematic review of the literature, qualitative interviews and/or focus groups should be completed to identify concepts important to patients with a specific condition. Transcripts from these interviews should then undergo thematic analysis to identify themes common to individuals with the condition in order to drive development of the initial item bank. Once this item bank is developed, additional cognitive interviews should be performed to validate the item bank prior to psychometric field testing.

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 a PROM used to measure QoL in patients with HNL include items specific to those issues. The 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. (Deng 2012) This scale included 64 symptoms which patients would indicate if they did or did not have. For those symptoms that were present, patients were asked to indicate the level of “intensity” as well as “distress” using two separate 5- point scales. During validation testing, the length of the test was raised as a concern by ~60% of those studied. Further, they found 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). (Deng 2022) Of the 33 items retained, the vast majority (28) refer to physical and functional symptoms with few items related to emotional health and well-being.

While the HN-LEF Symptom Inventory is a valuable tool for understanding symptom burden in those with HNL, there remains a need for a QoL instrument that will capture not only the physical and functional ramifications of HNL but also the social and emotional consequences. As a result, the purpose of this study was to develop a HNL specific QoL instrument to include physical, functional, and social/emotional domains. We have previously published the results of our systematic review and qualitative interviews conducted in early stages of scale development. (Starmer 2023, Starmer in press) This paper provides completion of the development process from item generation through cognitive interviewing in creation of an HNL specific QoL tool.

Methods:

Phase 1: Item generation

Item generation for a patient reported quality of life instrument includes consideration of extant scales and interrogation of the patient perspective. A systematic reviewStarmer 2023 was performed to identify extant tools which were examined to identify possible constructs and relevant items for consideration. Qualitative interviews were previously conducted with 22 individuals in the UK and US with lymphoedema.Starmer in press  Based on these interviews, candidate items were generated to reflect key themes from the patient interviews. Items were generated by the first author and reviewed by the remainder of 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 in order 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 otherwise inadequate for the purpose of the instrument being developed.

Phase 2: Initial validation and item reduction

Patients and experts 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 head and neck lymphedema, age>18, English proficiency, and ability to access an online survey instrument. Experts included clinicians across the globe with experience working with patients with HNC and HNL. Specialties invited to participate included surgical oncologists, radiation oncologists, medical oncologists, nurses, physical therapists, occupational therapists, and speech-language therapists.

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

The Content Validity Ratio (CVR) described by Lawshecite was used to initially assess which items were judged by the patient and expert volunteers to be most important. The formula utilized was:

Number of individuals rating an item 3-4-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 (2014). Given that the patients’ perspective should be weighted more heavily in this process, 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. Response options for the QoL survey were considered, and a 5-point Likert scale was selected.

Phase 3: Cognitive interviews

Following the initial item reduction process, three-step test cognitive interviews were conducted to further validate the items, survey format, and instructions. Participants previously diagnosed with head and neck lymphedema who did not participate in the initial qualitative interviews were invited to participate. Potential participants were referred by HNC practitioners (surgical, radiation, and medical oncologists as well as speech-language pathologists) and were invited to participate in person, by flyer, or through email correspondence.

Three-step test cognitive interviews were conducted either in person or via Zoom video platform by the first author. Three-step test cognitive interviews combine the “think aloud” method with probing methods to determine if the patients understand the questions as the researcher intendedDeVet 2018. During these interviews, participants were first asked to complete the survey, stating out loud 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. Detailed notes were taken during the interviews and each interview was recorded for future reference. The scale was further adapted based on these interviews. This study was approved by the Stanford Institutional Review Board.

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. 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, three bins were established: changes in life participation, discomfort, and functional impairments. Table 1 provides the initial item count for each bin as well as an example question. The winnowing process led to exclusion of 57 items due to redundancy and inclusion of 73 items for further testing.

Phase 2:

A convenience sample of 18 participants completed the Qualtrics survey regarding the candidate questions, 9 experts and 9 patients. The majority of participants were between 31-50 years of age, female, white, and residing in the United States. Demographic information regarding participants is available in Table 2.

Of the 73 candidate questions, 41 met the pre-set criteria using the content validity ratio. Of the remaining items that did not meet criteria, 10 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 candidate questions had >50% of participants rating the item as “very easy” to understand. 13 of the candidate questions (25%) had >1 participant indicating it was either “somewhat difficult” or “very difficult” to understand. Of the 52 candidate questions, 12 (23%) had more than one participant indicate it was “intrusive or upsetting”. Of the 52 items, 18 reflected physical domains, 10 reflected functional domains, and 23 reflected emotional domains.

Phase 3:

Three step 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. The majority of participants were female (80%) and white (60%). All participants had a history of treatment for head and neck lymphedema within the prior 12-month period.

*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 cognitive processing to remember. 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 indicated a preference for a 5-point scale versus a scale with fewer or more options. Participants indicated a preference for a landscape rather than portrait layout. Participants indicated that while the survey was slightly long, they did not feel it would be appropriate to cut additional items, 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 item redundancy (50%), difficulty differentiating from other possible causes (e.g. xerostomia) (20%), wording judged as too negative (10%), preference to avoid items that would require inverse scoring (10%), item judged as too vague (5%), and item considered irrelevant (5%). Of the remaining items, slight adjustments in wording were conducted to increase clarity. Items indicating “worry” about a concept were changed to “concern” based on feedback. A total of 34 items were retained for the final version of the survey. Of the items retained, one item was a global item, 9 reflected physical issues, 8 reflected functional issues, and 16 reflected emotional issues.

Discussion:

HRQoL is increasingly accepted as a primary or secondary endpoint in many treatment trials.Weiss 2023, McDowell 2023, Rischin 2022  PROMs provide clinicians and researchers the opportunity to understand the patient perspective of the impact of a disease and treatments employed to treat it. While a number of tools have been designed for limb lymphoedema, there has been limited focus on measuring QoL in patients with HNL, despite the unique consequences experienced in the head and neck region.Starmer 2023 The HN-LEF Symptom Inventorycite 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.

It is well established that individuals diagnosed with head and neck cancer are at risk for both short and long-term decrements to QoL.Roick 2020, Mehanna 2006  Further, there appears to be a relationship between poorer QoL and higher rates of depression and anxiety.Sunderland 2023, Patterson 2022, Lin 2012 It has been shown that patients with more severe HNL have higher degrees of functional impairment and poorer QoL.Deng 2013 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 social-emotional impacts of treatment. PROMs are considered to be the gold standard for assessing subjective patient perspectives.Higgenson 2001 To date, there is no tool developed specifically to encompass all aspects of QoL related to HNL.

Applying recommendations for PROM development previously published by the PROMIS and COSMIN groups, we developed an HNL specific quality of life instrument. This instrument is the first of its kind to wholistically assess the impact of HNL on physical, functional, social, and socioemotional outcomes in patients diagnosed with HNL. Inclusion of patient and expert opinions at multiple stages of development contribute to strong content validity.

As with most studies, there are limitations that we must acknowledge. While purposive sampling was utilized in recruiting patient and expert input at all points of development, those participating were largely white, female, and from the United States. This may limit the degree to which these results can be generalized. While data saturation was achieved in each stage of qualitative work, it is possible there are missing perspectives based on our use of convenience sampling. 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, future validation work will be conducted using a large, diverse population.

Future work is needed to further assess the validity, reliability, and utility of this scale in a large 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 to date that this instrument will provide valuable insight into the holistic impact of HNL on individual patients.

Conclusions:

The aim of this study was to develop a PROM specific to individuals with HNL to assess the impact of the condition 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 outlined by the PROMIS and COSMIN recommendations, we have developed a tool that shows promise for both clinical and research applications. Future studies of the instrument’s measurement properties will be needed in a large, diverse cross-sectional sample.

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Figure Legend

Table 1: 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 bothers me how visible my lymphoedema is”  “I often wish I could be normal again”  “I feel isolated from my loved ones because of lymphoedema”  “I worry about the impact lymphoedema has on my job”  “It is hard to stay positive because of the lymphoedema” |
| **Physical/functional**  Changes in life participation  Discomfort  Functional impairments | 16  14  21 | “I cannot work due to my lymphoedema”  “My lymphoedema makes me feel like I’m being strangled”  “It is difficult to drive when I am swollen” |

Table 2: Qualtrics participant characteristics

|  |  |
| --- | --- |
| Medical provider  Patient | 9 (50%)  9 (50%) |
| **Age**  18-30 years  31-50 years  51-70 years  >70 years | 0  11 (61%)  6 (33%)  1 (6%) |
| **Sex**  Male  Female | 6 (33%)  12 (66%) |
| **Ethnicity/race**  White  Black  Asian  Hispanic | 13 (72%)  1 (6%)  3 (17%)  1 (6%) |
| **Country**  USA  UK  Australia | 15 (83%)  2 (11%)  1 (6%) |