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UPPER LIMB LYMPHEDEMA 27 (ULL27): DUTCH TRANSLATION AND VALIDATION OF AN ILLNESS-SPECIFIC HEALTH-RELATED QUALITY OF LIFE QUESTIONNAIRE FOR PATIENTS WITH UPPER LIMB LYMPHEDEMA

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ABSTRACT

The health-related quality of life questionnaire for lymphedema of the upper limb (ULL27) was translated into Dutch according to international guidelines and validated. Eighty-four patients with lymphedema that occurred after axillary surgery for breast cancer and subsequent radiotherapy, chemotherapy, or hormonal therapy, completed the translated version of the ULL27 and the RAND36. Severity of upper limb edema was measured by specialized physiotherapists. The internal consistency of the domains of the questionnaire was good as were the convergent validity and discriminant ability. Upper limb volume and the domains of the ULL27 were not correlated. The Dutch translation of the ULL27 questionnaire has good internal consistency and validity but further research is needed to determine its responsiveness.

Keywords: validation, lymphedema, health-related quality of life, ULL27, RAND36, breast cancer

Breast cancer is diagnosed in 9,000 women a year in the Netherlands. The prevalence of upper limb lymphedema is 25% after modified radical mastectomy and 40% after adjuvant radiotherapy in the axillary region (1). Although upper limb lymphedema is sometimes treated surgically, it is usually treated conservatively, with manual lymphatic drainage (a mild form of massage), ambulant compression, exercise, and advice (2). The aim of such treatment is to reduce the edema and to improve the function of the upper limb (especially kinesiophobia, pain and limited shoulder function and usage). Functional limitations of the affected upper limb have a much greater impact on well-being than the increase in the size of the upper limb (3-5). Moreover, impairments such as swelling, numbness, and pain are not correlated with upper limb function (6). Both Bosompra et al (6) and Johansson et al (7) stressed the importance of assessing patients not only at the level of impairment but also for practical and psychosocial problems experienced by patients in daily life. Indeed, most investigators stress the importance of using health-related quality of life (HRQOL) questionnaires (8-14) to determine patient well-being. Several HRQOL questionnaires are being used to assess patients with cancer, and breast cancer in particular, such as the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC

QLQ-C30) (15), the Functional Assessment of Cancer Therapy-Breast with 4 additional questions about the upper limb (FACT-B+4) (8), the Short Form 36 (SF36) (16) and the Nottingham Health Profile (17). However, none of these, mostly generic, questionnaires specifically focus on lymphedema and its consequences on HRQOL. The only lymphedema-specific HRQOL questionnaire currently available is the French language Upper Limb Lymphedema 27 (ULL27) (9). Cross-cultural validation of an existing specific HRQOL scale has the advantage of avoiding the initial stage of development of a new questionnaire. The aim of this study was to translate the ULL27 into Dutch and to determine its internal consistency and validity for assessing upper limb lymphedema in the Dutch population of patients with lymphedema.

PATIENTS AND METHODS

ULL27

The ULL27 is a self-report questionnaire encompassing 27 questions with answers given on a 5-point Likert scale, ranging from "never" to "always" and is considered to measure the effects of lymphedema on HRQOL. The questionnaire measures three domains: physical (15 items), psychological (7 items) and social (5 items), with scores ranging from 0 to 100 (100 being the best score possible). Internal consistency (Cronbach's alpha) was reported to be > 0.82. Positive correlations between the ULL27 subscales and homologous SF-36 domains were significant. Sensitivity analysis in patients with active lymphedema demonstrated a significant effect size (9).

Translation

The questionnaire was translated according to established international guidelines (18-24). Two translators independently translated the questionnaire from French into Dutch, and a first version was established at a consensus meeting. The translation took into account the cultural and lifestyle context, making use of appropriate idioms [i.e., cross-cultural adaptation (20)]. Subsequently, a third translator translated the Dutch questionnaire back into French (19). This process of forward and back translation was repeated until a satisfactory translation was achieved [model of Brislin (19)].

As stipulated by Guillemin (20), the final translation was tested on patients, to clarify any ambiguities, in one-to-one interviews. Five patients commented on the difficulty, clarity and language of the questionnaire using a Dutch translation of the EORTC debriefing questionnaire for this purpose (15). Based on this information, a new version of the Dutch questionnaire was generated, which was translated into French by a fourth translator.

The final version of the questionnaire and its back translation, were then sent to the originator of the ULL27, Professor Launois (21), for comments. These were incorporated in the definitive version of the Dutch translation of the ULL27.

RAND36

The RAND 36-item Health Survey (RAND36) is a generic HRQOL questionnaire. It contains 8 domains: Physical Functioning (PF), Social Functioning (SF), Role Physical (RP), Role Emotional (RE), Mental Health (MH), Vitality (VT), Pain (P) and General Health (GH). Internal consistency was > 0.71 and construct validity, compared to similar scales, was significant (25).

Validation

The questionnaire was validated in twenty-three physiotherapy practices by physiotherapists specialized in edema therapy. Patients who matched the inclusion criteria were asked to participate in this study. These criteria were (1) women only,

(2) unilateral edema of the upper limb, (3) no distinction between primary and secondary lymphedema, and (4) women should have fluency in Dutch, sufficient to understand the questionnaire. Patients with: (1) progressive cancer or (2) who had lymphangitis or infections of the upper limb in the past 2 months were excluded from this study.

All participants were asked to complete a general questionnaire concerning demographic data, the ULL27 and the RAND36. The physiotherapists were asked to determine the severity of edema, following a specific protocol in which the size difference of both upper limbs was measured in a standardized way. According to the protocol of Kühnke (26) with the volume of the hand added to the total of the upper limb. Completed questionnaires were returned and data were anonymized. Informed consent was not needed, since all measurements were part of good clinical practice.

The discriminant validity was determined in an age-matched group of 61 women without symptoms of the neck, shoulder or upper limb and had been recruited by the practice, family, and friends.

Statistical Analysis

The data were checked for normal distribution. Thereafter the internal consistency of the three domains was determined with Cronbach's Alpha, with a value of 0.7 or higher being considered adequate. The item internal consistency was also determined, with an item-domain correlation of 0.4 or higher being considered sufficient. The item-domain discriminant validity was also determined. The concurrent validity was established by comparing the scores of the three ULL27 domains with the scores of the eight domains of the RAND36, and the discriminant ability was tested by comparing the total score and the scores of the three domains of the patients with those of the age-matched group of women without upper limb lymphedema. A Spearman correlation coefficient of 0.40 or higher was considered to indicate a significant correlation (19). Finally, the correlation between the mean scores of the ULL27 and the severity of edema was determined.

This research was conducted in accordance with the Declaration of Helsinki.

RESULTS

The Translation

Two translation rounds were needed to obtain the definitive version of the questionnaire that was tested on patients in the pilot study. During this study, one patient commented that questions on psychological topics might raise expectations that physiotherapists would also treat these aspects. This can be avoided by giving patients adequate information about treatment goals before therapy starts. Another patient suggested that the word "restricted" for questions 24 to 27 should be replaced by "hindered." She considered that "restricted" meant that a person could not perform an action whereas "hindered" implied that a person could still perform the action, albeit to a diminished extent. The questionnaire was then discussed with Professor Launois, in English. The use of the word "hindered" or "restricted" in questions 24 to 27 was replaced by "are you feeling any difficulty," and the questionnaire was approved.

The Validation Research

Twenty-nine physiotherapists specialized in edema were recruited between February and August 2006. They recruited 84 patients, the characteristics of whom are given in *Table 1.*

Most patients (mean age 59) were housewives (42.4 %), and 94% had undergone axillary surgery with or without surgical dissection of the breast. Three patients had not had surgery, and one patient had undergone extirpation of a melanoma on the

TABLE 1
Characteristics of the Research Population (N=84)

Characteristic	Mean	Sd	Range
Age	59	11.79	34-80
Size difference in ml	360.4	338.3	-170-1628
Start of edema after the operation in months	26	56.51	0-360
Duration of edema in months	35.51	45.14	0.5-276
Number of physiotherapy sessions	115	184.74	0-1100

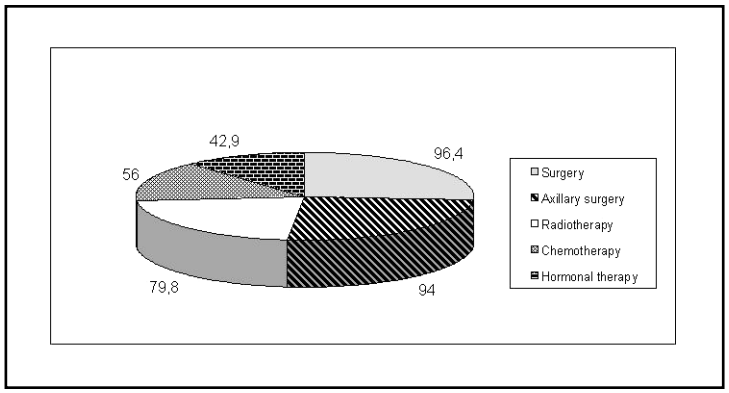

Fig. 1. Various treatments for breast cancer (%).

shoulder. Surgery involved breast amputation (n=49) and breast-saving techniques (n=31). Patients received various postoperative treatments (see *Fig. 1*); 47 patients wore therapeutic hosiery for treatment of their edema.

Patients were classified by the severity of edema (*Table 2*), and then the mean ULL27 total score and subdomain scores were calculated for each edema severity (*Fig. 2*).

Kolmogorov-Smirnov analysis showed the data not to be distributed normally. An ANOVA with Bonferroni correction showed that there was no significant difference between the total and subdomain scores of the ULL27 in each of the four grades of edema severity.

The internal consistency of the Dutch ULL27 was good (all Cronbach's alpha values >0.7; *Table 3*) and the item-domain internal consistency was considered sufficient except in two cases (> 0.4). Question 20 ("Did you feel confident about the future during the last 4 weeks?") was scored 0.29 and question 22 ("Did you feel well and at ease during the last 4 weeks?") was scored 0.25. The item-domain discriminant validity was determined by examining the correlations of the items with all three domains. In two cases (also questions 20 and 22) the items showed a better correlation with a domain other than its corresponding domain.

The concurrent validity was examined by associating the outcomes of the ULL27 with

TABLE 2
Classification of the Severity of Edema

Grade	Description	Volume difference	Number of patients
1	No measurable edema	150-299 ml	45
2	Small-volume edema	300-499 ml	17
3	Medium-volume edema	500-800 ml	15
4	Large-volume edema	> 800 ml	7

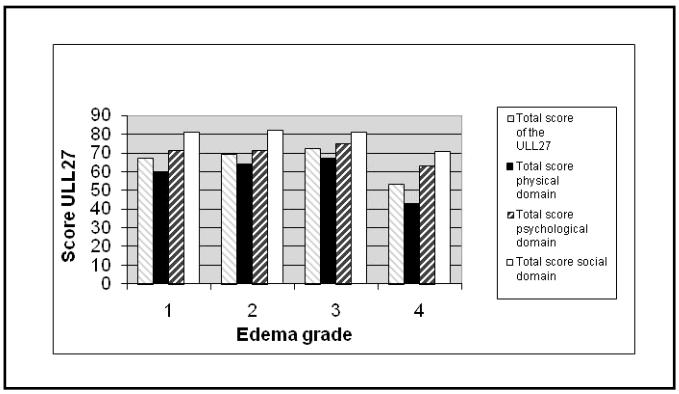

Fig. 2. Mean ULL27 score by severity of lymphedema.

the RAND36. The domains of the Dutch ULL27 were significantly correlated with most of the corresponding domains of the RAND36 (*Table 4*).

Lastly, the total score and subdomain scores of an age- matched group of women without symptoms of the neck, shoulder or upper limb (N=61, mean age (SD) 54 (9.4)) were compared with those of 61 patients, using an unpaired T-test. The total score and subdomain scores of the two groups were significantly different ($p<0.001$), with the control group scoring higher on the ULL27.

TABLE 3
The Internal Consistency of the ULL27

Domain	Dutch version	French version
Physical domain	0.92	0.93
Psychological domain	0.78	0.86
Social domain	0.79	0.82

DISCUSSION

The purpose of this study was to translate the French ULL27 questionnaire into Dutch and to validate it in a Dutch population of patients with lymphedema in the upper limb. The availability of such a questionnaire makes it possible to compare the data collected in other international studies.

TABLE 4
Correlations Between RAND36 and ULL27

RAND36	Physical domain ULL27	Psychological domain ULL27	Social domain ULL27
Physical Functioning (PF)	0.38	0.21	**0.64**
Role Physical (RP)	0.48	0.35	0.32
Bodily Pain (BP)	**0.69**	0.38	0.40
General Health (GH)	**0.60**	**0.54**	**0.56**
Vitality (VT)	0.47	**0.55**	0.44
Social Functioning (SF)	**0.55**	**0.51**	**0.45**
Role Emotional (RE)	0.39	0.42	0.36
Mental Health (MH)	0.52	**0.66**	0.53

*Highest correlation in bold

The questionnaire was validated in 84 patients but the distribution of edema severity in this population (grade 1 53.6%, grade 2 20.2%, grade 3 17.9% and grade 4 8.3%) was not similar to that of the French population (n=304) used to validate the original questionnaire (grade 1 13%, grade 2 20%, grade 3 27%, grade 4 40%), which means that it was not possible to compare the data directly.

Edema severity and ULL27 scores were not correlated, as has been found in other studies showing a lack of correlation between the difference in size between the affected and non-affected upper limbs and HRQOL (3-7). The internal consistency of the three domains was good and similar to that of the French study. The item-domain internal consistency and item-domain validity differed in two cases: questions 20 and 22 showed a better correlation with the social domain than with their own psychological domain. These two questions have a different direction in their presentation than the other 25 questions and serve as control questions. It may be appropriate to ask patients to pay special attention to these questions. Otherwise, these items may need to be deleted in a future version.

The physical domain of the ULL27 was poorly correlated with the Physical Functioning domain of the RAND36 (r =0.4). This can be explained by the fact that the questions of the RAND36 are focused more on the lower limb and those of the ULL27 more on the upper limb. The strongest correlations between the scores of the psychological and social domains of the ULL27 were found for the General Health (GH), Vitality (VT), Social Functioning (SF), Bodily Pain (BP) and Mental Health (MH) domains of the RAND36 and ranged from rs 0.55-0.69, supporting concurrent validity. The correlations were less strong for the other domains, as was also found with the original French questionnaire (manuscript in preparation).

Lastly, the Dutch ULL27 showed strong discriminant validity between groups of women with and without symptoms of lymphedema of the upper limb.

However, a distinction in severity of the edema could not be made using the ULL27. A potential limitation of this study is that the severity of edema was measured according to a written protocol, and the measurements had not been practiced in advance. However, since specialized edema physiotherapists

routinely measure the upper limb volume, it is expected that the measurements were accurate, with the only difference from normal practice being the measurement of the hand volume as part of the total volume. Moreover, it was the difference in hand/arm volume between the two upper limbs that was important.

The finding that HRQOL is not correlated with the difference in volume between the two upper limbs is consistent with earlier findings and supports the use of the ULL27 to provide additional information about lymphedema of the upper limb, because it offers better understanding of the patient in total. A minor limitation of the questionnaire is that it does not include information about upper limb complaints based on pathology other than edema. Therefore some open questions in the French, as well as in the Dutch version, are added to the 27 questions.

The design of this study was aimed at the validity of the ULL27. Its sensitivity to change in clinical use, however, is not yet determined. Further research is needed to establish the responsiveness of the Dutch ULL27.

CONFLICT OF INTEREST

The ULL27 was developed by Professor Robert Launois with an educational grant from REES France. Any person who wishes to use the questionnaire should contact Professor Robert Launois (reesfrance@wanadoo.fr). The Dutch translation and validation were prepared without funding.

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