PROGRESS IN
LYMPHOLOGY
XVIII
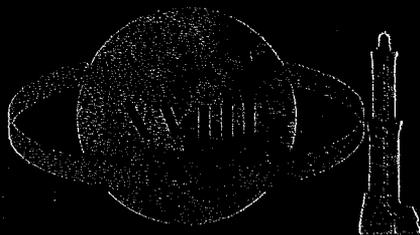
Proceedings of the
18th International Congress
of Lymphology
Genoa, Italy
September 3-7, 2001

Editors:
C.Campisi, M.D., M.H.Witte, M.D. and C.L.Witte, M.D.

A SPECIFIC QUALITY OF LIFE SCALE IN UPPER LIMB LYMPHŒDEMA : THE ULL-27 QUESTIONNAIRE

R. Launois[1-2] PhD ; A.C. Mègnigbêto[1-2] PhD ; K. Pocquet[3] MD ; F. Alliot[4] SRN

[1] Université PARIS XIII – Département de Santé Publique– Bobigny, France
[2] REES France, Paris, France
[3] Sanofi-Synthélabo, Le Plessis-Robinson, France
[4] Clinique Hartmann, Neuilly-sur-Seine, France

INTRODUCTION

There are 34,000 new cases of breast cancer each year in France. Recent studies have confirmed that upper limb lymphœdema secondary to radio-chemo-surgical treatment develops in 42% of cases. Lymphœdema or "big arm" is an increase in volume of the upper limb due to accumulation of water, protein and fats following damage to the lymphatic system caused by axillary lymph node clearance. Upper arm lymphœdema has major functional, aesthetic and psychological consequences. F. Alliot clearly identified the problems with body image which it produces, together with the physical and psychological consequences of "big arm" on the patients' everyday lives. It is important to assess the consequences of lymphœdema on womens' quality of life in the context of this chronic disorder with long lasting consequences. The generic quality of life scales which are currently available cannot be used for this purpose as they are relatively insensitive to clinical changes in lymphœdema. Sitzia J. and Sobrido L. were unable to identify any correlation between a reduction in lymphœdema volume and the N.H.P. (Nottingham Health Profile) when they used the N.H.P. to assess quality of life during treatment for upper limb lymphœdema.It therefore appears urgent to develop a specific quality of life indicator for upper limb lymphœdema which takes into account the patient's point of view and provides the attending physician with a fine measurement of the functional and psychosocial consequences of the disorder.

METHODS

Development Stages

To develop such an instrument we went through 3 stages.

First : A qualitative survey was conducted to identify the patient's complaints and to create a data bank of items. This work was performed by a psychologist who undertook semi-structured interviews with 24 patients. The interviews lasted one hour and 30 minutes and were recorded on audio cassette. After the interviews had been re-transcribed, the psychologist extracted more than 1,166 verbatim statements. This leads to the development of a preliminary version of the questionnaire containing 70 items.

Second : This preliminary version was administered to 154 patients in a subsequent quantitative survey to select the most relevant items and to specify the main domains of impairment. Factorial analysis was used to identify 28 items which were divided into four dimensions. We identified a "Physical" dimension (6 items), a "Psychological"

dimension (7 items), a "Symptoms" dimension (8 items), and finally a "Social" dimension (6 items). The interim analysis performed after including 2/3 of the patients showed complete fusion between the "symptoms" and "physical" dimensions. In order to retain the factorial stability of the scale, item 8 (difficulty dressing) has been removed. The upper limb lymphœdema questionnaire therefore has 3 dimensions: a "physical" dimension with 15 items, a psychological dimension with 7 items and a "social" dimension with 5 items. This process produces the final version of the questionnaire which contained 27 items.

A third study was launched over 304 patients to check the validity of this scale. The scale must have specific metrological properties which have to be confirmed in a validation study.

Validation of the Questionnaire

The upper limb lymphœdema quality of life scale has been evaluated in a multi-centre study.

Design of the study
- Non randomized multicentric open study. The Lymphedema Scientific Commitee : P. Carpentier MD ; V. Cluzan MD ; H. Boccalon MD ; M. Elias MD ; M. Espié MD ; C. Jamin MD ; C. Jasmin MD ; A. Pecking MD ; P. Priollet MD ; L. Vaillant MD
- Inclusion criteria: patients suffering from ULL-27 secondary to breast cancer, Age > 18 years
- Non-inclusion criteria: advanced cancer, ongoing radiotherapy or chemotherapy, signs of plexitis, past history of lymphangitis < 2 months
- Number of evaluable patients : 301

Grades of Patient Severity
Grades of oedema were defined by differences in volume between the affected limb and the healthy limb
- Oedema not measurable (>150 & <300 ml)
- Clinical low volume oedema (>300 & <500 ml)
- Clinical medium volume oedema (>500 & <800 ml)
- Clinical large volume oedema (> 800 ml)

Benchmark criteria
Six scales for the study were measured on the inclusion day on D0 and at the end of the observation period on D28.
- Oedema volume measurement : addition of cone truncks
- Global Symptom Index : GSI *(heaviness, tension, hardness - frequency and severity)*. Each question therefore contains 5 response options graded from 1 to 5. A composite index is calculated for each patient and is represented by the product of the severity scores and the frequency scores for each clinical characteristic of the arm. The composite index therefore ranges from 1 to 25. The global symptom index is the sum of the 3 composite indices and therefore ranges from 3 to 75.
- Patient's Arm Comfort Scale : ACS. A visual analogue scale was used to assess the global discomfort from the arm experienced by the patient; this is represented along a continuous 100 millimetre horizontal line along which the zero value (the left end)

represents no discomfort and the 100 value (the right end) represents extreme discomfort.

- Global Clinical Impression : GCI. A transitional scale for global clinical impression was completed by the attending physician on D28 and has 3 response options (improved, stable, worsened) which the physician considers to represent the change in the patient's state of health between D0 and D28.
- Generic quality of life scale : SF36 (8 dimensions : PF-RP-BP-GH-VT-SF-RE-MH)
- Specific quality of life scale : ULL-27. The specific ULL-27 quality of life scale contains 27 items divided into three dimensions: physical, psychological, and social. The items are equally weighted

Table 1
The quality of life scale to be validated

Physical functioning :	Psychological dimension :
1. Difficulties grasping high objects	16. Feeling sad
2. Difficulties maintaining certain positions	17. Feeling discouraged
3. Arm fells heavy	18. Feeling a lack of self-confidence
4. Arm feels swollen	19. Feeling distressed
5. Difficulties dressing	20. Feeling well in ones self
6. Difficulties getting to sleep	21. Feeling a wish to be angry
7. Difficulties sleeping	22. Having confidence in the future
8. Difficulties grasping objects	*Social dimension :*
9. Difficulties holding objects	23. Difficulty taking advantage of good weather, in life outside the house
10. Difficulties walking / heavy arm	24. Difficulty with personal projects, holidays or hobbies
11. Difficulties washing	25. Difficulties in emotional life with spouse or partner
12. Difficulties taking public tranport	26. Difficulty in social life
13. Tingling, burning feelings	27. Fearful of looking in a mirror
14. Feelings of swollen, hard, tense skin	
15. Difficulties in working relationships and tasks	

Statistical Validation Tests
- Intraclass Correlation coefficient on stable patients between D0 and D28 - Cronbach Alpha coefficient at D0
- Pearson's items-scale correlation coefficients at D0 - Stability of the factorial structure in various populations
- Spearman correlations coefficients between ULL-27 scale and other scales on D0 and by grade
- Effect size calculation

RESULTS

Clinical and Demographic Patient's Characteristics

304 patients were included. Three patients were lost to follow up between D0 and D28. The statistical analysis was therefore based on 301 patients, average age 61.61 ± 1.16 years old. Average height was 1.61 ± 0.20 m, average weight was 67.98 ± 1.36 kg and average body mass index was 26.25 ± 0.54.

Of these patients, 96% were right handed and 4% were left handed. The disorder was ipsilateral in 48% of the right handed people and contralateral in 52%. The ULL-27 affected their right arm in 47% of cases in the overall population. Almost all of the women had undergone systemic axillary lymph node clearance combined with surgical excision of the cancer. 92%, 46% and 24% of patients had been treated with radiotherapy, chemotherapy and hormone therapy respectively. 47% of women had a past history of lymphangitis.

The sample contained patients of all educational levels. 48.2% of the patients were retired. Of the other patients, social-occupational status was made up by a majority of employed workers (23%), with 10.6% housewives. Four per cent of the patients stated that they had no qualifications, 25% had the baccalauréat and 22% had a university degree.

Table 2
Treatment of breast cancer responsible for lymphœdema

Previous treatment	Number of patients	Percentage
Surgical treatment	297	98.67%
Lymph node clearance	296	98.34%
Radiotherapy	278	92.36%
Chemotherapy	137	45.51%
Ongoing hormone therapy	73	24.25%
Past history of lymphangitis	142	47.18%

Reliability

Two tests were used to confirm the precision of the ULL-27 scale: intra-class correlations between D0 and D28 were calculated for each dimension of the scale in stable patients and Cronbach alpha coefficients were calculated for all patients. The dimensions of the ULL-27 scale correlated closely in patients who were stable between D0 and D28. The correlation coefficients were 0.86, 0.80, and 0.80 for the physical psychological and social dimensions respectively. A statistical comparison of dimension scores between D0 and D28 in the stable patients revealed a statistical difference for the social dimension. The scores for the other two dimensions were not significantly different. The Cronbach alpha coefficients were 0.93, 0.86 and 0.82 respectively.

Construct Validity

- Confirmation of the dimensions

The confirmatory factorial analysis is based on 27 items. Using this, we obtained a KMO index of 0.93 and found the Bartlett test to be significant (rounded $\chi^2 = 3200$, dof = 351, p < 0.0001). This analysis re-identified the three dimensions from the interim analysis. The 3 dimensions of the scale accounted for 55% of the initial variance of the 27 items. The first dimension of the ULL-27 scale (the physical dimension) accounted for 27.70% of variance after rotation. The second dimension of the ULL-27 scale (the psychological dimension) accounted for 15.80% of variance after rotation and the third dimension of the ULL-27 scale (the social dimension) accounted for 11.20% of variance after rotation

■ The multi-traits/multi-items matrix

This correlation matrix contains all of the correlations between the items and dimensions. Two correlation coefficients are calculated for each item: R1, the correlation between each item and the dimension to which it belongs (this calculation is performed without including the score for this item in the dimension score) and R2, the correlation between each item and the dimension to which it does not belong. The correlation coefficients R1 ranged from 0.48 to 0.71 for the physical dimension, 0.42-0.77 for the psychological dimension, and 0.55-0.71 for the social dimension. These correlation coefficients define the internal consistency of the items in each dimension. Success rate is defined by the percentage of items which have a correlation coefficient of more than 0.40. The value of the correlation coefficient represents the strength of the relationship between the item and its dimension. In the case of the ULL-27 scale, all of the items correlated strongly with the dimension with which they belonged. The discriminatory validity of an item involves confirming that, the value R1 is greater than the value R2 for each item. This comparison is performed item by item, and represents a line by line comparison in the multi-trait matrix. Our success rate was 93% for the physical dimension and 100% for both the psychological and social dimensions. The strength of the link between item 12 "difficulties in working relationships and tasks" was identical for the three items.

Table 3
Internal consistency and discriminant validity of the items - intervals of correlation coefficients between items and dimensions (Spearman correlation coefficients)

	Physical	Psychological	Social
Internal coherence of items (range of correlations)	0.48 - 0.71	0.42 - 0.77	0.55 - 0.71
Success rate R1 ≥ 0.40)	100%	100%	100%
Discriminant validity of items (R1 > R2)	0.23 - 0.48	0.13 - 0.60	0.27 - 0.52
Success rate (R1 ≥ R2)	93%	100%	100%

Clinical Validity

We compared the mean dimension scores for patients with different grades of the disorder and we found a significant difference between the 4 grades for the physical (p < 0.02) and social (p < 0.02) dimensions. There was no significant difference between grades for the psychological dimension (p = 0.99).

The distribution of the scores of the physical dimension at D0 shows that the quality of life is more damaged for the severe stages of the disease. The median values are equivalent for stages 3 and 4.

Table 4
Clinical validity : Comparison of the ULL-27 dimensional scores at D0 accross severity stages

	Physical	Psychological	Social
Stage 1 (n = 30)	65.27	62.05	71.50
Stage 2 (n = 47)	57.17	61.72	63.83
Stage 3 (n = 69)	51.74	61.64	63.53
Stage 4 (n = 90)	50.54	61.62	55.99
(Anova)	0.008	0.99	0.02

In order to confirm cross-sectional convergence between the ULL-27 scale and other indicators, we calculated Spearman correlation coefficients between dimension scores on D0. All of the correlation coefficients were significant; the strongest correlations were found between the physical dimension of the ULL-27 scale and the ACS (0.531), the global symptom index (0.557), followed by the dimensions PF (0.515), BP (0.649) and VT (0.535) of the SF36, between the physical dimension of the ULL-27 scale and the VT dimension of the SF36 (0.529) and MH (0.732) of SF36, and finally between the social dimension of the ULL-27 scale and the SF dimension of the SF36 (0.579).

Responsiveness

We confirmed the ability of the scale to measure change by testing for correlations between the observed differences in the scores from the scales between D28 and D0. All of the correlations were statistically significant in the 181 patients who improved clinically. In order to confirm the sensitivity of the ULL-27 scale, we also compared dimension scores between D0 and D28 by the paired Wilcoxon test. We found that the scores were statistically different for the three dimensions (p < 0.001). We then compared the mean dimension scores of the SF36 between D0 and D28 using this method and found no significant difference for the dimensions PF, RP and GH . The difference was significant for the other 5 dimensions, BP, GH, VT, SF, and RE (p < 0.001). Mean scores for the indicators of volume, symptoms and arm comfort were significantly different in this patient group between D0 and D28. We also calculated the standardized response mean and the effect size (Cf. Table 5) and found that the standardized response mean values were 0.41, 0.42 and 0.28 respectively. The corresponding figures for the effect size were 0.58, 0.62 and 0.38.

Table 5
Standardized response mean and effect size in patients who improved clinically

Dimensions	Standardized Response Mean	Effect Size
ULL-27 Physical Dimension (PHD)	0.41	0.58
Psychological dimension (PSD)	0.42	0.62
Social dimension (SD)	0.28	0.38

Acceptability

Acceptability was measured on several occasions, and in particular during the validation, which was the second quantitative study. The majority of items in the ULL-27 on D0 were completed by 252 to 297 patients. There was a large number of missing values for three items: item 7 entitled "difficulty taking public transport" which had 39 missing values, item 12, entitled "difficulty in your working relationships and tasks" with 27 missing items and item 27 entitled "difficulties in your emotional life with your spouse or partner" with 50 missing items. The median time taken to complete the questionnaire was 11 ± 1 minutes.

CONCLUSION

The ULL-27 scale was designed and validated observing all of the classical stages used to construct measurement instruments. This scale is a precise, sensitive, accurate scale. Internal coherence of items and dimensions is excellent. Scores for the physical and psychological dimensions do not change in clinically stable patients. The social dimension is less stable; conversely, it is very sensitive to any clinical change in the disorder. The sensitivity of the ULL-27 scale is greater than that of other scales. The convergence between the dimensions of the different scales demonstrate the accuracy of measurement. Convergence was found both for scores on D0 and for the differences in scores. Clinicians now have a reliable indicator which is able to detect the effects of treatment given for lymphoedema, even in the absence of tangible clinical effects.