

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

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Abstract

OBJECTIVE : The aim of the study, was to validate a self-completed questionnaire in Upper Limb Lymphoedema. **METHODS:** A qualitative survey was conducted to identify patients' complaints. This questionnaire was administered to 154 patients. Principal component analysis was used to identify dimensions. A validation study was carried in 304 patients. Six instruments have been used in the case report form: volume differences between the healthy and the affected arms. Composite symptom scales completed by clinicians from patient interviews. ULL-27 and SF-36 scales completed by patients. Overall opinion of doctors and patients Internal validity was checked through factorial analysis. Trait validity was investigated by correlating the domains rated with ULL-27 with the SF-36 scale. Nomological validity was tested by comparing the means of the ULL-27 subscales across severity stages Sensitivity was tested only in patients with progressive disease between D0 and D28 by comparing mean sub-scores for the ULL-27 scale and by calculating the effect size. **RESULTS:** 304 patients were included in the study. Factorial analysis isolate 3 dimensions: physical (15 items), psychological (7 items) and social withdrawal (5) The Cronbach coefficients are greater than 0,80 for all dimensions. The Spearman correlations clearly distinguish the different life domains from each other. At D0 the physical and social dimensions of ULL-27 scale were significantly correlated with severity of illness but it was not the case for the psychological dimension. Correlation coefficients in-patients clinically stable between D0 and D28; were all-greater than 0.84. For all dimensions of ULL-27 The sensitivity analysis between D0 and D28 in-patients with active disease, demonstrated significant differences between mean scores for all ULL-27 dimensions. **CONCLUSION:** Volume of oedema poorly reflects the impact of the illness upon the patient. The ULL-27 scale seems to be a consistent instrument. **KEYWORDS :** Quality of life – Specific questionnaire - Upper limb lymphoedema - Validation study -

Background

There are 34,000 new cases of breast cancer each year in France. Recent studies have confirmed that upper limb lymphoedema secondary to radio-chemo-surgical treatment develops in 42% of cases. Lymphoedema 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 lymphoedema has major functional, aesthetic and psychological consequences. F. Alliot⁽¹⁾ 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 therefore to assess the consequences of lymphoedema on women's 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 lymphoedema. Sitzia J. and Sobrido L. were unable to identify any correlation between a reduction in lymphoedema 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 lymphoedema. It therefore appears important to develop a specific quality of life indicator for upper limb lymphoedema 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

1. 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 lymphoedema questionnaire therefore has 3 dimensions : a "physical" dimension with 14 items, a psychological dimension with 7 items and a "social" dimension with 6 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.

2. VALIDATION OF THE QUESTIONNAIRE

The upper limb lymphoedema quality of life scale has been evaluated in the setting of an open, non-randomised, multi-centre study.

Design of the study

- Non randomized multicentric open study
- Inclusion criteria: patients suffering from ULL 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

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 ml & < 300 ml)
- Clinical low volume oedema (> 300 ml & <500 ml)
- Clinical medium volume oedema (>500 & <800)
- Clinical large volume oedema (> 800)

Benchmark criteria

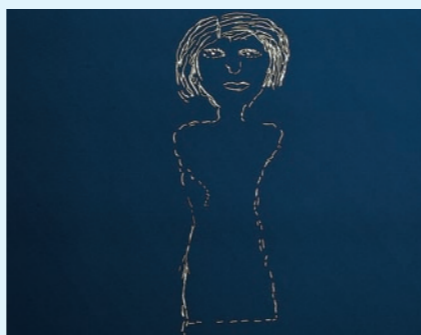
Six scales for the study were measured on the inclusion day on D0 and at the end of the observation period on D28.

- **Oedema volume measurement :** addition of cone trunks
- **Global Symptom Index : GSI** (heaviness, tension, hardness - frequency and severity). Each question 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 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 feels 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 transport	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 scale and other scales on D0 and by grade
- Effect size

Results

1. 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 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 (Cf. table 2).

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 lymphoedema

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%

2. RELIABILITY

Two tests were used to confirm the precision of the ULL 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 ULL27 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.

3. 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 $c = 3200$, $dof = 351$ $p < 0.0001$). 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 ULL27 scale (the physical dimension) accounted for 27.70% of variance after rotation. The second dimension of the ULL27 scale (the psychological dimension) accounted for 15.80% of variance after rotation and the third dimension of the ULL27 scale (the social dimension) accounted for 11.20% of variance after rotation.

The multi-trait/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 (Cf. Table 3), 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

4. CLINICAL VALIDITY

We compared the mean dimension scores for patients with different grades of the disorder (Cf. table 10) 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 ($p = 0.99$).

Table 4 :

Clinical Validity : Comparison of the ULL27 Dimensional Scores at D0 Across 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 ULL27 scale and other indicators, we calculated Spearman correlation coefficients between dimension scores on D0 (Cf. table 6). All of the correlation coefficients were significant; the strongest correlations were found between the physical dimension of the ULL 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 ULL27 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 scale and the SF dimension of the SF36 (0.579).

Table 6 : Correlations between dimensions in the quality of life scales on D0

Dimensions	PF	RP	BP	GH	VT	SF	RE	MH	Phys. Dim. ULL	Psy. Dim. ULL	Social Dim. ULL	ULL GS	ACS	GSI	Change vol. Oedema
SF36															
Physical functioning (PF)	1.000														
Restriction due to physical state (RP)	0.418	1.000													
Bodily pain (BP)	0.554	0.556	1.000												
General health (GH)	0.334	0.247	0.277	1.000											
Vitality (VT)	0.503	0.480	0.593	0.269	1.000										
Social functioning (SF)	0.295	0.495	0.513	0.201	0.588	1.000									
Role emotional (RE)	0.388	0.773	0.525	0.205	0.493	0.549	1.000								
Mental health (MH)	0.349	0.430	0.529	0.267	0.709	0.645	0.528	1.000							
ULL27															
Physical Dimension (PHD)	0.515	0.442	0.649	0.211	0.555	0.464	0.417	0.486	1.000						
Psychological dimension (PSD)	0.223	0.405	0.434	0.237	0.529	0.552	0.482	0.732	0.487	1.000					
Social dimension (SD)	0.335	0.393	0.384	0.229	0.448	0.579	0.365	0.528	0.495	0.603	1.000				
ULL Global Score (GS)	0.502	0.513	0.703	0.241	0.659	0.610	0.522	0.681	0.912	0.780	0.736	1.000			
Arm comfort scale (ACS)	0.235	0.293	0.418	0.103	0.325	0.339	0.265	0.283	0.531	0.289	0.356	0.51	1.000		
Global symptom index (GSI)	-0.252	-0.322	-0.394	-0.098*	-0.278	-0.300	-0.280	-0.302	-0.557	-0.322	-0.294	-0.54	-0.566	1.000	
Volume of oedema	-0.188	-0.059*	-0.066*	-0.017*	-0.023*	-0.038*	-0.074*	-0.052*	-0.181	-0.001*	-0.162	-0.17	-0.257	0.319	1.000

(*) : Non-significant difference

5. 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 ULL27 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 7) and

6. ACCEPTABILITY

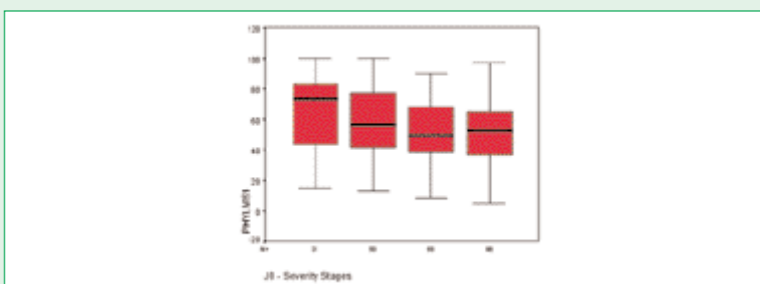
Acceptability was measured on several occasions, and in particular during the validation, which was the second quantitative study. The majority of items in the ULL27 on D0 were completed by 292 to 297 patients. There was a large number of missing values for three items: item 7 entitled "difficulty taking 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.

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 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%

Table 5 : Physical Dimension across severity stages



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 7 : Standardised response mean and effect size in patients who improved clinically

Dimensions	Standardised Response Mean	Effect Size
ULL27		
Physical Dimension (PHD)	0.41	0.58
Psychological dimension (PSD)	0.42	0.62
Social dimension (SD)	0.28	0.38

Conclusion

The ULL27 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 ULL27 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. The medical service provided for patients is nowadays a priority. It is now essential to evaluate the impact of the disorder and the benefits of treatments. The use of the concept of quality of life is highly relevant in lymphoedema. The specific quality of life scale for secondary upper limb lymphoedema following breast cancer has developed from this change in medicine.