CONSTRUCTION AND VALIDATION OF A QUALITY OF LIFE SCALE IN SECONDARY UPPER LIMB LYMPHOEDEMA FOLLOWING BREAST CANCER

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ABSTRACT

OBJECTIVE: The aim of this study was to validate a self-completed questionnaire in patients with upper limb lymphoedema (ULL).

METHODS: A qualitative survey of patients' complaints was conducted using a questionnaire in 154 patients and dimensions were identified by principal component analysis. Validation was carried out in 304 patients. Reliability was established using test-retest and the Cronbach coefficient. Within scale analysis involved factorial and multi-trait, multi-item analysis. Known group differences were assessed by comparing ULL-27 subscale means across severity stages. Convergent validity was investigated by correlating the domains measured by the ULL-27 and SF-36 scales. Sensitivity was determined by calculating the effect size in patients with progressive disease between days 0 and 28.

RESULTS: Factorial analysis isolated three dimensions. Cronbach alpha coefficients were >0.80. Correlation coefficients in patients who were clinically stable were >0.84 for all dimensions. The physical and social dimensions of ULL-27 on day 0 correlated significantly with disease severity but the psychological dimension did not. Positive Correlations between the ULL-27 subscales and homologous SF-36 dimensions were significant. Sensitivity analysis between days 0 and 28 in patients with active lymphoedema demonstrated a significant effect size.

CONCLUSION: This study demonstrates the reliability, accuracy and responsiveness of the ULL-27 scale.

KEYWORDS: quality of life, specific questionnaire, upper limb lymphoedema, validation study

ABBREVIATIONS: ULL: upper limb lymphoedema; NHP: Nottingham health profile; FLIC: functional living index cancer; WCLS: Wesley Clinic lymphoedema scale; DV: difference in volume; CDV: change in difference in volume; GCI: global clinical impression; GSI: global symptom index; VAS: visual analogue scale; PF: physical functioning; RP: limitation in social activities due to the presence of a physical problem; BP: bodily pain; GH: general perception of health; VT: vitality; SF: social activities; RE: limitations in social activities associated with psychological problems due to the disease; MH: mental health.

INTRODUCTION

There are 34 000 new cases of breast cancer each year in France. Depending on the type of procedure performed, the incidence of lymphoedema will be between 5−15% for the typical breast cancer practice [1]. 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 and/or irradiation.

Treatment for lymphoedema includes a number of options: drugs (lymphotonic agents), physiotherapy (manual lymphatic drainage, lifestyle) and compression (compressive sleeve). Practitioners therefore combine and adapt treatment strategies on an individual basis because of the variability in patient response and the clinical results achieved. At present, only the volume indicator can be used to assess the impact of these treatment strategies. However, this in itself does not take into account the complexity and severity of the repercussions the disorder has on patients' lives. Upper arm lymphoedema has major functional, aesthetic and psychological consequences. A number of publications clearly identify the problems it produces with body image, together with the physical and psychological consequences of 'big arm' on everyday life of the patient [2−9]. It is therefore important to assess the consequences of lymphoedema on quality of life.

Though the concept of 'Quality of life' is very vast, there are, two fundamental components: subjectivity and multidimensionality [10]. First, quality of life assumes an ability to describe the hardship experienced and to appraise its relative impact on the subject's daily life which can be done only by the patient. Second, it cannot be evaluated in general but its various dimensions have to be investigated. Factor analysis has supported the validity of four distinct areas [10] relating to symptoms, functional well being, emotional stability and appropriate social integration.

The generic quality of life scales which are currently available [11, 12] means that they may not be the most relevant, valid and responsive questionnaires to explore these domains in lymphoedema as they are relatively insensitive to clinical changes in a particular disease. Sitzia and Sobrido [13] were unable to find any correlation between a reduction in lymphoedema volume and NHP (Nottingham Health Profile) when they used the NHP to assess quality of life during treatment for upper limb lymphoedema (ULL). The main drawback of the generic scales is their failure to identify small but significant clinical changes over time.

Disease-specific scales seem to be better suited to discriminating between the benefits of a particular treatment in lymphoedema. A number of specific quality of life scales have been designed for use with cancer patients but none of these standardized instruments are directly related to the psychosocial morbidity associated with arm swelling [14−16].

Various tools for the assessment of quality of life in patients suffering from ULL have been reported, some of which include Mirolo et al. [17], which is an adaptation of the FLIC (Functional Living Index Cancer) scale. The scale developed by these authors, known as the WCLS (Wesley Clinic Lymphoedema Scale), was found to be relatively sensitive to clinical changes, whereas the FLIC scale was not. The origin of the statements in the WCLS is, however, entirely arbitrary. Others include the LYMQOL (quality of life assessment tool for lympoedema of the limbs by Keeley et al [18]. It was therefore important to develop a specific quality of life indicator for ULL, which takes into account the patients' point of view and provides the attending physician with fine measurement of the functional and psychosocial consequences of the disorder. This paper aims to present the final results of the work done on construction and validation of the ULL quality of life scale which has been presented and translated to Dutch [19] and Italian languages.

METHODS

Questionnaire development

The questionnaire was developed in three stages:

Stage 1: A qualitative survey was carried out over a period of 8months to identify the patients' complaints and to create a database of items. This was performed by a psychologist who undertook semi-structured interviews with 24 patients. Three groups of patients were recruited according to the severity of their lymphoedema: (i) 11 patients who were physically or psychologically unaffected but who were afraid of becoming worse; (ii) five patients who were physically or psychologically affected; and (iii) eight patients who had progressive problems. Sixty-six percent of the patients were over 51-years of age and 33% had progressive problems. The interviews lasted 1 h 30 min and were recorded onto an audio cassette. The psychologist extracted more than 1166 verbatim statements which were used to develop the preliminary version of the questionnaire containing 70 items. For each item, questions were based on two criteria: the frequency of the disorder (never, rarely, sometimes, often, always), and the importance assigned to each

complaint by the patient (unimportant, slightly important, moderately important, very important, extremely important). Replies were graded on a 5-point scale.

Stage 2: This preliminary version was given to 154 patients in a quantitative survey 6months later, to select the most relevant items and to specify the main domains of impairment. The survey was implemented in 15 centres. The average age of the patients was 62.2 ± 0.84 years (range: 27-81 years; median age: 64 years). The time required to complete the questionnaire was no more than 30 min. Relevant items were selected using one of two methods: removal of 'ceiling effects or floor effects' and factorial analysis. A total of 22 questions were removed and the answers to the other 48 questions were subjected to factorial analysis. Factorial analysis identified 27 final items divided into four dimensions: a 'symptoms' dimension (eight items), a 'functional' dimension (six items), a 'psychological dimension' (seven items), and a 'social' dimension (six items). An further question regarding occupational activities was added, 'difficulties in working relationships and tasks', but was placed *a priori* in the social dimension. The questionnaire to be validated in a second quantitative analysis then contained 28 questions.

Stage 3: A final survey comprising of 306 participants was conducted to check the validity of the scale. The results of an interim analysis extracted from the available data on 196 patients showed that symptom items correlated closely with functional dimensions [20], hence distinction between the two could no longer appeared to be appreciated. Therefore, a simplified version was then created. In this, the symptom and functional dimensions were combined to 'physical dimension', item 8 on 'dress style' which correlated closely with all dimensions was remove and item 12,'difficultites in working relationships and tasks' was moved to the physical dimension in the final factorial analysis. (Table 1).

ULL-27 scale

The questionnaire incorporated 27 items divided into three dimensions: 'physical' (15 I

tems), 'psychological' (seven items) and 'social' (five items). The recall period was the previous 4 weeks. Items on the ULL scale were scored from 1−5 and were weighted equally. The response options for all items other than items 21 and 23 were reversed. We standardized the values of each scale using the method described by Ware et al. for the SF-36 scale [10]. Improvement in quality of life is represented by an increase in the score.

Validation study

The ULL quality of life scale was evaluated in an open, non-randomised, multi-centre study. Inclusion criteria included: (i) women were at least 18-years-old; (ii) women presenting with unilateral ULL which had developed after surgical and radiotherapy and/or chemotherapy and/or hormone therapy for breast cancer, and defined as a difference in circumference of at least 2 cm between the upper limbs, disappearance of skin relief on the back of the hand, or pitting oedema in the hand; and (iii) women who were able to understand the questionnaire and gave their agreement to take part in the study. Exclusion criteria included: (i) patients with progressive malignant disease; (ii) a history of lymphangitis within the previous 2 months; or (ii) signs of plexitis.

G**rades of patient severity**

Grades of oedema were defined by differences in volume (DV) between the affected and healthy limbs: oedema not measurable (150−299 ml), low volume oedema (300−499 ml), medium volume oedema (500−800 ml) and large volume oedema (>800 ml).

Concurrent criteria

We assessed the clinical outcome (volume of oedema), clinical judgement (global clinical impression; GCI), symptoms scales (symptoms indexes or global rating) or quality of life scale (SF-36) and the ULL-27 scale at the start and end of the evaluation.

The **volume of oedema**, was measured using the truncated cone volume addition method [21]. Clinical worsening (or improvement) in volumetric terms was defined by a change in the difference in volume (CDV). The transitional scale for GCI was completed by the attending physician on day 28 and it had three response options (improved, stable, worsened), which the physician considered to represent the change in a patient's state of health between days 0 and 28.

The **Global Symptom Index** (GSI) was calculated from a questionnaire developed specifically for this study and completed by the clinician in the patients' presence. Questions addressed symptoms of heaviness, tension and hardness of the affected arm. Participants were instructed to rate on a 5-point verbal scale the frequency of each symptom) over the previous 4 weeks (never, rarely, fairly often, often, always) and its intensity (not at all, a little, moderate, a lot, enormous). A composite index was constructed for each symptom by calculating the product of the frequency and the intensity scores. The overall score for the GSI

scale was standardised as a percentage of the difference between the highest and lowest score. A low score represented both infrequent development of clinical signs and minor severity of symptoms, and a score of 100 represented severe symptoms.

A **visual analogue scale** (VAS) , represented by a continuous 100 mm horizontal line was used to assess the global discomfort in the arm experienced by the patient. Zero represented no discomfort and 100, extreme discomfort. The VAS was reversed in order to produce a higher score with increasing patient comfort. The difference in score from this scale was used to define the patients' subjective improvement or worsening of clinical state. When the VAS score changed by >+5 it was considered as an improvement in patient's clinical state , and a changed by < -5 it was a worsening of patient's condition. A stable clinical state was between these two values.

The GSI and VAS scales were fully evaluated within the study for reliability, validity and responsiveness to be considered scientifically robust for use in clinical practice.

Statistical analysis

Items in the questionnaire were treated as discrete quantitative or ordinal qualitative variables. Metrological properties of the Quality of life and symptoms scales such as face validity, content validity, reliability, construct validity and responsiveness [22-31] were confirmed.

Optimality indices were used to measure that the data correctly represented the underlying model. Confirmatory factorial analysis was performed to check the stability of the factorial structure of the scale using the principal component factorisation method and a 'Varimax' rotation . Confirmation of the structure of the questionnaire was done using multi-trait scaling analysis which is based on item-scale correlations. A non-parametric analysis of variance (Kruskal Wallis test) was used to compare the dimension scores between the different grades of severity of lymphoedema on day 0. The same comparisons were performed on differential scores to confirm the longitudinal validity of the scale. Comparisons between day 0 and day 28 were made using paired tests. For clinical criteria relating to the arm or forearm, the Chi^2 test for paired series was used. A continuity correction was applied if it was required. The paired Wilcoxon test was used for dimension scores or for other quantitative criteria. All statistical tests were two-tailed with a statistical probability threshold (alpha risk) of 0.05. Confidence intervals of 95% were calculated. The statistical sofware used was SPSS, version 10.0.

RESULTS

Socio-clinical characetistics

Twelve practitioners participated in the study and 304 patients were included, however statistical analysis was performed on 301 patients as three patients were lost to follow-up between day 0 and day 28. The average age,height and weight of the patients were 61.61 ± 1.16years, 1.61 ± 0.20m and 67.98 ± 1.36kg respectively. Other patient characteristics and baseline quality of life are highlighted in Tables 2 and 3. Overall results of GSI,GCI and VAS showed an clinical improvement in 60% and 10% deteroriation with respect to these different criteria. The Grade III patients showed the most improvement (36%). The GSI fell from 32.3 on day 0 to 14.59 on day 28. The mean arm comfort scale score (VAS) rose from 47.72 ± 1.46 on day 0 to 65.63 ± 1.40 on day 28. The overall change in patients was also defined by the clinicians: 61% (181/297) were defined as having improved between days 0 and 28, 31% of patients as being stable (92/297) and 8% as have deteriorated (24/297). The opinions of the clinicians and patients concerning the change in the disorder were then compared and a significant kappa coefficient of 44.3% was found.

Validation of the ULL-27 scale

Acceptability

ULL-27 items were phrased directly based on patients' descriptions in accordance with FDA recommendations [32]. Most of the items in ULL-27 were completed by 292−297 patients on day 0. However there was a large number of missing values for three items: item 7 (39 values), 12 (27 values), and 27(50 values). The median time taken to complete the questionnaire was 11 ± 1 min.

Content validity

Evidence from pre-testing with patients and expert opinion support the content validity of the ULL-27 scale.

Reliability

The 'Internal consistency' was tested by Cronbach alpha values [22]. Cronbach alpha coefficients in all patients were 0.93, 0.86 and 0.82 for the physical, psychological and social dimensions, respectively. All values exceeded the standard criterion of 0.70. Intra-class correlation coefficients between days 0 and 28 were calculated for each dimension of the ULL-27 scale in the 92 patients considered to be stable by clinicians. Correlation coefficients for the physical, psychological and social dimensions were 0.86, 0.80

and 0.80, respectively. Intra-class correlation coefficients for the GSI, VAS and the eight dimensions of SF-36 were highly statistically significant ($p<0.001$) except for the GH dimension of SF-36.

Construct validity

The Within scale analysis explained 55% of the variance. The physical, psychological and social dimensions of the ULL-27 scale accounted for 27.7%, 15.8% and 11.2% of variance after rotation. (Table 4).

Two correlation coefficients which define the internal consistency of the items were calculated: R1, the correlation between each item and the dimension to which it belonged and R2, the correlation between each item and the dimension to which it does not belong. The correlation coefficient, R1, ranged from 0.48−0.71 for the physical dimension (Table 5), 0.42−0.77 for the psychological dimension and 0.55−0.71 for the social dimension. The success rate is defined by the percentage of items which have a correlation coefficient of >0.40. The success rate here was 93% for the physical dimension and 100% for both the psychological and social dimensions.

Known group differences

The mean dimension scores for patients with different grades of the disorder were compared (Table 6) and a significant difference was found between the four grades for the physical ($p<0.02$) and social ($p<0.02$) dimensions. There was no significant difference between grades for the psychological dimension ($p=0.99$). Similarly, the SF-36 scale produced the same results: only the dimension PF was different between the four grades ($p=0.01$). There were no significant differences between the severity of grades of the disorder for any of the other dimensions. The average values of the GSI and the arm comfort scale were statistically different between the four severity grades.

Quality of life was better in older women on day 0, regardless of whether the cut-off was set at 60 or 65-years of age. Patients who were not being treated on day 0 also had a better quality of life than those who were being treated. Finally, contralateral involvement in right handed people was associated with a higher quality of life than in right-handed people with ipsilateral involvement. Table 7.

Convergent validity

Spearman correlation coefficients were calculated between the dimension scores on day 0 and the observed differences in the scores from the scales between day 28 and day 0. Convergent validity is fulfilled when

the scale scores for a related concept produce a Spearman correlation coefficient of >0.4. At day 0, all of the correlation coefficients were significant (Table 8). In terms of longitudinal validity, all of the correlations between the observed differences in scores from the scales between days 28 and 0were statistically significant in the 181 patients who improved clinically according to the GCI scale (Table 9). The correlation coefficients between the difference in arm volume and all psychological and social indicators were very weak regardless of the scale. This was also seen longitudinally over time.

Responsiveness

The responsiveness of the ULL scale was determined in a subgroup of 181 patients whose clinical status improved in the opinion of the clinician. The mean item subscores were calculated and dimension scores between days 0 and 28 were compared by the paired Wilcoxon test to confirm the sensitivity of the ULL-27 scale. Scores were found to be statistically significantly different for the three dimensions ($p<0.001$). The mean dimension scores of SF-36 between days 0 and 28 were then compared using the same method; no significant difference for the dimensions PF, RP and GH were found. The difference was significant for the other five dimensions, BP, MH, VT, SF and RE ($p<0.001$). The mean scores for the indicators of volume, symptoms and arm comfort were significantly different in this patient group between days 0 and 28.

Effect size was calculated to assess the responsiveness of the scales. A coefficient of 0.20 reflects low sensitivity, 0.50 represents moderate sensitivity and 0.80 or more represents high sensitivity to change. Effect size values of 0.58, 0.62 and 0.38 were found for the physical, psycological and social dimensions respectively.

DISCUSSION

The ULL-27 scale has been designed and validated following all of the classical stages used to construct measurement instruments. The three dimensions of ULL-27, physical, psychological and social, have robust quantitative properties. Precision, measured by the Cronbach alpha coefficient, demonstrated good internal consistency between items within their dimension. This was confirmed by multi-trait/multi-item analysis which assesses both internal coherence of the items and their discriminatory validity. The response rates of all of the dimensions were 100% for internal coherence. Discriminatory validity was excellent for

all of the items, except for item 12 relating to difficulty in working relationships and tasks. This item appears to correlate with the three dimensions of the ULL scale.

Strong and significant correlations were found for all of the indicators between the scores on days 0 and 28 and ranged from 0.80−0.86 for the ULL-27 scale. Apart from the GH dimension of SF-36 (r=0.49), the correlation coefficients between the other dimensions of SF-36 and between the other indicators were between 0.70 and 0.92.

The wilcoxon test confirmed that the scores from the physical and psychological dimensions of the ULL-27 scale were stable, as were six of the dimensions of SF-36, the perceived comfort scale and the volume indicator. The social dimension of ULL-27 and the RP and GH dimensions of SF-36 exhibited significant differences between days 0 and 28 in stable patients.

Known group differences were checked. A fall in scores for the physical and social dimensions of the ULL-27 scale was observed when the grade increased. This indicates that the disorder has greater repercussions in the higher severity grades. The score for the psychological dimension was not significantly different between grades: the psychological component of the disorder experienced by patients was not dependent on grade. The GSI and VAS (perceived arm comfort scale) produced statistically different scores depending on the grade of the disorder. Of the SF-36 dimensions, only PF was significant. The scores for the other dimensions were not statistically significant between the grades of disorder.

A very close convergence with most of the reference indicators was found. The physical, psychological and social dimensions of the SF-36 and ULL-27 correlated closely with each other. For the physical dimension of ULL-27, however, the correlations were stronger with the PF, BP and VT dimensions of the SF-36 and with VAS and GSI. From these strong correlations it can be concluded that VAS and GSI predominantly assess the physical component of the disorder.

Correlations for psychological dimension of ULL-27 were stronger with the VT, SF and MH dimensions of SF-36. Finally, correlations were stronger with the SF and MH dimensions of SF-36 for the social dimension of ULL-27.

For SF-36, PF is less sensitive than that on the LMS scale and the functional consequences of lymphoedema are clearly identified by this new instrument. This takes into account the psychological consequences of the disorder: all correlations between the psychological dimension of ULL-27 and the

homologous dimensions of SF-36 are 0.50, even on longitudinal sections. Conversely, the social impact of the disorder is better measured by SF-36. For this dimension, there is a weaker correlation between the two scales and stability of response is better in patients whose clinical state is unchanged; the amplitude of this effect is greater when SF-36 is used. Overall, the sensitivity of LMS is good with an amplitude of effects close to 0.70. The GH, RP or RE dimensions of SF-36 do not meet any of the metrological criteria required.

The GSI has very good metrological properties and can be used systematically with the ULL-27 scale. Convergence with the physical dimension of the ULL-27 scale is seen in both cross-sectional and longitudinal sections. As expected, it has no links with other dimensions of the ULL-27 scale. The arm comfort scale (VAS), which assesses patient comfort, is as revealing as the GSI. Its convergence with the psychological dimension of ULL-27 on longitudinal sections identifies arm discomfort as the key factor in determining a person's psychological balance.

The poor correlations observed between 'volume of oedema' and the ULL-27 subscales and GSI are undoubtedly due to the fact that differences in volume between the healthy arm and the affected limb only assess the clinical signs of lymphoedema, whereas the ULL-27 scale evaluates the negative effect of the problems in the affected arm on the overall quality of life of breast cancer patients. The lack of any correlation between the volume of the limb and the degree of distress [6] again demonstrates the importance of differentiating between physical morbidity and its psychosocial impact on a patient's life.

In conclusion, the ULL-27 scale is a precise, accurate and sensitive scale. Cronbach alpha coefficients and the multi-trait/multi-item matrix indicate that the items offer good internal coherence. Reproducibility, or response stability over time, was demonstrated clearly by the correlation coefficients calculated for the physical and psychological dimensions, which were all >0.8 in clinically stable patients. The social dimension is less stable; it seems to be very sensitive to any clinical change in the disorder, even to those which are undetectable by physicians. The convergence between the dimensions of the different scales demonstrates the accuracy of measurement. Convergence was found for scores on day 0 and for the differences in scores. The ULL-27 quality of life scale was also shown to be sensitive: quality of life scores were significantly higher when the clinical score improved.

The medical service provided for patients is important. It is essential to measure the impact of a disorder and any treatment benefits. The concept of quality of life is highly relevant to lymphoedema. The specific quality of life scale for secondary ULL following breast cancer has developed from this change in medicine. In its current form, the ULL-27 scale offers good metrological properties. It is true that in the quality of life domain, no scale can be claimed to have been truly validated; it is only suggested that a body of convergent evidence has been collated in different environments and studies. Such a situation characterises the present status of the ULL-27 questionnaire. Future development of this scale will require additional work.

REFERENCES

1. Velanovich V, Szymanski W. Quality of life of breast cancer patients with lymphedema. Am J Surg 1999; 177: 184−188.
2. Alliot F, Cluzan RV, Sthevenin PH, Bleton JP. The body image in lymphoedema: remarks. In: XVI World Congress of the International Union of Angiology. Paris 1992.
3. Alliot F. Traitements des atteintes lymphatiques. In: Janbon C, Cluzan H. eds. *Lymphologie (Collection de Médecine Vasculaire*). Paris: Masson, 1995: 134−162.
4. Maunsell E, Brisson J, Deschènes L. Arm problems and psychological distress after surgery for breast cancer. CJS 1993; 36: 315−320.
5. Tobin M, Lacey H, Meyer L, Mortimer P. The psychological morbidity of breast cancer – related arm swelling. Cancer 1993; 72: 3248−3252.
6. Woods M, Tobin M, Mortimer P. The psychological morbidity of breast cancer patients with lymphoedema. Cancer Nursing 1995; 18: 467−471.
7. Hack FT, Cohen L, Katz J, et al. Physical and Psycological morbidity after axillary lymph node dissection for breast cancer. J Clin Oncol 1999; 17: 143−149.
8. Warmuth M, Bowen G, Prosnitz L, Chu L, et al. Complications of axillary lymph node dissection for carcinoma of the breast. A report based on a patient survey. Am Cancer Soc 1998; 83: 1362−1368.
9. Tasmuth T, von Smitten K, Hietanen P, Kataja M, et al. Pain and other symptoms after different treatment modalities of breast cancer. Ann Oncol 1995; 6: 453−459.
10. Cella DF. Quality of life: the concept. J Pall Care 1992; 8: 8−13.
11. Ware JE, Snow KK, Kosinski M, et al. *SF 36 Health Survey Manual and Interpretation Guide*. Boston New England Medical Center: The Health Institute, 1993.
12. Hunt SM, McEwen J, McKenna SP. *Measuring Health Status*. London: Croon Helm, 1986.
13. Sitzia J, Sobrido L. Measurement of health-related quality of life of patients receiving conservative treatment for lymphoedema using the Nottingham Health Profile. Qual Life Res 1997; 6: 373−384.
14. Ganz P, Coscarelli A, Fred C, et al. Breast cancer survivors: psychosocial concerns and quality of life. Breast Cancer Res Treat 1996; 38: 183−199.

15. Ganz PA, Coscarelli Schag A, Lee J. Breast conservation versus mastectomy – is there a difference in psychological adjustment or quality of life in the year after surgery?. Cancer 1992; 69: 1729−1738.

16. Aaranson NK, Ahmedzai S, Bergman B, et al. The European organization for research and treatment of cancer QLQ C30 a quality of life instrument for use in international clinical trials in oncology. J Nat Cancer Inst 1993; 85: 365−376.

17. Mirolo BR, Bunce IH, Chapman M, et al. Psychosocial benefits of postmastectomy lymphoedema therapy. Cancer Nurs 1995; 18: 197−205.

18. Keeley V, Crooks S, Locke J, et al. A Quality of Life Measure for Limn Lyphoedema (LYMQOL). Journal of lyphoedema 2010; 5 (1): 26-27

19. Viehoff PB, Van Genderen FR, Wittink H. Upper limb Lyphoedema 27 (ULL27): Dutch translation and validation of an illness-specific health-related quality of life questionnaire for patients with upper limb lymphedema. Lymphology 2008; 41 (3): 131-138.

20. Launois R, Alliot F. Quality of life scale in upper limb lymphoedema. A validation study. Lymphology 2000; 33 (Supp): 266−274.

21. Casley-Smith JR. Measuring and representing peripheral oedema and its alterations. Lymphology 1994; 27: 56−70.

22. Moret J, Chwalow C, Baudoin-Balleur <initials?>. Evaluer la qualité de vie: construction d'une échelle. Rev Epidém Santé Publ 1993; 41: 65−71.

23. Nunnaly JC. *Psychometric Theory*. 2nd edn. New York: McGraw Hill Book Company, 1978.

24. Kaplan RM, Bush JW, Berry C. Health status: type of validity and the index of well-being. Health Serv Res 1979; 16: 64−73.

25. Launois R, Reboul-Marty J, Henry B. Construction et validation d'un indicateur spécifique de qualité de vie: le cas de l'insuffisance veineuse chronique des membres inférieurs. J d'Econ Médicale 1994; 12: 109−126.

26. Guyatt G, Bombardier C, Tugwell PX. Measuring disease specific quality of life in clinical trials. Can Med Assoc J 1986; 134: 889−995.

27. Guyatt G, Walter S, Norman G. Measuring change over-time: assessing the usefulness of evaluative instruments. J Chron Dis 1987; 40: 171−178.

28. Reboul-Marty J, Launois R. Les indicateurs de qualité de vie: processus de mesure et validation. Cardioscopies 1995; 33: 635−637.

29. Launois R, Reboul-Marty J, Henry B. Construction and validation of a quality of life questionnaire in chronic lower limb venous insufficiency (CIVIQ). Qual Life Res 1996; 5: 539−554.

30. Liang MH, Fossel AH, Larson MG. Comparisons of five health status instruments for orthopedic evaluation. Med Care 1990; 28: 632−642.

31. Deyo RA, Diehr P, Patrick DL. Reproducibility and responsiveness of health status measures - statistics and strategies for evaluation. Control Clin Trials 1991; 12: 142S−158S.

32. Guidance for Industry. Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labelling Claims. U.S. Department of Health and Human Services Food and Drug Administration.

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APPENDIX

ULL-27 questionnaire

Please enter the exact time when you started completing this questionnaire:

⌊ ⌋ h ⌊ ⌋ min

During the last four weeks, have you experienced difficulties because of your arm:	Never	Rarely	Sometimes	Often	Always
1. In getting to sleep: difficulty finding a comfortable place, in positioning your affected arm?	–	–	–	–	–
2. In washing, brushing your hair or putting on makeup?	–	–	–	–	–
3. In grasping objects: opening a door or turning a tap off?	–	–	–	–	–
4. In sleeping: waking often, with pain?	–	–	–	–	–
5. Walking, when your arm is heavy, a burden or swollen?	–	–	–	–	–
6. Grasping high objects, taking down the washing?	–	–	–	–	–
7. Taking public transport?	–	–	–	–	–
8. Dressing, putting on clothes, undressing?	–	–	–	–	–
9. Staying in certain positions for a long time?	–	–	–	–	–
10. Holding objects: cutlery, a book, vase or plate etc?	–	–	–	–	–
11. In your working relationships and tasks?	–	–	–	–	–

During the last four weeks, have you, because of your arm:	Never	Rarely	Sometimes	Often	Always
12. Felt that your arm is swollen?	–	–	–	–	–

13. Felt like getting angry?	–	–	–	–	–
14. Felt your skin is swollen, tense or hard?	–	–	–	–	–
15. Felt sad?	–	–	–	–	–
16. Felt a lack of confidence in yourself?	–	–	–	–	–
17. Felt sensations of tingling, burning, tightness or itching?	–	–	–	–	–
18. Felt that your arm is heavy, a burden or swollen?	–	–	–	–	–

During the last four weeks, have you, because of your arm:					
	Never	Rarely	Sometimes	Often	Always
19. Felt distressed?	–	–	–	–	–
20. Had confidence in the future?	–	–	–	–	–
21. Been afraid of looking at yourself in the mirror?	–	–	–	–	–
22. Felt ‘well in yourself’?	–	–	–	–	–
23. Felt discouraged?	–	–	–	–	–

During the last four weeks have you had difficulties because of your arm:					
	Never	Rarely	Sometimes	Often	Always
24. In your social life: going to a restaurant, cinema or theatre, a party or doing the shopping etc.?	–	–	–	–	–
25. Taking advantage of good weather, spending time outside in the open air?	–	–	–	–	–
26. In your emotional life with your spouse or partner?	–	–	–	–	–
27. In your personal projects: holidays, hobbies, etc.?	–	–	–	–	–

Please enter the exact time you finished completing this questionnaire: ⌊_⌋⌊_⌋h⌊_⌋⌊_⌋min.

Table 1. Quality of life scale to be validated

Physical functioning	**Psychological dimension**
06. Difficulties grasping high objects	16. Feeling sad
10. Difficulties maintaining certain positions	24. Feeling discouraged
19. Arm feels heavy	17. Feeling a lack of self-confidence
10. Arm feels swollen	20. Feeling distressed
09. Difficulties dressing	23. Feeling well in oneself
01. Difficulties getting to sleep	14. Feeling a wish to be angry
04. Difficulties sleeping	21. Having confidence in the future
03. Difficulties grasping objects	**Social dimension**
11. Difficulties holding objects	26. Difficulty taking advantage of good weather, in life outside the house
05. Difficulties walking/heavy arm	28. Difficulty with personal projects, holidays or hobbies
02. Difficulties washing	27. Difficulties in emotional life with spouse or partner
07. Difficulties taking public transport	25. Difficulty in social life
18. Tingling, burning feelings	22. Fearful of looking in a mirror
15. Feelings of swollen, hard, tense skin	
12. Difficulties in working relationships and tasks	

Table 2. Characteristics of patients in the study (Total= 301)

Patient characteristics	n (%)
Age (yr)	61.61 ± 1.16*
Height (m)	1.61 ± 0.20*
Weight (kg)	67.98 ± 1.36*
BMI (m/kg²)	26.25 ± 0.54*
Dominant hand	
Right	289 (96)
Left	12 (4)
Location of disorder	
Ipsilateral	144 (48)
Contralateral	157 (52)
Previous treatment	
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)
Oedema volume	
Grade I	39 (13)
Grade II	60 (20)
Grade II	81 (27)
Grade IV	120 (40)

* mean ± standard deviation

Table 3. Measurement of quality of life on day 0

Dimensions	Range of scores	N	Mean	Standard error
Difference in arm volume	1271-6180	297	805	40.38
Global symptom index	0-100	300	32.2	1.31
Arm comfort scale	0-100	299	47.72	1.46
ULL-27				
Physical dimension	5-100	243	54.27	1.42
Psychological dimension	3.57-100	287	61.91	1.33
Social dimension	0-100	242	61.78	1.63
Global score	14.81-99.07	196	57.80	1.37
SF-36				
Physical functioning	0-100	254	60.02	1.34
Restriction due to physical state	0-100	287	40.77	2.39
Bodily pain	0-100	294	53.09	1.44
General health	30-77	270	50.76	0.58
Vitality	0-95	293	48.79	1.14
Social functioning	0-100	290	62.54	1.45
Role emotional	0-100	289	46.71	2.49
Mental health	4-100	288	55.9	1.23

Table 4: Confirmatory factorial analysis

ACP - VARIMAX - PAIRWISE - KMO = 0.93 55% of explained variance	Physical dimension	Psychological dimension	Social dimension
Difficulties grasping high objects	**0.75**	-0.02	0.12
Difficulties maintaining certain positions	**0.73**	0.14	0.17
Arm feels heavy	**0.73**	0.21	0.13
Arm feels swollen	**0.71**	0.16	-0.02
Difficulties dressing	**0.71**	0.03	0.20
Difficulties getting to sleep	**0.71**	0.22	0.11
Difficulties sleeping	**0.69**	0.25	0.08
Difficulties grasping objects	**0.68**	0.07	0.16
Difficulties holding objects	**0.68**	0.09	0.27
Difficulties walking/heavy arm	**0.68**	0.22	0.15
Difficulties washing	**0.66**	0.09	0.25
Difficulties taking public transport	**0.65**	0.11	0.26
Tingling, burning feelings	**0.64**	0.13	0.05
Feelings of swollen, hard, tense skin	**0.61**	0.21	0.09
Difficulties in working relationships and tasks	**0.42**	0.34	0.35
Feeling sad	0.26	**0.77**	0.20
Feeling discouraged	0.19	**0.76**	0.32
Feeling a lack of self-confidence	0.19	**0.75**	0.28
Feeling distressed	0.33	**0.71**	0.16
Feeling well in oneself	0.04	**0.67**	0.16
Feeling a wish to be angry	0.34	**0.61**	0.07
Having confidence in the future	-0.06	**0.55**	0.04
Difficulty taking advantage of good weather, in life outside the house	0.09	0.06	**0.77**
Difficulty with personal projects, holidays or hobbies	0.21	0.26	**0.77**
Difficulties in emotional life with spouse or partner	0.25	0.29	**0.66**
Difficulty in social life	0.34	0.34	**0.57**
Fearful of looking in a mirror	0.15	0.40	**0.52**

Table 5: Internal consistency and discriminatory validity of the items - intervals of correlation coefficients between items and dimensions (Spearman correlation coefficients)

	Physical dimension (14 items)	Psychological dimension (7 items)	Social dimension (6 items)
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%
Discriminatory 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 6. Comparison of mean values from the quality of life scales by grade of lymphoedema on day 0 (ANOVA)

Dimensions	Grade I			Grade II			Grade III			Grade IV			p
	N	Mean	SEM	N	Mean	SEM	N	Mean	SEM	N	Mean	SEM	
Arm comfort scale	38	56.74	4.03	59	51.37	2.86	59	51.37	2.86	115	41.87	2.48	0.06
Global symptom index	38	20.25	2.86	59	27.10	2.49	59	27.10	2.49	116	39.67	2.12	0.001
ULL 27													
Physical dimension	31	65.27	4.57	50	57.17	3.28	50	57.17	3.28	90	50.54	2.26	0.02
Psychological dimension	35	62.04	3.51	57	61.72	3.16	57	61.72	3.16	111	61.62	2.15	0.99
Social dimension	30	71.50	4.24	46	63.80	3.92	46	63.80	3.92	91	55.99	2.75	0.02
SF 36													
Physical functioning	30	69.67	3.36	51	60.88	2.99	51	60.88	2.99	95	55.47	2.29	0.01
Restriction due to physical state	36	44.44	6.91	56	46.88	5.22	56	46.88	5.22	110	37.95	3.87	0.52
Bodily pain	36	53.64	4.16	57	56.44	3.34	57	56.44	3.34	116	51.72	2.35	0.66
General health	34	49.53	1.16	55	51.67	1.31	55	51.67	1.31	107	49.95	1.02	0.47
Vitality	38	51.05	3.32	58	48.88	2.66	58	48.88	2.66	113	48.45	1.84	0.83
Social functioning	36	65.97	4.16	57	64.91	3.64	57	64.91	3.64	113	61.17	2.31	0.50
Role emotional	38	52.63	7.18	57	55.56	5.68	57	55.56	5.68	110	41.82	4.00	0.18
Mental health	37	61.62	3.27	55	56.00	3.33	55	56.00	3.33	113	54.94	2.00	0.33

Table 7. Discriminatory power of scales by age, treatment and side of involvement

Dimensions	Age*		Treatment**		Side***	
	Effect size	p	Effect size	p	Effect size	p
Change in difference of volume	-0.50	0.001	-1.16	0.001	0.08	0.275
Global symptom index	0.23	0.063	-0.89	0.001	0.12	0.425
Arm comfort scale	-0.21	0.078	0.78	0.001	-0.03	0.743
ULL 27						
Physical dimension	-0.004	0.971	0.55	0.019	-0.21	0.167
Psychological dimension	-0.22	0.057	0.26	0.168	-0.32	0.011
Social dimension	-0.22	0.127	0.46	0.020	-0.28	0.034
ULL global score	-0.10	0.49	0.63	0.005	-0.33	0.26
SF 36						
Physical functioning	0.64	0.001	0.59	0.005	-0.34	0.006
Restriction due to physical state	0.19	0.121	0.47	0.013	-0.29	0.012
Bodily pain	-0.06	0.690	0.66	0.001	-0.21	0.095
General health	-0.05	0.836	0.24	0.204	-0.03	0.989
Vitality	0.25	0.033	0.26	0.255	-0.27	0.023
Social functioning	-0.20	0.126	0.29	0.094	-0.31	0.008
Role emotional	0.15	0.233	0.79	0.001	-0.13	0.310
Mental health	-0.21	0.087	0.21	0.266	-0.32	0.005

*Quality of life of patients less than 65-years-old - quality of life of patients more than 65-years-old; **Quality of life of patients non-treated - quality of life of patients treated; ***Quality of life of patients suffering from ipsilateral lymphoedema - quality of life of patients suffering from contralateral lymphoedema.

Table 8. Correlation between differences in scores on day 28 and day 0 in patients who improved clinically

Dimensions	PF	RP	BP	GH	VT	SF	RE	MH	Phys dimen. ULL	Psycol dimen. ULL	Social dimen. ULL	Global score ULL	Arm comfort scale	GSI	CDV
SF 36															
PF	1.000														
RP	0.084*	1.000													
BP	0.182	0.120*	1.000												
GH	0.058*	0.168*	0.090*	1.000											
VT	0.209	0.254	0.287	-0.045*	1.000										
SF	0.079*	0.373	0.341	-0.019*	0.213	1.000									
RE	0.192	0.520	0.101*	0.026*	0.258	0.219	1.000								
MH	0.256	0.240	0.350	0.078*	0.540	0.311	0.193	1.000							
ULL-27															
Physical dimension	0.384	0.057*	0.286	0.131*	0.211	0.187*	0.129*	0.173*	1.000						
Psychological dimension	0.272	0.187	0.392	0.263	0.401	0.237	0.230	0.476	0.405	1.000					
Social dimension	0.165*	0.119*	0.131*	0.000*	0.276	0.290	0.107*	0.286	0.274	0.350	1.000				
ULL global score	0.433	0.138*	0.292	0.095*	0.340	0.326	0.339	0.364	0.809	0.794	0.622	1.000			
Arm comfort scale	0.103*	-0.048*	0.262	-0.005*	0.156	0.225	0.001*	0.169	0.366	0.322	0.175		1.000		
GSI	-0.100*	-0.077*	-0.220	0.040*	-0.074*	-0.197	0.055*	-0.211	-0.323	-0.164	-0.123*		-0.542*	1.000	
CDV	-0.051*	-0.107*	0.151	-0.002*	0.131*	0.017*	-0.037*	0.278	0.038*	0.185	0.203		0.325*	-0.369	1.000

GSI: global symptom index; CDV: change in difference in volume; PF: physical functioning; RP: limitations in social activities due to the presence of a physical problem; BP: bodily pain; GH: general perception of health; VT: vitality; SF: social functioning; RE: limitations in social activities associated with psychological problems; MH: mental health.

*: Difference not statistically significant