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NEW CLINICAL AND LABORATORY STAGING SYSTEMS TO IMPROVE MANAGEMENT OF CHRONIC LYMPHEDEMA

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ABSTRACT

We have developed new clinical (C) and laboratory (L) staging systems to improve the clinical management of chronic lymphedema. These systems were retrospectively assessed in 220 chronic lymphedema patients followed up for 4 years. Clinical evaluation of the treatment response/disease progression was performed at 6 month intervals and laboratory evaluation at a yearly interval except for recurrent sepsis cases. The reliability of C-stage and L-stage for the progression of disease were analyzed separately. The C-staging was based on the subjective and objective findings of local and systemic conditions, while L-staging was based on lymphoscintigraphic findings. Clinical implementation of this new staging system facilitated interpretation of the progress/ deterioration of the clinical response to CDT treatment, and it was found to be a useful guideline for the decision/selection of further surgical treatment. We propose that these two separate staging systems could now become a new guideline for improved management of lymphedema with a better prediction of treatment outcome and decision point for additional medical/surgical therapy. Further clinical implementation and evaluation is necessary to demonstrate clinical usefulness especially to guide surgical therapy and L-staging in followup.

Quality of life (QOL) is now a major parameter for assessing the management result of any disease (1,2). Chronic lymphedema management should also mandate QOL assessment as an added parameter (3-5) for improved selection of therapies and better prediction of treatment outcome.

MLD (manual lymphatic drainage)-based CDT (complex decongestive therapy) and SPC (sequential pneumatic compression)-based compression therapy have been widely used as basic treatment regimens for chronic lymphedema with satisfactory results (6-16). However, the current assessment criteria for the management outcome and/or progress of lymphedema are far from ideal (14,17,18). The International Society of Lymphology (ISL) recommended clinical staging is far too simple to be used as a reliable guideline for complicated treatment strategies and to accommodate surgical options. Timely addition of appropriate reconstructive or ablative surgical therapy is essential for the patient who fails to respond to CDT-based therapy, and this next step requires improved staging with new criteria including the QOL for this purpose (14,19,20).

We have developed and adopted new clinical and laboratory staging systems. Clinical staging utilized clinical manifestation and/or progress of the lymphedema including systemic and local complications of lymphedema and the QOL in a 4 stage system

TABLE 1
Guideline Criteria for the New Clinical and Laboratory Staging System (I-IV)*

Laboratory (Lymphoscintigraphic Staging)	Clinical Staging
Grade I (stage) • Lymph node uptake (LN): decreased (±) • Dermal backflow (DBF): none (-) • Collateral lymphatics (CL): good visualization (+) • Main lymphatics (ML): decreased visualization (±) • Clearance of radioisotope from injection site (CR): decreased lymphatic transport (±)	**Stage I** • Edema (swelling): mild and/or easily reversible (+) • Skin change: none without dermatofibrosclerosis DFS (-) • Sepsis (systemic and/or local): none (-) • Daily activity limitation (DAL): No limitation (-) • Quality of Life (QOL): good with minimal and/or occasional limitation (e.g., exercise, hobby) physically psychologically and/or socioeconomically
Grade II (stage) • LN: decreased to none (-) • DBF: visualization (+) *IIA – extent of DBF does not exceed $^1/_2$ of each limb *IIB – exceed $^1/_2$ of each limb • 1CL: decreased visualization (±) • ML: poor to no visualization (±) • CR: greater decrease (±)	**Stage II** • Edema: moderate and/or reversible with effort (+) • Skin change: none to minimal without DFS (±) • Sepsis: none to occasional (±) • DAL: occasional and/or moderate limitation (±) • QOL: fair with moderate limitation physically, psychologically and/or socioeconomically
Grade III (stage) • LN: no uptake (-) • DBF: visualization (+) • CL: poor visualization (-) • ML: no visualization (-) • CR: no clearance (-)	**Stage III** • Edema: moderate to severe and/or minimally reversible to irreversible (±) to (-) • Skin change: moderate with significant DFS (+) • Sepsis: common (+) – less than four times a year • DAL: frequent and significant (+) • QOL: poor with significant limitation
Grade IV (stage) • LN: none (-) • DBF: poor to no-visualization (-) • CL: no visualization (-) • ML: no visualization (-) • CR: no clearance (-)	**Stage IV** • Edema: severe and/or irreversible (-) • Skin change: severe with advanced DFS (++) • Sepsis: very frequent (++) – four times or more a year • DAL: constant and severe (++) • QOL: bad with severe limitation

* Minimum two or more lymphoscintigraphic findings for laboratory staging and three or more clinical findings for clinical staging.

TABLE 2
Quality of Life (QOL)

Excellent	No limitation or difficulty on extra activity (e.g., hobby) physically, psychologically and/or socioeconomically in addition to the daily activity.
Good	Some limitation on extra activity but occasionally, physically, psychologically and/or socioeconomically but with no limitation to daily activity.
Fair	Significant limitation on extra activity but no limitation on daily activity physically, psychologically and/or socioeconomically, or occasionally some limitation on both daily and extra activity.
Poor	Significant frequent limitation on both daily activity and extra activity, physically, psychologically and/or socioeconomically.
Bad	Profound limitation on daily activity as well as extra activity or no daily activity feasible without assistance physically, psychologically and/or socioeconomically.

(clinical stages I through IV). A separate laboratory staging was based on the lymphoscintigraphic findings (10,13,14,19,21,22). Separate staging systems allowed a timely addition of various surgical therapies to the patients who failed CDT treatment (14,21,23-28). The new clinical staging expands ISL staging (based on limited information on the local factors, i.e., edema and skin change) by the addition of various systemic factors: sepsis, daily activity limitation, and quality of life–physical, functional, socioeconomic and psychological (4,5,29,30). Attempts to include the lymphoscintigraphic findings in the new clinical staging failed and only added confusion (19,31-34). Therefore, laboratory staging was made a separate independent parameter for assessing the clinical management outcome and/or its natural progress.

The new staging systems were evaluated for their effect on the clinical management of patients with lymphedema and predictability of CDT treatment outcomes and the need for appropriate supplemental surgical therapy.

MATERIALS AND METHODS

Proposed Staging System

Clinical staging was accomplished by a total composite score of various clinical features: edema (swelling), skin change, sepsis, daily activity limitation, and QOL (*Table 1*). The subjective and objective findings of the local condition of the skin and subcutaneous soft tissues, were assessed by the degree of skin change (dermatofibrosclerosis), swelling, and spontaneous reversibility. Local and/or systemic sepsis was assessed by the severity of erysipelas and/or cellulitis. Functional limitation on daily activity as a result of the various subjective symptoms was assessed by pain, uncomfortable sensory complaints (heaviness, tightness, numbness), skin texture feeling of the swollen limb, and difficulty in wearing clothes due to the swelling (*Table 1*). QOL was evaluated by the physical, psychological, and socioeconomical limitations (*Table 2*). Physical factors for the QOL included the strength of the affected limb and/or restriction of movement compared to the unaffected limb as well as the further

TABLE 3
Clinical Outcome: Demographic Data on the New Clinical Staging for Assessment of the Progress (Deterioration or Improvement) of Lymphedema*

Initial C Stage	n	Final C stage				Further deterioration
		I	II	III	IV	
I	77	70	6	1	0	0
II	98	3	81	11	2	1
III	29		2	14	12	1
IV	16			1	6	9

*Four year follow-up evaluation of CDT-based therapy results among 220 patients.

additional impact on the duties at home and/or duties at work and/or recreational activity. Psychological factors included feelings of depression, frustration and/or anger due to the lymphedema in addition to difficulties in sleeping. Socioeconomic factors included difficulty with intimate relationships and/or socializing activities.

Laboratory staging was made with a composite sum of various normal and abnormal lymphoscintigraphic findings (*Table 1*). Lymph node uptake, dermal backflow, collateralization as well as main lymphatic visualization, and the clearance of radioisotope from the injection site were utilized as parameters of the lymphatic transport capacity.

Subjects

A total of 840 chronic lymphedema patients registered at the Lymphedema Clinic, Samsung Medical Center, Seoul, Korea during the period of February 1995 through August 2001. 220 patients (85-primary and 135 secondary: 169 female and 51 males: mean age of 41.3 years) were randomly selected based on the availability of a 4 year follow up assessment using the new staging guidelines.

All 220 patients were evaluated with new clinical and laboratory staging systems (*Table 1*) and underwent various combinations of standard CDT and compression therapy. A periodic clinical evaluation was made with an average 6 month but no longer than yearly interval. Lymphoscintigraphic study was performed mostly on a yearly basis, except for those patients with recurrent sepsis for whom additional study was included whenever feasible. The isotope agent used in scintigraphy for most follow-up tests was Tc-99m Antimony sulfur-colloid (182/220). This was changed to tin-colloid (38/220) for the last part of the follow-up period, and those images have not been included in the analysis. Therefore, the clinical staging only was used to assess the progress (deterioration) of the disease despite acceptable maintenance care (*Table 3*).

RESULTS

As summarized in *Table 4*, a comparison of clinical (C) and laboratory (L) stages during the initial diagnosis of 220 patients showed broad overlapping between the two different stagings; each group of the same C stage accompanied various L stages, and the same L stage also accompanied a wider

TABLE 4
Demographic Data on Initial Clinical and Laboratory Stages of Chronic Lymphedema*

	Laboratory Stage					
	I	II	III	IV	Unidentified***	Total
Clinical Stage**						
I	53	19	1	0	4	77
II	6	66	24	1	1	98
III	0	2	15	10	2	29
IV	0	1	6	9	0	16
Total	59	88	46	20	7	220

*220 patients, selected for 4 year follow-up assessment through the Lymphedema Clinic, Vascular; Center, Samsung Medical Center, Seoul, Korea (Feb. 1995 – Aug. 2001); **based on new 4 staging system; ***unavailable for comparison study.

range of C stages. But a more advanced L-stage was generally accompanied by the compatible/equivalent C-stage.

Clinical implementation of this new staging system (*Table 3*) reflected reliable interpretation of the progress, either a deterioration or improvement, of the clinical status following therapy. Among 220 patients, 49 patients were appropriately classified with this new staging (43 showed deterioration and 6 improvement of clinical stage). Deterioration of the clinical stage occurred despite adequate therapy in various C-stages but was more frequent among the advanced C-stage and was mainly related to decreased compliance. The majority of deterioration in the clinical staging occurred among the higher L-stage groups with 5 of 7 in C-stage I who progressed having L-stage II (4/5) or III (2/5) initially, while 10 out of the 14 in C-stage II who progressed also had a higher L-stage III (9/10) and IV (1/10). Another 11 of 13 in C-stage III who progressed also had L-stage IV or higher before treatment.

Good maintenance of the initial clinical stage throughout the 4 year follow-up period was achieved in the majority of patients (171/220) with good to excellent compliance. Further improvement in the C-stage was noticed in a limited number particularly among the excellent compliance group with good motivation reversing the C-stage. (*Table 3*). Interestingly, 2 of 3 who converted from C-stage II to I also showed a concomitant improvement in the L-stage from II to I.

DISCUSSION

Staging

In order to make the new staging system more user-friendly, many revisions and modifications were made by the multidisciplinary team of the Lymphedema Clinic to develop the current system.

The daily activity limitation (DAL) was originally included in the QOL assessment together with sepsis, but it made the interpretation of the clinical status more complicated and therefore both items were excluded from the QOL assessment. Only a limited part of the physical condition was left for the QOL assessment including physical factors of strength and movement and

restriction of duties at home and/or at work together with psychological and socioeconomical factors *(Table 2*).

This study could not separate and exclude the economic factors in the review of the QOL and learned that it has more potential to impact not only the social but also the psychological status so that the value of the economic factors was increased by the same amount as the social factors in the assessment.

Laboratory staging is also not ideal, although a separate grouping from the clinical staging has significantly reduced the confusion when both are mixed. Thus far, it seems to work better as an independent parameter supplementary to the basic clinical staging with a relatively dependable accuracy.

Clinical Implementation

This new clinical/laboratory staging assists in making rational decisions on surgical therapy. It was useful in deciding which patients failed to respond to CDT and when to choose various surgical therapies at the appropriate stage of chronic lymphedema as a supplement to the failed CDT.

When the C-stage showed progression/advancement despite maximum CDT for a minimum two year period, reconstructive surgery was added. This included lymphovenous anastomotic surgery in C-stage I and II, and free lymph node transplant surgery in C-stage II and III. Excisional surgery was added to the end stage of lymphedema in C-stage III and IV (20,21,27,28,35).

The addition of laboratory staging to this new clinical staging further improved the overall predictability of the treatment outcome, including the clinical response to the various therapies as well as progress of the disease. An advanced L-stage in the same C- stage showed a tendency to progress faster in this study. Therefore, L-stage could be used as a separate guideline to add extra modalities of treatment particularly surgical therapy 'ahead of time' to prevent further deterioration.

CONCLUSION

These two separate staging systems are potentially useful guidelines for improved management of patients with lymphedema. They appear to provide better predictability of treatment outcome and more rational decision-making for supplemental surgical therapy. Further clinical implementation is necessary to test clinical efficacy (especially for adjunct surgical therapy) and the integration of the L-staging in followup.

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