Validity of the Novel Taiwan Lymphoscintigraphy Staging and Correlation of Cheng Lymphedema Grading for Unilateral **Extremity Lymphedema**

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Objective: The aim was to validate the new Taiwan Lymphoscintigraphy Staging, correlate it with Cheng Lymphedema Grading (CLG) and evaluate the treatment outcomes of unilateral extremity lymphedema.

Background: No consensus has been reached for diagnosis and staging for patients with lymphedema among medical specialties.

Methods: We included 285 patients with unilateral extremity lymphedema using lymphoscintigraphy. Lymphoscintigraphy was correlated to clinical symptoms and signs, and classified into normal lymphatic drainage, partial obstruction, and total obstruction. Inter- and intraobserver reliability of Taiwan Lymphoscintigraphy Staging, correlation between Taiwan Lymphoscintigraphy Staging and clinical findings were conducted. Patients were categorized in "surgical" (n = 154) or "nonsurgical" (n = 131) groups for outcome evaluation.

Results: Lymphoscintigraphy found 11 patients (3.9%) with normal lymphatic drainage, 128 (44.9%) with partial obstruction, and 146 (51.2%) with total obstruction. Taiwan Lymphoscintigraphy Staging showed high interobserver agreement [intraclass correlation coefficient: 0.89 (95% confidence interval, 0.82-0.94)], and significantly correlated to computed tomography volumetric difference (r = 0.66, P < 0.001) and CLG [intraclass correlation coefficient: 0.79 (95% confidence interval 0.72-0.84)]. At a mean follow-up of 31.2 ± 2.9 months, significant improvement in the circumferential difference (from $23.9\% \pm 17.6\%$ to $14.6\% \pm 11.1\%$; P = 0.03) with a mean circumferential reduction rate of $40.4\% \pm 4.5\%$ was found in surgical group. At a mean follow-up of 26.6 ± 8.7 months, the nonsurgical group had increase

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of mean circumferential difference from $24.0\% \pm 17.2\%$ to $25.3\% \pm 19.0\%$ (P = 0.09), with a mean circumferential reduction rate was $-1.9\% \pm 13.0\%$. Conclusions: The Taiwan Lymphoscintigraphy Staging is a reliable diagnostic tool, correlated with clinical findings and CLG, aiding in the selection of the appropriate treatment to achieve favorable long-term outcomes in unilateral extremity lymphedema.

Keywords: breast cancer-related lymphedema, extremity lymphedema, lymphatic microsurgery, lymphedema diagnosis, Cheng Lymphedema Grading System, lymphoscintigraphy

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A pproximately 3 to 5 million people in the United States and 200 million worldwide suffer from extremity lymphedema; the incidence is particularly high in cancer survivors. 1-4 Ten to fifty percent patients with breast cancer might develop lymphedema of the upper extremities postaxillary lymph node dissection and radiation.^{4–7} Ten to forty-nine percent of patients might develop lower extremity lymphedema post for gynecologic cancer ablation, pelvic lymph node dissection, and subsequent radiation treatments. 8-10 A swollen limb can result from different conditions that require different treatments. 11-14 Diagnosis of lymphedema is currently based on history, physical examination, limb measurements, and imaging studies. The ideal method for disease staging to guide the most appropriate treatment is, however, controversial among different medical specialties including breast surgery, gynecology, oncology, rehabilitation, pediatrics, and plastic surgery, because of several different proposed protocols. 15 The International Society of Lymphology Staging System¹⁶ is based solely on subjective symptoms, making it prone to substantial observer bias. Imaging modalities have been suggested as useful adjuncts to International Society of Lymphology Staging to clarify the diagnosis. 17-24 The senior author (M.-H.C) developed Cheng Lymphedema Grading (CLG)^{25,26} to assess the severity of extremity lymphedema based on objective limb measurements. A great challenge in the management of lymphedema, however, consists of combining clinical and imaging findings in a comprehensive clinicoimaging grading system to guide the selection of appropriate surgical treatment.

Lymphoscintigraphy has been adopted as a first-line imaging modality to examine the functional status of the lymphatic system. $^{27-30}$ Lymphoscintigraphy enables both qualitative and quantitative analyses^{18,28,29} and is reported to be 96% to 100% sensitive in the diagnosis of lymphedema, respectively.³¹ Reliability studies of previous lymphoscintigraphy staging systems 18,32-34 are lacking, and these stages are difficult to apply in clinical practice, resulting in variable findings

Furthermore, the results of lymphoscintigraphy can vary depending on the protocol used and the image resolution of the lymphatics.20