

Factors Associated with Lower Extremity Dismorphia Caused by Lower Extremity Lymphoedema

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WHAT THIS PAPER ADDS

This is the first report that has clarified independent factors associated with lower extremity dysmorphia (LED). Indocyanine green (ICG) lymphography based leg dermal backflow (LDB) stage has the strongest association with LED, and is useful for evaluation of late stage lymphoedema with LED. Patients with higher LDB stage should be carefully followed with consideration of aggressive treatment to prevent lymphoedema progression.

Objectives: Indocyanine green (ICG) lymphography has been reported to be useful for the early diagnosis of lymphoedema. However, no study has reported the usefulness of ICG lymphography for evaluation of lymphoedema with lower extremity dysmorphia (LED). This study aimed to elucidate independent factors associated with LED in secondary lower extremity lymphoedema (LEL) patients.

Methods: This was a retrospective observational study of 268 legs of 134 secondary LEL patients. The medical charts were reviewed to obtain data of clinical demographics and ICG lymphography based severity stage (leg dermal backflow [LDB] stage). LED was defined as a leg with a LEL index of 250 or higher. Logistic regression analysis was used to identify independent factors associated with LED.

Results: LED was observed in 106 legs (39.6%). Multivariate analysis revealed that independent factors associated with LED were higher LDB stages compared with LDB stage 0 (LDB stage III; OR 17.586; 95% CI 2.055–150.482; $p = .009$) (LDB stage IV; OR 76.794; 95% CI 8.132–725.199; $p < .001$) (LDB stage V; OR 47.423; 95% CI 3.704–607.192; $p = .003$). On the other hand, inverse associations were observed in higher age (65 years or older; OR 0.409; 95% CI 0.190–0.881; $p = .022$) and higher body mass index (25 kg/m² or higher; OR 0.408; 95% CI 0.176–0.946; $p = .037$).

Conclusions: Independent factors associated with LED were elucidated. ICG lymphography based severity stage showed the strongest association with LED, and was useful for evaluation of progressed LEL with LED.

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INTRODUCTION

Lymphoedema is a debilitating oedematous disease. With the increasing number of cancer survivors, cancer related lymphoedema is becoming a major public health issue.^{1,2} In particular, lower extremity lymphoedema (LEL) patients are likely to suffer from refractory lymphoedema, because the lower extremities are directly affected by gravitational effects during standing and walking. The lower extremity becomes dysmorphic with progression of LEL, which causes significant cosmetic and functional problems.^{1,3–5} For better management of LEL, it is important for medical staff to be aware of the factors associated with lower extremity

dysmorphia (LED), which is commonly seen in progressed LEL cases.^{4–8}

Indocyanine green (ICG) lymphography clearly visualises superficial lymph flow in real time without radiation exposure, and has been applied in the evaluation of lymphoedema.^{9–14} Severity staging systems based on ICG lymphography findings have been developed for evaluation of arm, leg, genital, and facial lymphoedema, and are reported to be useful for the early diagnosis of obstructive lymphoedema.^{15–20} ICG lymphography is becoming popular among physicians and therapists who look after lymphoedema patients, especially among lymphoedema surgeons.^{21–23} ICG lymphography has become one of the most important pre-operative lymphoedema assessments, and plays an important role as an intra-operative navigation tool.^{24–30}

Although several reports have shown the usefulness of ICG lymphography for lymphoedema evaluation in the early stages of LEL and intra-operative navigation, no study has

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Table 1. LDB stage based on ICG lymphography findings.

LDB stage	ICG lymphography findings
Stage 0	Linear pattern only
Stage I	Linear pattern + Splash pattern ^a
Stage II	Linear pattern + Stardust pattern (1 region) ^b
Stage III	Linear pattern + Stardust pattern (2 regions) ^b
Stage IV	Linear pattern + Stardust pattern (3 regions) ^b
Stage V	Stardust pattern (associated with Diffuse pattern)

ICG = indocyanine green; LDB = leg dermal backflow.

^a Splash pattern is usually seen around the groin.

^b Lower extremity is divided into three regions: the thigh, the lower leg, and the foot.

reported on the usefulness of ICG lymphography for evaluation of progressed LEL with LED.^{15–19,24,26,27,29,30} Since LED is associated with cosmetic and functional morbidity and should be prevented, LED associated factors should be clarified. This study aimed to elucidate independent factors associated with LED.

MATERIALS AND METHODS

Two hundred and sixty eight limbs of 134 female patients with LEL secondary to pelvic cancer treatments who underwent bilateral pedal ICG lymphography between June 2009 and August 2014, under ethics committee approved protocol, were included in this study. All patients suffered from progressive lymphoedema secondary to pelvic lymphadenectomy refractory to compression therapy. No patient had past history of lymphoedema surgery. Clinical charts were reviewed to collect clinical and ICG lymphography findings; clinical findings when ICG lymphography was performed were used for analysis.

Recorded clinical findings included age, body mass index (BMI), duration of oedema, past history of radiotherapy, past history of cellulitis, and limb circumferences. Duration of oedema was defined as time from symptomatic oedema onset to appointment for physical examination. Circumferences were measured at and 10 cm above and below the superior edge of the patella (C_1 , C_2 , C_3), at the superior edge

of the lateral malleolus (C_4), and at the midpoint of the first metatarsal (C_5). LEL index, index for body type corrected lymphoedematous lower extremity volume evaluation, was calculated based on the following formula; LEL index = $(C_1^2 + C_2^2 + C_3^2 + C_4^2 + C_5^2)/\text{BMI}$.^{7,8} Unlike conventional volume measurement, LEL index is less influenced by body physique, and allows direct limb comparison between patients with different body physiques.⁸

ICG lymphography was performed as previously reported^{12,15,18–20}: 0.2 mL of ICG (Diagnogreen 0.25%; Daiichi Pharmaceutical, Tokyo, Japan) was injected subcutaneously in the first web space and the lateral border of the Achilles tendons in both feet. After ICG injection, circumferential fluorescent images of lymphatic drainage channels were obtained using an infrared camera system (Photodynamic Eye [PDE]; Hamamatsu Photonics K.K., Hamamatsu, Japan). ICG lymphographic images were recorded at a plateau phase of the lymphography (12–18 h after injection). Based on ICG lymphography findings, leg dermal backflow (LDB) stage was determined as previously reported (Table 1 and Figs. 1–7).^{19,31}

LED was defined as a limb with a LEL index of 250 or higher, and set as a dependent variable. LEL index of 250 was reported to be a borderline of normal limb and significantly enlarged lymphoedematous limb according to previous studies.^{7,8} Independent variables included age (<65 years vs. 65 + years), BMI (<25 kg/m² vs. 25 + kg/m²), duration of oedema (<60 months vs. 60 + months), past history of radiation (positive vs. negative), past history of leg cellulitis (positive vs. negative), and LDB stage (stage 0 vs. stage I/II/III/IV/V).^{3–6} Univariate analyses were done using chi-square test and Fisher exact probability test; chi-square test was used where all expected values were 5 or higher, whereas Fisher exact probability test was used where at least one of the expected values was lower than 5. Multivariate analysis was done using multiple logistic regression analysis. Statistical significance was defined as $p < .05$. All patients gave written consent to this study.

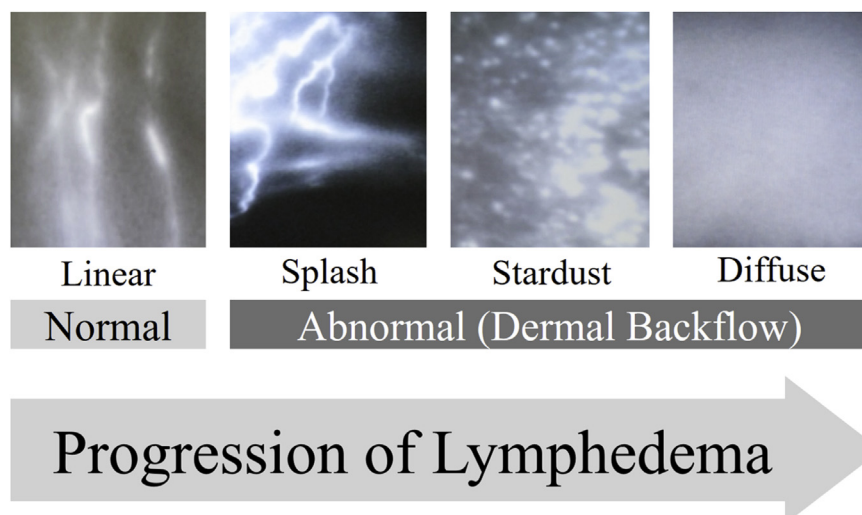


Figure 1. Indocyanine green (ICG) lymphography findings. With progression of lymphoedema, ICG lymphography finding changes from Linear pattern (left), to Splash pattern (centre left), to Stardust pattern (centre right), and finally to Diffuse pattern (right).

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