

# Association Between Access to Specialists and History of Cellulitis Among Patients with Lymphedema: Secondary Analysis Using the National LIMPRINT Database

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## Abstract

**Background:** Cellulitis is frequently encountered in patients with lymphedema despite existing prevention protocols. To resolve this issue, social aspects surrounding patients, such as communication with patients and professionals, are necessary to consider new approaches. This study aimed to clarify the association between the history of cellulitis in patients with lymphedema and access to specialists after adjustment for relevant confounding factors.

**Methods and Results:** This study was a secondary analysis of the Lymphoedema IMPact and PRevalence—INTERNational (LIMPRINT) study using a national Japanese database of adult lymphedema compiled between 2014 and 2015 ( $n=113$ ). Descriptive data were collected for patient characteristics. Multivariate logistic regression analysis was conducted to explore possible risk factors for patients having experienced cellulitis. The duration of edema ranged from <6 months (16.2%) to 10 years or longer (25.2%), with varying severity. History of cellulitis was observed in 31.9% of patients. The prevalent treatment techniques within the context of complex decongestive therapy included skin care advice (52.2%), compression garments (55.8%), exercise advice (41.6%), multilayer bandages (38.1%), cellulitis advice (49.6%), and massage (61.1%). Overall, 57.1% of patients had access to lymphedema specialists. Longer duration of lymphedema (adjusted odds ratio [AOR]=4.10,  $p=0.005$ ) and access to lymphedema specialists (AOR=0.28,  $p=0.009$ ) were significantly associated with a history of cellulitis.

**Conclusions:** A history of cellulitis in patients with lymphedema is associated with limited access to specialists. To support self-care in this patient population, reasonable consideration systems, including telehealth, should be developed to facilitate communication between specialists and patients and decrease the occurrence of cellulitis in lymphedema.

**Keywords:** lymphedema, cellulitis, self-care, communication, telehealth

## Introduction

LYMPHEDEMA IS THE STRONGEST RISK FACTOR for the development of cellulitis,<sup>1</sup> which comprises inflammation of the skin of bacterial origin mainly caused by *Staphylo-*

*coccus aureus* and group B streptococci.<sup>2,3</sup> Lymphedema and cellulitis are involved in a vicious circle of recurrent cellulitis and worsening edema.<sup>4</sup> Two studies have reported the prevalence of cellulitis in patients with lymphedema to be 49.0%<sup>5</sup> and 52.0%.<sup>6</sup> Although this is a high proportion,

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treatment with prophylactic antibiotics is recognized as an effective preventive approach.<sup>2,3</sup> The relationship between cellulitis and lymphedema was confirmed by a secondary analysis of the national database of the international epidemiological study, that is, Lymphoedema Impact and Prevalence—INTERNATIONAL (LIMPRINT).<sup>7</sup>

Cellulitis in patients with lymphedema affects physical, psychological, and social well-being. Developing cellulitis may lead to worsening edema and risk of recurrent cellulitis. Therefore, it affects not only the inflammatory cellulitis period but also the long-term health status of these patients. Prevention of cellulitis is an important clinical challenge in lymphedema management<sup>2</sup> and requires a social approach. To prevent cellulitis, control of edema and early intervention before the appearance of clinical symptoms are required.<sup>8,9</sup> In lymphedema management, patients mainly follow self-care at home.<sup>8,10,11</sup> Therefore, it is important for patients to be educated regarding appropriate complex decongestive treatment (CDT) techniques, attend regular follow-ups, be aware of the clinical signs of cellulitis to seek clinical care, and use prescribed antibiotic treatment and/or care.<sup>2,8</sup>

Health care services can only be improved with communication between patients and health care professionals. The coronavirus disease-2019 (COVID-19) pandemic situation has recently made telehealth systems attractive,<sup>12</sup> and they have been applied in many spheres of health care, including lymphedema management. Telehealth refers to the practice of caring for patients remotely when the health care provider and patient are not physically present with each other. Therefore, the effectiveness and wider applications of this new approach must be evaluated.

However, the actual communication gap between patients with lymphedema and health care professionals has not been identified. Furthermore, it is not known whether specialized care for patients with lymphedema with a history of cellulitis is available within reasonable traveling distance. The lack of accessibility could be a barrier to using telehealth systems for lymphedema management. We aimed to clarify the association between a history of cellulitis in patients with lymphedema and access to specialized care after adjusting for confounding factors using the national database of the LIMPRINT study.

## Materials and Methods

### Study design

We conducted this secondary analysis of the national database of LIMPRINT, which was a cross-sectional epidemiological study<sup>7</sup> among Japanese patients with lymphedema in 2014.<sup>5</sup>

### Patient population

In this study, the target population included patients who regularly visited lymphedema clinics. Two specialized lymphedema clinics in the rural areas of Japan were included in the LIMPRINT study. We included patients older than 18 years, who had lymphedema for longer than 3 months, and were able to understand the content of the study, as described in the information sheet, and provide informed consent. We excluded patients unwilling or unable to participate for any reason, those receiving end-of-life care, and those for whom participation was considered disadvantageous.

### Data collection

We used the data of patients and their lymphedema characteristics as registered in the LIMPRINT national database. Patient characteristics assessed included sex (male or female), age (years old), obesity (underweight, normal weight, obese, and morbidly obese), history of cellulitis (yes or no), and history of cellulitis within a year (yes or no). The following lymphedema characteristics were assessed: edema type (primary or secondary), edema location (upper extremity or lower extremity), edema duration (3–6 months, 6 months–1 year, 1–2 years, 2–5 years, 5–10 years, or  $\geq 10$  years), severity classification according to the International Society of Lymphology (ISL) (I, II, late II, or III), procedures included in CDT (physiotherapy, surgery, skin care advice, compression garment/stockings, exercise advice, antibiotics, and/or massage), and access to lymphedema specialists.

Access to lymphedema specialists was defined based on the following question: “Is treatment by a lymphedema specialist available for this patient within a reasonable traveling distance?” In Japan, specialists in lymphedema outpatient clinics mainly include medical professionals who work at lymphedema outpatient clinics or are certified in related lymphedema management.

### Statistical analysis

Categorical variables are expressed as frequencies and proportions, and continuous variables are presented as medians and interquartile ranges (IQRs).

Characteristics of patients with and without a history of cellulitis were compared. The chi-square test or Fisher’s exact test was performed for categorical variables, and Wilcoxon rank-sum test was performed for continuous variables. Factors associated with a history of cellulitis were analyzed using bivariate and multivariate logistic regression analyses. In the logistic model, the dependent variable was history of cellulitis, and the independent variables were selected among those that were clinically meaningful and/or had  $p$  values  $< 0.05$  in the bivariate analysis. Multicollinearity was examined by correlation analysis.

Statistical analysis was performed using Stata/SE 14.2 (StataCorp., College Station, TX, USA), and a  $p$  value  $< 0.05$  was selected as the level of significance.

### Ethical considerations

The study protocol was approved by the Medical Ethics Committee of Kanazawa University (#525-2). Informed consent was obtained from each patient or his or her proxies.

## Results

### Patient and lymphedema characteristics

We collected the data of 113 patients, of whom 85.7% were female. The median age was 73 (IQR 65–80) years. The proportion of lower extremity lymphedema was 82.7% ( $n=91$ ), and 98.2% of patients had secondary lymphedema. The proportion of patients who had a history of cellulitis was 31.9% ( $n=36$ ) (Table 1).

The duration of edema ranged from less than 6 months to 10 years or longer. Approximately half of the patients had lymphedema for more than 5 years, namely 5–10 years ( $n=31$ , 27.9%) and 10 years or longer ( $n=28$ , 25.2%). Lymphedema

TABLE 1. PARTICIPANT CHARACTERISTICS (N=113)

Sex (female)	96 (85.7)
Age (years)	73 (65–80)
Obesity	
Underweight	12 (11.0)
Normal weight	66 (60.6)
Obese	23 (21.2)
Morbidly obese	8 (7.3)
Edema type (secondary)	111 (98.2)
Edema location (lower extremity)	91 (82.7)
Edema duration	
<6 Months	18 (16.2)
6 Months–1 year	13 (11.7)
1–2 Years	7 (6.3)
2–5 Years	14 (12.6)
5–10 Years	31 (27.9)
10 Years or longer	28 (25.2)
ISL <sup>a</sup> classification	
Stage I	6 (8.8)
Stage II	28 (41.2)
Stage II later	32 (47.1)
Stage III	2 (2.9)
History of cellulitis (ever)	36 (31.9)
History of cellulitis (within 1 year)	15 (15.8)
Categories of treatment within CDT <sup>b</sup>	
Physiotherapy	13 (11.5)
Debulking/lipedema/lymphatic surgery	9 (8.0)
Skin care advice	59 (52.2)
Compression garment	63 (55.8)
Multilayer bandage	47 (38.1)
Exercise advice	43 (41.6)
Cellulitis advice	56 (49.6)
Antibiotics	14 (12.4)
Lymphatic drainage	69 (61.1)
Access to lymphedema specialists <sup>c</sup>	60 (57.1)

N (%), median (interquartile range).

<sup>a</sup>International Society of Lymphology.

<sup>b</sup>The sum of the percentages exceeds 100% as the treatment procedures were overlapping.

<sup>c</sup>Is treatment by a lymphedema specialist available for this patient within a reasonable traveling distance?

CDT, complex decongestive treatment; ISL, International Society of Lymphology.

severity according to the ISL classification was at approximately stage II ( $n=28$ , 41.2%) or II later ( $n=32$ , 47.1%). The administered CDT included skin care advice ( $n=59$ , 52.1%), compression bandage/stockings ( $n=63$ , 55.8%), multilayer bandages ( $n=47$ , 38.1%), lymphatic drainage ( $n=69$ , 61.1%), and exercise advice ( $n=43$ , 41.6%). To prevent and/or treat cellulitis, patients received cellulitis advice ( $n=56$ , 49.6%) and antibiotics ( $n=14$ , 12.4%). The proportion of patients having access to lymphedema specialists was 57.1% ( $n=60$ ).

#### Comparison of characteristics between patients with and without history of cellulitis

The comparison of characteristics between patients with and without cellulitis history is shown in Table 2. Access to lymphedema specialists among patients with a history of cellulitis was significantly lower ( $n=11$ , 34.4%) than that among patients without a history of cellulitis ( $n=49$ , 67.1%) ( $p=0.002$ ). Multicollinearity was not observed among the independent variables that had  $p$  values  $<0.05$ .

TABLE 2. BIVARIATE ANALYSIS FOR HISTORY OF CELLULITIS

	Cellulitis negative (N=77)	Cellulitis positive (N=36)	p
Sex (female)	62 (81.6)	34 (94.4)	0.069
Age (years)	95.5 (17.0)	70.5 (2.2)	0.319
Obesity			0.294
Underweight	8 (11.0)	4 (11.1)	
Normal weight	47 (64.4)	19 (52.8)	
Obese	15 (20.6)	8 (22.2)	
Morbidly obese	3 (4.1)	5 (13.9)	
Edema type (secondary)	77 (100.0)	34 (94.4)	0.037
Edema location (lower extremity limb)	63 (85.1)	28 (77.8)	0.338
Edema duration			0.081
<6 Months	14 (18.7)	4 (11.1)	
6 Months–1 year	11 (14.7)	2 (5.6)	
1–2 Years	7 (9.3)	0 (0.0)	
2–5 Years	10 (13.3)	4 (11.1)	
5–10 Years	18 (23.4)	13 (36.1)	
10 Years or longer	15 (19.5)	13 (36.1)	
ISL <sup>a</sup> classification			0.052
Stage I	6 (15.8)	0 (0.0)	
Stage II	16 (42.1)	12 (33.3)	
Stage II later	16 (42.1)	16 (53.3)	
Stage III	0 (0.0)	2 (6.7)	
Access to lymphedema specialists <sup>b</sup>	49 (67.1)	11 (34.4)	0.002

N (%), median (interquartile range), chi-square test, or  $t$ -test.

<sup>a</sup>International Society of Lymphology.

<sup>b</sup>Is treatment by a lymphedema specialist available for this patient within a reasonable traveling distance?

#### Association between history of cellulitis in patients with lymphedema and having access to specialists

History of cellulitis among patients with lymphedema was negatively associated with access to specialists (adjusted odds ratio [AOR]=0.28, 95% confidence interval [CI]=0.11–0.74,  $p=0.009$ ). Furthermore, a longer duration of lymphedema was significantly associated with a history of cellulitis (AOR=4.10, 95% CI=1.53–11.0,  $p=0.005$ ) (Table 3).

#### Discussion

In this secondary analysis of the LIMPRINT national database, we clarified the relationship between a history of cellulitis in patients with lymphedema and having access to specialists. Patients with a history of cellulitis had significantly less access to lymphedema specialists, thus suggesting the necessity to improve access and communication between patients with lymphedema and specialists to prevent cellulitis.

The proportion of patients having access to lymphedema specialists was more than double in the group without cellulitis history than in that with cellulitis history (67.1% vs. 34.4%,  $p=0.002$ ). After adjusting for age, ISL severity, and lymphedema duration, history of cellulitis was associated with less access to lymphedema specialists (AOR=0.28,  $p=0.009$ ). The current data are supported by those reported

TABLE 3. MULTIVARIABLE LOGISTIC REGRESSION FOR HISTORY OF CELLULITIS

<i>Variables</i>	<i>Crude odds ratio</i>	<i>95% CI</i>	<i>p</i>	<i>Adjusted odds ratio</i>	<i>95% CI</i>	<i>p</i>
Age, years	0.99	0.97–1.01	0.609	0.96	0.98–1.01	0.462
Edema duration, years	3.12	1.33–7.35	0.009	4.10	1.53–11.0	0.005
ISL classification	0.80	0.34–1.87	0.607	1.51	0.55–4.17	0.428
Access to lymphedema specialists	0.26	0.11–0.62	0.002	0.28	0.11–0.74	0.009

CI, confidence interval; ISL, International Society of Lymphology.

by a systematic review that examined self-care for lymphedema<sup>13</sup> where proper self-care was found to influence edema control and decrease the rate of recurrent cellulitis. Proper self-care is related to easy access to health care professionals and medication. Therefore, patients who have a history of cellulitis would have insufficient self-care to prevent cellulitis based on edema control.

Lymphedema management mainly consists of self-care based on CDT<sup>8</sup> and early consultation such as using antibiotics before cellulitis onset.<sup>2</sup> Some studies have suggested that patients with lymphedema need to live within a physical distance to meet with health care professionals 6 monthly,<sup>13</sup> denoting that regular visits provide consultation and educational opportunities for patients to improve their self-care behaviors. However, in the real-world setting, making changes to physical distancing seems difficult for both patients and trained professionals, as it may contribute to physical, social, and emotional aspects for patients with chronic illness.<sup>14</sup> Therefore, developing feasible and sustainable systems to support patient adherence and understanding of self-care regardless of physical distance is needed.

The COVID-19 pandemic has led to the progress of telehealth systems for medical consultations<sup>1</sup> and has helped improve the self-care behaviors of patients with chronic illness.<sup>15</sup> These technical advances would contribute to lymphedema management. In addition to visiting outpatient clinics, consultation systems such as teleconferences, videoconferences, exchanges of photographic documentation, mobile phone messages, and emails or other support mobile or computer applications could help contribute to the improvement of self-care for patients with lymphedema and decrease the number of patients developing cellulitis.

In this study, we targeted patients with lymphedema who regularly visited lymphedema outpatient clinics. Most patients had secondary lymphedema (98.2%) and ISL stage II or late II (total 88.2%). The proportion of patients with a history of cellulitis was 31.9%. Most patients in the study population had normal weight (60.1%). These characteristics were not as severe as those reported by other cited studies.<sup>6</sup> However, lymphatic abnormalities cause changes in the inflammatory status and increase the risk of developing cellulitis regardless of lymphedema severity.<sup>16–18</sup> Therefore, the health care system should be expanded to reach patients who cannot visit the outpatient department or who have lymphedema of any severity.

This study had three limitations. First, data on actual physical distance and communication details of the regular visits to the outpatient clinics were not collected. Second, cellulitis information included only the presence or absence

of history of cellulitis. The frequency of recurring cellulitis might be related to a high risk of recurrent cellulitis and less consultation environment to professionals. Finally, data were only collected from two facilities located in rural areas. The social background may differ from that in an urban area and other countries; however, we could refer to other publications to consider the clinical implementations.

Further investigations are required to consider feasible and sustainable approaches for the development of telehealth systems that will support the self-care of patients with lymphedema for the prevention of recurrent cellulitis.

## Conclusions

A history of cellulitis in patients with lymphedema is associated with limited access to specialists. To prevent cellulitis in this patient population, services such as telehealth systems can be applied to improve communication between specialists and patients and decrease episodes of cellulitis in patients with lymphedema.

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## Authors' Contributions

C.J.M. and S.M. conceived and designed the LIMPRINT study, and H.S. coordinated all procedures in Japan. J.S. arranged this investigation among the multiple facilities, and M.D. and A.S. performed the investigation. P.J.F. managed all the data and then G.N. and M.D. performed the statistical analysis. H.K. and M.K. interpreted the results based on their specialties. M.D. drafted the first article. G.N., H.S., and J.S. reviewed the article. All authors revised the article and approved the final version of the article.

## Data Sharing

The data are not publicly available or accessible.

## Author Disclosure Statement

No competing financial interests exist.

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