

Risk Factors of Lymphangitis in Patients with Lymphedema at Vajira Hospital

Chakrit Eaimkijarn¹ MD¹, Radchapoom Ketkaew² MD²

¹ Division of Plastic and Reconstructive Surgery, Department of Surgery, Faculty of Medicine Vajira Hospital, Navamindradhiraj University, Bangkok 10300, Thailand

² Department of Surgery, Phichit Hospital, Phichit 66000, Thailand

ABSTRACT

OBJECTIVE: Lymphangitis is a complication often found in lymphedema. It affects patient's quality of life, morbidity, cosmetic, and functional ability. Potential risk factors of lymphangitis were studied in lymphedema patients of Vajira Hospital.

METHODS: This study is a retrospective study. That is, data of lymphedema patients of Vajira Hospital from January 2007 to December 2018 were collected. Demographic data of patients' gender, age, underlying diseases, BMI, symptoms, site, onset, stages, causes, and types were analyzed to address risk factors using the SPSS program.

RESULTS: There were 140 patients participating, consisting of 12 males and 128 females, 78 of which had lymphangitis while the other 62 patients did not have lymphangitis. The average age of patients was 60.09 ± 12.05 years and the average body mass index (BMI) was 28.73 ± 7.81 kg/m². There were 75 patients having arm lymphedema and 65 patients having leg lymphedema. Additionally, 11 patients had primary lymphedema and 129 patients had secondary lymphedema. The most common complication of lymphedema was lymphangitis ($p < 0.001$). There was a higher chance for Campisi stages 3, 4 rather than Campisi stages 1, 2 ($p < 0.01$). The significant presence of wounds was a risk of infection ($p < 0.044$) in lymphedema patients. The average body weight of patients who had infection was estimated at 74.26 kg, which was higher than that of the non-infected patients, which was at 66.16 ± 14.67 kg ($p = 0.037$).

CONCLUSION: It is suggested to treat lymphedema since the initial stage, before the symptom reaches its late stage, to reduce the chance of lymphangitis. Besides, patients should be advised to beware of wounds and immediately receive wound treatment to lessen the rate of lymphangitis. Moreover, patients with lymphedema and higher weight are of major concerns as they have more chance to get infected.

KEYWORDS:

cellulitis, lymphangitis, lymphedema, risk factors

INTRODUCTION

Lymphedema, which is a result from the abnormality of lymphatic vessels, is divided into two categories: primary and secondary lymphedema. For primary lymphedema, it is considered a rare disease which is normally found in young children. It is supported by the prevalence

rate of 1.2 cases per 100,000 persons among people aged lower than 20 years old¹. For secondary lymphedema, it can be found in more than 90% of the whole lymphedema patients²⁻³.

Lymphedema can be caused by various factors: infection, malignant tumor, radiation, and surgery. This disease has a huge effect on the

patient's quality of life⁴⁻⁵, cosmetic and functional ability. The patients who received gynecologic cancer and breast cancer treatment⁶ have suffered from lymphedema. They also have more chances to get complications of lymphedema which are lymphangitis and lymphangiosarcoma⁷.

Lymphangitis is a result of the infection of bacteria or bacteria toxin that spreads into skin and subcutaneous tissue in lymphedema patients. The main cause of skin infections is β -hemolytic streptococci which is found in 75-90% of cellulitis cases⁸⁻¹³. For the typical symptoms of lymphangitis, there are erythema, swelling, hot sensation, and tenderness at the affected site¹⁴⁻¹⁵. The severe conditions are tachycardia and hypotension. Lymphangitis is the frequent complication in lymphedema, which is found at around 40-50% in Asian patients with lymphedema¹⁶. The common risk factors for lymphangitis are overweight, damage to the cutaneous barrier, wound, venous insufficiency, and swelling of the lower extremity¹⁷⁻¹⁸. Former research points out that lymphedema is a risk factor of the occurrence of cellulitis in which a lymphoscintigraphy study has shown the abnormality of lymphatic supply on leg, which occurs around 50-77% in patients with cellulitis¹⁹⁻²⁰. There is a systematic review and meta-analysis research that finds risk factors of getting cellulitis on leg. It is found that patients with previous cellulitis, wound, current leg ulcer, lymphedema, and body mass index of $> 30 \text{ kg/m}^2$ ²¹, have a chance for recurrent infection of up to 57%, compared to patients with post cellulitis in lymphedema²²⁻²³. Therefore, the lymphatic system plays an important role in interstitial fluid balance and immunological function²⁴. Each episode of cellulitis will destroy the lymphatic system, which can increase the risk of recurrent infection that leads to the possibility of lymphedema. For the diagnosis of lymphedema by performing lymphoscintigraphy, it is suggested to do with patients who have recurrent cellulitis²⁵⁻²⁶. This study presents risk factors of lymphangitis in patients with lymphedema at Vajira Hospital.

METHODS

Study Design

This research is a retrospective study. To illustrate, the studied data were derived from all patients with lymphedema who had received treatment in Vajira Hospital from January 1, 2007, to December 31, 2018. There were 150 subject patients, 10 of which were excluded due to uncompleted data. Thus, our subjects remained 140 patients and 78 patients had lymphangitis. In this regard, the study protocol had been approved by the Ethical Review Committee, Vajira Hospital, for research involving human subjects.

Data Collection

The data were categorized into patient characteristics (gender, age, body mass index), underlying diseases (diabetes mellitus, hypertension, cardiovascular disease), cancer stage, and characteristics of lymphedema (duration of lymphedema, Campisi clinical staging, primary lymphedema, secondary lymphedema, upper extremity lymphedema, lower extremity lymphedema). Inclusion criteria are; (1) patients aged 18 years and older; (2) patients who received diagnosis of lymphedema at arms and legs from two factors, congenital and complication from cancer surgery, in Vajira Hospital, from January 1, 2007, to December 31, 2018; (3) patients who received diagnosis of lymphangitis, had a history of admission with antibiotic use, had symptoms of redness, swelling, warm, and fever. Exclusion criteria are; (1) patients who had incomplete data recorded in Vajira Hospital; (2) death; (3) unreachable. This study was approved by research ethics committee; the COA number is 111/2561.

Statistical Analysis

The statistical analysis was done using the SPSS program for window version 22.0. The program was used for analyzing risk factors that increased the chance of lymphangitis in patients with lymphedema. Furthermore, it was also used for the multiple logistic regression analysis. The analytical results were presented using odds

ratio (OR), confident interval of 95%, and p-value (p-value < 0.05 refers to a significant value).

RESULTS

Based on 140 patients with lymphedema who received treatment in Vajira Hospital from January 1, 2007, to December 31, 2018, there were 78 patients who had lymphangitis.

According to the demographic data of **Table 1**, there were 12 males and 128 females patients with lymphedema. The average patients' age was 60.09±12.05 years. The average age of 78 patients who had lymphangitis was 60.13±12.15 years. For 62 non-infected patients, their age was 60.03±12.02 years. From all 140 patients, there were 11 patients who had primary lymphedema while the rest of 129 patients had secondary lymphedema. In case of BMI ≥ 30 kg/m², the infection group consisted of 30 patients, while the non-infection group was 15 patients (p = 0.075). The average weight of all patients was 70.70±23.79 kg. The average weight of the infection group was 74.26±28.6 kg while the non-infection group was 66.16±14.67 kg (p = 0.037).

Table 2 for patients with underlying diseases of diabetic mellitus, hypertension,

coronary artery disease, chronic kidney disease, and dyslipidemia, there were 55 infected patients while 36 patients were not infected (p = 0.125).

In addition, **Table 3** reveals that the average period of lymphedema was 5 years. For the patients who had lymphedema for more than 5 years, there were 27 patients who had lymphangitis. The number of patients with lymphedema for less than 5 years who had lymphangitis were 37 patients (p = 0.267). We based our research on Campisi stage 2010²⁷ (**table 4**). **Table 5** portrays the number of patients with lymphangitis in stages 1 to 4. There were 3, 7, 38 and 30 patients, respectively. **Table 6** reflects when Campisi staging is used to compare between early stage (stages 1, 2) and late stage (stages 3, 4). It can be statistically accounted as p < 0.001 by late stage. It had an odd ratio of 19.39 when compared between the early stage and the late stage.

The major complication of lymphedema (**table 7**) that risked lymphangitis were wound, pain, heaving, limit of motion, doing activities, abnormal skin, and difficulties in wearing clothes. Among these, the significant symptom was the occurrence of wound (p = 0.044).

Table 1 Demographic data of lymphedema patients

Characteristic	Total (n = 140)	Lymphangitis	No lymphangitis	P-value*
Age (years)	60.09 +/- 12.05	60.13 +/- 12.15	60.03 +/- 12.02	0.963
Male	12	12	0	0.001
Female	128	66	62	
Primary lymphedema	11	6	5	0.377
Secondary lymphedema	129	72	57	
Height (cm)	155.89 +/- 7.53	156.49 +/- 8.57	155.14 +/- 5.95	0.288
BMI (kg/m ²)	28.73 +/- 7.81	29.77 +/- 9.07	27.45 +/- 5.73	0.097

Abbreviations: cm, centimeter; kg, kilogram; m, meter

* P-value < 0.5 = statistically significant

Table 2 Underlying diseases of lymphedema patients

Diagnosis	Total (n = 129)
Breast cancer	74
Cervical cancer	26
Endometrial cancer	11
Ovary cancer	8
Scar contracture	1
Bladder cancer	1
Inflammation (local dermatitis)	4
Chronic venous insufficiency	2
Obesity	2

Table 3 Duration of lymphedema

Years	Lymphangitis	No lymphangitis	OR	95% CI	P- value*
< = 5	37	34	1.00		
> 5	41	28	1.55	(0.72-3.36)	0.267

* P-value < 0.5 = statistically significant

Table 4 Campisi staging 2010

Campisi stage	Features
1A	No edema but presence of lymphatic impairment; no difference in volume/consistency of edema between limbs
1B	Mild edema that is reversible with appropriate limb position
2	Persistent edema that is partially reversible with appropriate limb position
3	Persistent edema that continually becomes more severe; recurrent acute lymphangitis
4	Fibrotic lymphoedema with lymphostatic warts, column-shaped limbs
5	Elephantiasis with severe limb deformation, scleroindurative pachydermatitis, widespread lymphostatic warts

Table 5 Number of lymphedema patients with lymphangitis in stages 1 to 4

Staging of lymphangitis	Number (78)
Stage 1	3
Stage 2	7
Stage 3	38
Stage 4	30

Table 6 Comparison of Campisi stages

Staging	Lymphangitis	No lymphangitis	OR	95% CI	P- value*
Stages 1,2	8	49	1.00		
Stages 3,4	70	13	19.39	(7.31-51.40)	< 0.001

* P-value < 0.5 = statistically significant

Table 7 Complication of lymphedema

Complication	Total 140 (%)	Lymphangitis		P-value*
		Infection 78 (%)	Non-infection 62 (%)	
Cellulitis/lymphangitis	78 (55.7)	77 (98.7)	1 (1.6)	< 0.001
Wound	18 (12.9)	14 (17.9)	4 (6.5)	0.044
Pain	38 (27.1)	22 (28.2)	16 (25.8)	0.751
Heaviness	67 (47.9)	40 (51.3)	27 (43.5)	0.363
Difficulties in living	27 (19.3)	17 (21.8)	10 (16.1)	0.399
Abnormal skin	26 (18.6)	12 (15.4)	14 (22.6)	0.277
Wearing clothes problem	22 (15.7)	15 (19.2)	7 (11.3)	0.200

* P-value < 0.5 = statistically significant

DISCUSSION

This research explored the risk factors of lymphangitis in patients with lymphedema. Our study found out that hypertension, diabetes mellitus, body mass index, treatment, and duration of the occurrence of lymphedema were

not associated with the risks of lymphangitis.

The subject patients were 128 females and 12 males who had the infection. The result showed that all males with lymphedema had the infection (p = 0.001). However, there were more females with lymphedema due to breast

cancer surgery and oncological conditions. For male subjects, all of them had lymphedema from a groin node dissection procedure.

The ages with high incidence of cellulitis were 45-64 years²⁸. In this research, the patients with lymphedema were aged approximately 60.09 +/-12.05 years.

According to J. Dobner's study conducted in Austria in 2018, with respect to body weight that affects the risk of infection in children and adults, both low weight and obesity heighten the risk of infection²⁹. They state that there are other confounding factors namely malnutrition, hygienic status, and underlying diseases. However, our research found that obesity did not increase the risk of infection ($p = 0.097$). Yet, in comparison, the body weight of the infected patients, which is approximately 74.26 ± 28.6 kg, is higher than the non-infection group, which is 66.16 ± 14.67 kg ($p = 0.037$). Thus, patients with lymphangitis have more weight.

The study of Teerachisakul done in 2013 states that the duration of the occurrence of lymphedema of more than 5 years means the risk of lymphangitis³⁰. Nevertheless, our research on 'nonsignificant duration' showed that the number of sample size was too low to address the significantly different value.

We found that the risk factor of highest odd ratio was Campisi stages 3,4 [OR 19.39]. According to research on leg edema, overweight and obesity are common predictive factors of cellulitis in the normal population³¹⁻³³. For our study, we used a multiple logistic regression analysis to confirm the statistic result; high weight and Campisi staging had a significantly higher risk for infection, while lymphoscintigraphy, staging of cancer, treatment, and duration of the occurrence of lymphedema could not be concluded as a significant risk of infection due to the small number of subject patients. This can lead to further study in the future.

In this research, we observed the relation between cellulitis or lymphangitis and the underlying diseases namely hypertension,

diabetes mellitus, coronary artery disease, chronic kidney disease, and dyslipidemia. We have found out that when comparing the lymphangitis group of patients who had underlying disease to the group without lymphangitis and did not have underlying disease, the value we got was not significantly different ($p = 0.125$) even though there was some former research finding the stated relation and mentioning that diabetes mellitus was associated with cellulitis³⁴⁻³⁶. According to our finding, there was a possibility of cellulitis in the patients with diabetes mellitus which delayed wound healing especially at the lower limbs, increasing the chance for getting skin and soft tissue infection. Yet, there is former research opposing the stated hypothesis. It claims that chronic lymphedema is the factor of delayed wound healing. Also, there is a study about hypertension, stating that it is not related to the occurrence of cellulitis, but the patients with lymphedema are hypothesized to be related to hypertension³⁷⁻³⁸. We have noticed in our research that the condition of diabetes mellitus ($p = 0.767$) and hypertension ($p = 0.171$) had no relation to the risk of lymphangitis. From our study, cellulitis could be provoked by how the cutaneous barrier was disrupted, in which it could be a passage for germs to enter and colonize the area³⁹. For the clinical aspect of cellulitis, it is mostly caused by local contamination of infection⁴⁰⁻⁴¹. The treatment of risk factor for interdigital maceration, fungal nail infection, skin ulceration, and dry skin are really essential to prevent recurrent infections⁴²⁻⁴³. Skin care can prevent wounds. As accumulation of dermal and subdermal fluid and disruption of lymphatic channels are risks of the infection. The remedy of lymphedema is vital in blocking the occurrence of recurrent infections.

This study has potential limitations. Some of the data collection are based on retrospective medical records. Therefore, there could be data errors.

CONCLUSION

The goal of lymphedema's treatment is to prevent or lower the progression of the disease. Our research shows that there is the need to immediately cure the symptoms since the initial stage to forbid the disease to reach its end stage and to lower the infection.

CONFLICT OF INTEREST

None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this article.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to patients' privacy.

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