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ORIGINAL RESEARCH

Factors Predicting Treatment Adherence in Outpatients with Cancer-Related Edema: Decision Tree Analysis

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Purpose: This study aimed to determine the combination of factors associated with continuity of care in outpatients with cancer-related edema six months after the initial visit.

Patients and Methods: A total of 101 outpatients were divided into two groups: continuation (n=65) and non-continuation (n=36) groups. Details regarding age, body mass index, sex, affected extremities (upper or lower), site of edema (unilateral or bilateral), International Society of Lymphology (ISL) classification, presence of distant metastasis, and overall score on the lymphedema quality of life questionnaire (LYMQOL) were obtained before initial lymphedema care. In this study, we performed a decision tree analysis using a classification and regression tree (CART) to detect the combination of factors associated with the continuity of edema care for cancer-related edema.

Results: Significant differences were observed in the site of edema (unilateral or bilateral) and distant metastasis between the two groups. In the decision tree using CART analysis, the factors selected to influence the possibility of continuation were the side of edema as the first layer, and body mass index of 23.0 and distant metastasis (with/without) as the second layer. Outpatients with unilateral edema and a body mass index higher than 23.0 were most likely to be able to continue care. In contrast, outpatients with bilateral edema and distant metastasis had greater difficulty in continuing care.

Conclusion: In this study, factors that were suggested to influence the continuity of cancer-related edema care were the side with edema, body mass index higher than 23.0, and distant metastasis. This information may be helpful for developing care strategies and improving patient adherence.

Keywords: cancer-related edema, continuation, decision tree analysis, outpatient, predicted factor

Introduction

Cancer-related edema is a chronic disease that presents with cancer treatment.[1] Typical examples are secondary lymphedema associated with surgery for breast, gynecological, prostate, head, and neck cancers, and melanoma. It also includes edema caused by chemotherapy and radiation therapy. The prevalence of cancer related edema is difficult to ascertain because there are no universal diagnostic criteria. However, it has been estimated to range from 5% to 83% in various studies.[2–4]

Care for cancer-related edema with CDT (complete decongestive therapy) is standard practice. CDT is a fourfold conservative care that includes skin care, manual lymphatic drainage, compression therapy (consisting of compression bandages, compression sleeves, or other types of compression garments), and lymph-reducing exercises.[5] CDT is effective in reducing cancer-related edema, including lymphedema, but requires continued care to achieve its benefits.[6]

Nevertheless, it is sometimes difficult to maintain the continuity of care for patients with cancer-related edema. In Japan, care is often provided mainly on an outpatient basis for insurance reasons.[7] Therefore, more cases of dropout from care are expected compared to intensive hospitalization for the purpose of drainage. However, the dropout rates and the

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factors contributing to such dropouts have not yet been clarified. Their clarification would be useful in improving adherence to continued care and developing new care strategies for patients with cancer-related edema.

Decision tree analysis was used to identify the predictors of adherence to care in outpatients with cancer-related edema. Decision tree analysis is a data mining method that represents the items and decision criteria necessary for a decision-making model in the form of trees. Outpatients with cancer-related edema have a variety of background factors, and we considered it important to examine them using this method, which considers the combined effects of multiple factors. Therefore, the aim of this study was to use decision tree analysis to identify predictors that influence continuity of care for patients with cancer-related edema.

Materials and Methods

Study Design

This is a descriptive, observational, and cross-sectional study. Additionally, medical records were reviewed for information such as edema conditions at the time of the initial diagnosis.

Patients

One hundred and one outpatients newly diagnosed with cancer-related edema who were treated in Osaka International Cancer Institute between June 2022 and May 2023 were enrolled in this study. The inclusion criteria were diagnosis of cancer-related edema and initiation of edema care. Exclusion criteria included any difficulty in continuing care for reasons unrelated to the disease or edema, such as relocation. The reason for exclusion was that it was difficult to follow up patients who relocate to distant areas. In addition, Japan has universal healthcare insurance, which allows patients to receive uniform treatment at any medical institute. The patients were divided into two groups according to their continued status of outpatient edema care six months after the initial diagnosis. The period of 6 months was chosen based on the fact that the application for medical expense benefits for compression garments in Japan is on a six-month basis. Therefore, the first application for medical expense benefits was set as the period of focus in this study.

Data Collection

Patient characteristic data were obtained before initial lymphedema care to measure age, body mass index, sex, involved extremity (upper or lower), site of edema (unilateral or bilateral), International Society of Lymphology (ISL) classification, distant metastasis, and overall score (range; 0–10) on the Lymphedema Quality of Life Questionnaire (LYMQOL).

Care and Patients Follow Up

In this study, the diagnosis of cancer-related edema was made by a doctor who had completed a new lymphedema training course according to the Japanese lymphedema guidelines.[7] The decision to classify a patient as unsuitable for edema treatment was made based on patient-related factors such as deep vein thrombosis, heart failure, and internal organ-related edema.

Patients diagnosed with cancer-related edema underwent CDT during an outpatient visit. CDT was performed by rehabilitation physicians, physical therapists, occupational therapists, and nurses with certifications required by public medical insurance. Instructions on skin care methods and daily living using pamphlets; instructions on multilayer bandaging; selection and application of elastic garments; instructions on exercising while using the bandages; and instructions on self-lymphatic drainage were provided as needed. The duration of each intervention was 40–60 min, and the frequency of intervention was 1–3 times per month, depending on the severity of the edema. Additionally, a protocol was developed to measure the edema status in all patients at 1, 3, and six months after the initial care. This follow-up system is standard in hospitals that care for outpatients with cancer-related edema in Japan, as reported in previous studies.[6] In Japan, the maximum number of times of edema care per month is determined by medical insurance.

Statistical Analysis

Continuous variables were expressed as means ± standard deviation (SD). Categorical variables are presented as numbers and percentages. Comparisons between patient groups were performed using the Mann–Whitney *U*-test for continuous and ordinal

variables and the chi-square test for categorical variables. Next, a decision tree analysis using a classification and regression tree (CART) was conducted with the dependent variable being whether to continue edema care at six months, and the independent variables being related to cancer-related edema factors (age, body mass index, sex, involved extremity, site of edema, ISL classification, distant metastasis, and overall LYMQOL score). The decision tree was stopped by setting the minimum number of cases in the group before analysis (parent node) to 10 and the minimum number of cases in the group after analysis (child node) to five. Additionally, for sensitivity analysis, the root node factors were divided into two groups for comparison. Statistical significance was set at $P < 0.05$. All statistical analyses were performed using R version 4.2.4.

Ethical Statement

The present study was carried out following the principles of the Declaration of Helsinki regarding investigations including humans and was approved by the ethics committees of the Osaka International Cancer Institute (approval number 23234) and Morinomiya University of Medical Science (approval number 2023–142). Participants were informed about the given the opportunity to opt out through online and a paper posting.

Results

Patient Characteristics

The baseline characteristics of the patients are summarized in Table 1. Of the 101 patients, 65 (64.4%) continued cancer related edema care at six months after the initiation of care. A significant difference between the continuation and non-continuous groups was found in the sites of edema and presence of distant metastasis ($p<0.01$). No significant differences were found in other factors.

Factors for Care Continuity in Decision Tree Analysis

The results of the decision-tree analysis are shown in Figure 1. In the CART analysis, the factors selected to influence the possibility of continuation were edema, body mass index, and distant metastasis, resulting in a two-layer hierarchy. In

Table 1 Patient's Characteristics

	Total (n=101)	Continuation Group (n=65)	Non-Continuous Group (n=36)	p value
Age, y	60.6 ± 13.8	59.2 ± 13.4	63.2 ± 14.3	0.17
Body mass index, kg/m^2	22.7 ± 3.5	22.8 ± 3.5	22.7 ± 3.6	0.91
Sex				
Male	16 (15.8)	8 (12.3)	8 (22.2)	0.19
Female	85 (84.2)	57 (87.7)	28 (77.8)	
Extremity of edema				
Upper	43 (42.6)	29 (44.6)	14 (38.9)	0.57
Lower	58 (57.4)	36 (55.4)	22 (61.1)	
Site of edema				
Unilateral	64 (63.4)	48 (73.8)	16 (44.4)	< 0.01
Bilateral	37 (36.6)	17 (26.2)	20 (55.6)	
ISL classification				
I	11 (10.9)	6 (9.2)	5 (13.9)	0.22
II early	68 (67.3)	45 (69.2)	23 (63.9)	
II late	20 (19.8)	14 (21.5)	6 (16.7)	
III	2 (2.0)	0 (0.0)	2 (5.6)	
Distant metastasis				
With	30 (29.7)	13 (20.0)	17 (47.2)	< 0.01
Without	71 (70.3)	52 (80.0)	19 (52.8)	
LYMQOL				
Overall score	5.3 ± 2.1	4.9 ± 2.1	5.6 ± 2.0	0.12

Abbreviations: ISL, International Society of Lymphedema; LYMQOL, Lymphedema quality of life questionnaire.

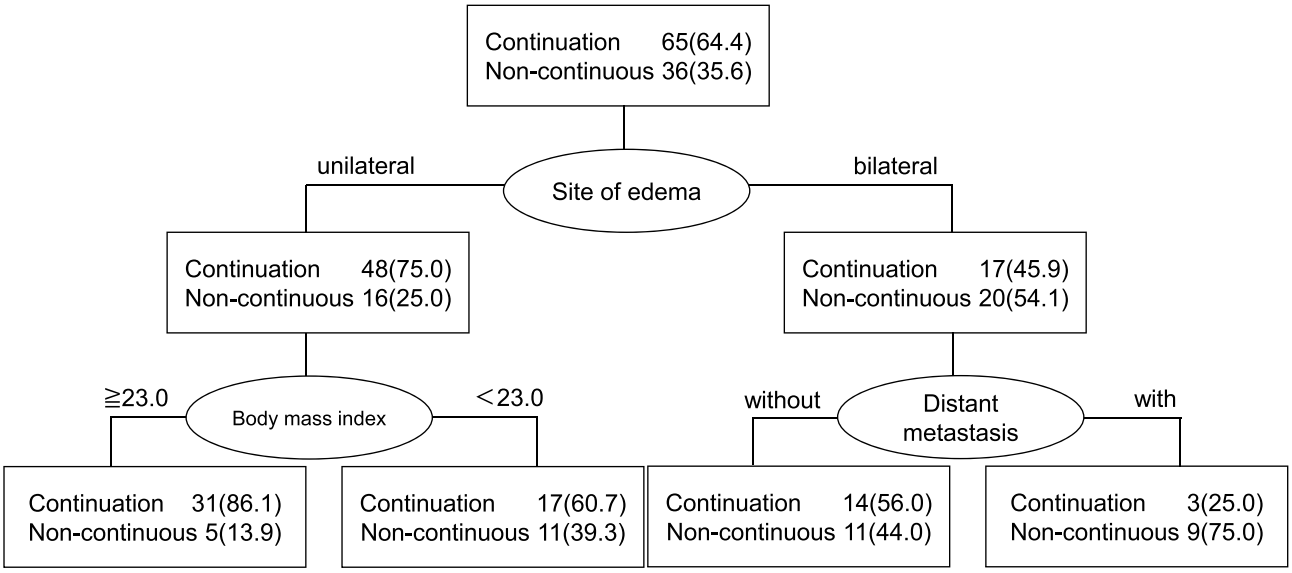

Figure 1 Decision tree analysis of 6-month care continuation in patients with cancer-related edema, n(%).

this model, the root node was on the side of edema onset, and in the unilateral edema node, the two leaves were divided by a body mass index of 23.0 kg/m^2 in the second layer. In contrast, the bilateral edematous nodes were divided into two leaves based on the presence or absence of distant metastasis in the second layer. Comparison between the two groups in the root node factor showed significant differences in extremity edema and the overall LYMQOL score. (Table 2)

Table 2 Subgroup Analysis of Root Node Factor

	Total (n=101)	Unilateral group (n=64)	Bilateral group (n=37)	p value
Continuity of edema care				
Continuation	64 (63.4)	48 (75.0)	17 (45.9)	< 0.01
Non-continuous	37 (36.6)	16 (25.0)	20 (54.1)	
Age, y	60.6 ± 13.8	60.0 ± 14.0	61.5 ± 13.5	0.61
Body mass index, kg/m^2	22.7 ± 3.5	22.7 ± 3.4	22.7 ± 3.8	0.95
Sex				
Male	16 (15.8)	6 (9.4)	10 (27.0)	0.02
Female	85 (84.2)	58 (90.6)	27 (73.0)	
Extremity of edema				
Upper	43 (42.6)	42 (65.6)	1 (2.7)	< 0.01
Lower	58 (57.4)	22 (34.4)	36 (97.3)	
ISL classification				
I	11 (10.9)	6 (9.4)	5 (13.5)	0.22
II early	68 (67.3)	43 (67.2)	25 (67.6)	
II late	20 (19.8)	14 (21.9)	6 (16.2)	
III	2 (2.0)	1 (1.6)	1 (2.7)	
Distant metastasis				
with	30 (29.7)	18 (28.1)	12 (32.4)	0.64
without	71 (70.3)	46 (71.9)	25 (67.6)	
LYMQOL				
Overall score	5.3 ± 2.1	5.7 ± 2.0	4.6 ± 2.1	0.01

Abbreviations: ISL, International Society of Lymphedema; LYMQOL, Lymphedema quality of life questionnaire.

Discussion

In this study, we report the use of decision tree analysis to identify factors that influence continuity of care six months after initial care in patients with cancer-related edema. The novelty of this study lies in its discovery of the combined patterns of continuous and dropout factors.

The combination with the highest probability of continuing outpatient care for cancer-related edema was when the site of edema developed unilaterally, and the body mass index was 23.0 or higher. A total of 86.1% of outpatients with this combination were able to continue care at six months after the initiation of care. Unilateral edema cases are considered to be breast cancer-related lymphedema[8] in the upper extremity, gynecologic,[9] or urologic cancer with unilateral lymph node dissection in the lower extremity.[10] These cancer types are generally expected to have better long-term survival.[11] Additionally, body mass index was selected, consistent with previous studies on risk factors for the development of secondary lymphedema.[12,13] The body mass index was classified by machine learning as 23.0. This index is low by global obesity standards.[14] However, it is an average index in the Japanese population included in this study.[15] In a previous study on risk factors for developing breast cancer-related lymphedema in Japanese patients, a body mass index of 23.0 was selected.[16] Since patients with a body mass index of 23.0 or higher were able to continue care, it was thought that their cognition of the need for care may have influenced this classification. This is a Japanese patient group with an above-average body mass index, and edema in this group may be more severe than that in the lower body mass index group. Therefore, the need for continuity of care and good adherence to it have led to continuity regardless of whether the patient is a responder or non-responder to care. Alternatively, the group of patients with a BMI of 23.0 or less may have had milder symptoms and may not have continued care due to completion in less than six months or self-interruption. Nevertheless, since 75.0% of outpatients with unilateral cancer-related edema were able to continue their care six months after initial of care, and it can be concluded that the majority of patients were able to apply for medical benefits for elastic garments under Japanese medical insurance, it is considered acceptable to use standard CDT.

In contrast, the combination with the highest probability of discontinuing outpatient care for cancer-related edema occurred when the site of edema developed bilateral and distant metastases. A total of 75.0% of outpatients with this combination were unable to continue at the same observation time point. Bilateral edema is considered to develop in treatment-related bilateral lower extremity edema, such as gynecologic cancer, urologic edema and more,[10] drug-induced edema, and end-stage edema. Notably, more than half of the patients who presented with bilateral edema were unable to continue care, regardless of the second layer of the decision tree, indicating that the condition may not be favorable. Furthermore, distant cancer metastasis is commonly a determinant prognostic factor.[17] Therefore, conditions with bilateral edema and distant metastasis may make it difficult to continue care in an outpatient setting for reasons such as death, end-stage disease, and decline in "performance status". Inevitably, it is necessary to develop a care strategy for these combinations of outpatients, based on the assumption that long-term continuity of care will be difficult. More specifically, this includes the provision of weak-pressure rather than strong-pressure compression garments and palliative drainage.

The current study has some limitations. First, this was a single-hospital study. Therefore, the possibility of unintentional selection bias in the selection of patients could not be fully avoided and the results may differ for outpatients in other hospitals. Second, the type of cancer diagnosis and treatment were not considered as independent factors. The purpose of this study was to predict factors related to edema at initial presentation in patients with cancer-related edema. Fourth, the sample size of 101 patients may not be large enough to generalize to all patients with cancer-related edema, especially given the diversity in cancer types and treatments. In this study, this issue was specified by the number of parent and child nodes, following the method of decision tree analysis, Finally, the time period for determining continuity of care was set at six months after the initial visit. Therefore, the results of this study may not be generalizable to a period greater than six months.

Conclusion

Our study found that the continuity of care for outpatients with cancer-related edema six months after initial care could be determined by the site of edema, body mass index, and presence of distant metastasis.

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Disclosure

The authors report no conflicts of interest in this work.

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