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Original Article

Upper limb symptoms in breast cancer survivors with lymphedema: A latent class analysis and network analysis

Aomei Shen [a,b], Nada Lukkahatai [c,*,#], Zijuan Zhang [b], Hongmeng Zhao [a], Nezar Ahmed Salim [c], Gyumin Han [d], Wanmin Qiang [a], Qian Lu [b,**,#]

[a] Tianjin Medical University Cancer Institute & Hospital, National Clinical Research Center for Cancer, Tianjin's Clinical Research Center for Cancer, Key Laboratory of Breast Cancer Prevention and Therapy, Tianjin Medical University Ministry of Education, Tianjin, China
[b] Peking University School of Nursing, Beijing, China
[c] Johns Hopkins University School of Nursing, Baltimore, MD, USA
[d] College of Nursing, Research Institute of Nursing Science, Pusan National University, Yangsan-si, Gyeongsangnam-do, Republic of Korea

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ABSTRACT

Objective: Breast cancer survivors (BCS) with lymphedema experience multiple symptoms in upper limbs that significantly impact their quality of life. The complexity of symptomology and the connection among these symptoms are unclear. This study aimed to identify upper limb symptom subgroups and symptom networks among BCS.

Methods: This secondary analysis included individuals with lymphedema (defined as an inter-limb circumference difference of $\geq$ 2 cm) from three cross-sectional studies among post-surgery BCS. Upper limb symptoms were assessed by the Breast Cancer and Lymphedema Symptom Experience Index. Descriptive analysis, latent class analysis, logistic regression analysis, and network analysis were performed.

Results: A total of 341 BCS with upper limb lymphedema were included. Swelling, heaviness and tightness were the most prevalent symptoms. Four distinct latent classes were identified: "Severe symptom" group (Class 1: 9.4%), "Movement-limitation and lymph-stasis" group (Class 2: 24.6%), "Lymph-stasis" group (Class 3: 37.5%), and "Mild symptom" group (Class 4: 28.4%). BCS with axillary lymph node dissection, radiotherapy, longer post-surgery duration, and without medical insurance were less likely to belong to the mild symptom group ($P <$ 0.001). Symptom network density decreased from Class 1 to 4. Core symptoms for each symptom network were tenderness, firmness, arm-swelling, and heaviness, respectively.

Conclusions: This study identified four distinct categories of upper limb symptoms and influencing factors among individuals with breast cancer-related lymphedema (BCRL). Our findings suggest the need to consider individualized approaches to symptom management and support for BCRL, taking into account their specific symptom clusters and associated risk factors.

Introduction

One in every five breast cancer survivors (BCS) develops breast cancer-related lymphedema (BCRL) post-cancer treatments, especially axillary surgery and radiotherapy.[1,2] The BCRL results in distressing physical symptoms (e.g., numbness, pain, tightness), functional limitations, psychological distress (e.g., altered body image, depression), ultimately impacting work capacity and overall quality of life.[3–6] The current treatment options for the BCRL include complete decongestive therapy (CDT)[7] (including bandaging, compression garments, and manual lymphatic drainage), pneumatic compression, low-level laser therapy, physical exercise, acupuncture, surgery, and so on.[1] Most clinicians base their decision to recommend the treatment options on patients' objective measurement of lymphedema, ignoring their self-reported symptoms. However, research findings imply that current lymphedema treatments, while beneficial, might not fully alleviate lymphedema-associated symptoms.[8] Currently, there are no clear guidelines on selecting the effective approach for individual patients based on their specific

* Corresponding author.
** Corresponding author.
E-mail addresses: nada.lukkahatai@jhu.edu (N. Lukkahatai), luqian@bjmu.edu.cn (Q. Lu).
# These corresponding authors contributed equally to this work.

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symptoms and circumstances. This lack of standardized intervention contributes to variability in treatment outcomes and underscores the need for better understanding and classification systems of BCRL-related symptoms to tailor treatments more precisely to each patient's needs.

Individuals with BCRL report a wide range of symptoms, including swelling, heaviness or tightness, pain or discomfort, numbness or tingling sensations, reduced range of motion, skin changes (e.g., thickening or discoloration), and impaired function in performing daily activities in the affected limb.[9–11] These symptoms can vary in severity and may not be experienced by every individual with lymphedema. Early recognition and management of these symptoms are essential for minimizing their impact on quality of life and for preventing complications associated with the condition.[8,12] The majority of current literature focuses primarily on identifying upper limb symptoms associated with BCRL,[10] and on identifying factors contributing to the development of BCRL,[9,13,14] leaving a gap in understanding the complex lymphedema symptomatology. To address this gap, latent class analysis (LCA) and network analysis offer promising approaches to identify unobserved subgroups of patients with distinct patterns of limb symptoms related to BCRL and explore symptom inter-relationships within the BCRL population, enabling the detection of clinically Meaningful symptom profiles that are not directly observable but may inform individualized symptom management strategies. These methods enable the detection of clinically Meaningful symptom profiles that are not directly observable, the characterization of specific symptom clusters and their severity, facilitating a more comprehensive understanding of BCRL symptomatology and informing targeted interventions for improved symptom management.

Our study aims to address the lack of understanding regarding the complexity and interrelationships of upper limb symptoms in BCS with lymphedema by using latent class analysis and network analysis to identify the patterns of lymphedema-related symptoms, their associations with demographic and clinical characteristics, and the core symptoms within subgroups.

Methods

Study design and participants

We conducted a secondary analysis of datasets from three cross-sectional studies, with methodology and sample details described in prior publications.[15–17] This present study report followed the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[18] Participants were aged 18 or older, diagnosed with unilateral primary breast cancer, and over one month post breast cancer surgery (mastectomy or lumpectomy). The diagnosis of BCRL was based on an ipsilateral limb circumference increase of over 2 cm compared to the contralateral limb (inter-limb circumference difference $\geq$ 2 cm). Exclusions applied to those with cancer metastasis, arm surgery history, lymphatic diseases, or cognitive impairment, and to missing data on sociodemographic and clinical variables, self-reported lymphedema symptoms, and circumferential limb measurements.

Data collection and outcomes

We extracted the following data from the datasets of the parent studies: (1) Sociodemographic and clinical data: age, education, employment, marital status, medical insurance, post-surgery years, types of breast surgery, type of lymphadenectomy, and received treatments (e.g., chemotherapy, radiotherapy, endocrine therapy); (2) Self-reported lymphedema symptoms measured by part I of the Breast Cancer and Lymphedema Symptom Experience Index (BCLE-SEI);[17] (3) Circumferential Limb Measurements. An increase in arm circumference of more than 2 cm in the affected arm compared to the unaffected arm was considered as the diagnosis of BCRL.[19]

Per the American Physical Therapy Association (APTA), lymphedema stages were categorized based on the inter-limb circumference differences: 2 cm $\leq$ inter-limb circumference differences $<$ 3 cm denoted a mild stage; 3 cm $\leq$ inter-limb circumference differences $<$ 5 cm indicated a moderate stage; and, inter-limb circumference differences $\geq$ 5 cm represented a severe stage.[14,20,21]

Statistical analysis

The SPSS 26.0, Mplus version 8.3, and R 4.2.3 were used to analyze the data. We conducted a descriptive analysis to examine the socio-demographics, clinical characteristics, and lymphedema-related symptoms frequency and severity. We conducted a latent class analysis (LCA) to identify symptom patterns based on the frequencies of 19 symptoms. To improve the result stability, we excluded five symptoms with a prevalence $<$ 20% (breast-swelling, chest wall-swelling, redness, blistering, and burning) from the LCA. Models ranging from one to six classes were assessed to determine the optimal fit. The fitness of the LCA model was determined using the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), adjusted Bayesian Information Criterion (aBIC), Lo-Mendell-Rubin (LMR), bootstrap likelihood ratio test (BLRT), and entropy. Smaller values of AIC, BIC, and aBIC indicated better fit; an entropy value closer to one (ideally $>$ 0.80) indicated improved classification.[22] The LMR and BLRT were used to compare the estimated model with a model containing k-1 class(es), with significant levels indicating a better fit.[23] The optimal number of latent classes was determined by considering both the sample size within each class (ensuring that identified classes represented at least 5% of the sample)[24] and the clinical and theoretical Meaningfulness of the findings.

We assessed differences between groups using chi-square tests, Fisher's exact tests, and one-way ANOVA (analysis of variance) to determine the association among socio-demographic and clinical factors and identified latent classes. Multinomial logistic regression analyses were performed using variables that were statistically significant in the univariable analysis, with the "Mild symptom" group specified as the reference category for all comparisons. A significance level of $P < 0.05$ was used to determine statistical significance.

Finally, the contemporaneous symptoms networks were constructed for each latent class group, with each node denoting a distinct symptom, and each edge representing the partial correlations between two nodes. Edge thickness reflected the intensity of the association between interconnected nodes. We used the *qgraph* package to visualize the network, employing the *Fruchterman-Reingold algorithm* and spring layout to generate undirected association networks. We conducted centrality analysis to calculate three centrality indices: Strength, betweenness, and closeness. Σs, the sum of the absolute values of edge weights, was employed to investigate network density.

Results

Participants' characteristics and symptom prevalence

A total of 341 breast cancer participants (from 1129 participants from 3 studies) with upper limb lymphedema were included in this analysis. Among them, 60.41% exhibited a maximum inter-limb circumference difference ranging between 2 and 5 cm, while the remaining participants displayed a maximum inter-limb circumference difference exceeding 5 cm. The majority of participants were married (n = 315, 92.4%), unemployed (n = 260, 76.2%), had medical insurance (n = 327, 95.9%), and were more than one-year post-surgery (n = 286, 83.9%). The participants' average age was 56.18 (SD = 10.46, range 32–85), with 221 (64.8%) having educational levels beyond high school. Regarding clinical characteristics, 89.4% underwent mastectomies and 10.6% received lumpectomies. Additionally, 89.7% received axillary lymph node dissection (ALND), whereas only 10.3% underwent sentinel lymph node biopsy (SLNB). Moreover, 93.0% received adjuvant chemotherapy, 62.5% received radiotherapy, and nearly half (49.9%) underwent endocrine therapy. On average, the severity and number of symptoms were 0.69 (SD = 0.55, IQR: 0.29–0.94), and 9.75 (SD = 5.50, range 0–24), respectively. The most prevalent symptoms were arm-swelling (85.0%), heaviness (76.0%), and tightness (69.8%), with arm-swelling, heaviness, and fatigue being the most severe symptoms (Mean = 1.83, SD = 1.188; Mean = 1.50, SD = 1.185; Mean = 1.21, SD = 1.074, respectively), as shown in Supplementary Table S1 and Supplementary Table S2.

Identification of latent class in BCRL-related symptoms

The result of the latent class analysis (LCA) showed all model fit indices from one-class to six-class models (Table 1). The AIC, BIC, and aBIC values consistently decreased as the number of latent classes increased, with the decrease from the four-class model to the five-class model not considerable. Notably, the BIC value increased in the five-class model. The entropy values of all models were above 0.90, with the five-class model achieving the highest entropy. However, the smallest subgroup proportion was less than 5% in the five-class model. Finally, comprehensive evaluation of the classification criteria favored the four-class model, which was selected as the optimal model due to its lowest BIC and meeting all other index criteria.

The LCA identified four latent classes with distinct symptom profiles, which were depicted in Fig. 1. Class 1 (9.4%, $n = 32$) was labeled the "Severe symptoms" group as it displayed the highest probabilities of all 19 symptoms, suggesting a complex and burdensome symptom experience. Class 2 (24.6%, $n = 84$) was characterized by elevated probabilities of symptoms related to limited limb movement and lymph stasis, and was thus named the "Movement-limitation and lymph-stasis" symptom group. Class 3 (37.5%, $n = 128$) exhibited high probabilities in lymph stasis-related symptoms (including arm-swelling, stiffness, tightness, heaviness, fibrosis, firmness, and fatigue) with less movement restriction, and was labeled "Lymph-stasis" symptom group. Class 4 (28.4%, $n = 97$) showed the lowest probabilities across all symptoms and was subsequently labeled as the "Mild symptoms" group. The overall symptom severity for participants in class one to class four was 1.58 (SD = 0.75), 1.03 (SD = 0.42), 0.64 (SD = 0.25), and 0.18 (SD = 0.14), respectively. The average numbers of symptoms for the four latent classes were 19.00 (2.49), 13.79 (2.60), 9.84 (2.33), and 3.10 (2.13), respectively.

Association between demographic and clinical factors with the latent classes

The results of the univariate analysis indicated that there were significant differences in medical insurance, post-surgery years, type of lymphadenectomy, and radiotherapy ($P < 0.05$). The four significant variables were then included as independent variables in the multinomial logistic regression by using the "Mild symptom" group as a reference. The characteristics of non-insurance, more than 5 years post-surgery, receiving SLNB, and without radiotherapy were set as references. Participants with insurance (OR: 0.141, 95% CI: 0.034–0.588), less than one-year post-surgery (OR: 0.284, 95% CI: 0.102–0.789; OR: 0.252, 95% CI: 0.109–0.583) were more likely to belong to Class 4. BCS who underwent ALND (OR: 4.296, 95% CI: 1.768–10.438; OR: 4.447, 95% CI: 2.110–9.370) and radiotherapy (OR: 2.262, 95% CI: 1.312–3.899; OR: 1.974, 95% CI: 1.226–3.179) were less likely to belong to Class 4 (Table 2).

Symptom network analysis across the latent classes

The overall density of the symptom network for Class 1 to Class 4 was 87.58, 40.59, 23.67, and 20.05, respectively. In the network for Class 1 (Severe symptoms), tenderness ($r_s = 1.051$, $r_c = 1.007$, $r_b = -0.463$) had the largest value for strength; firmness ($r_s = 0.970$, $r_c = 1.287$, $r_b = 0.637$) had the largest value for closeness, and limited-arm-movement ($r_s = -0.429$, $r_c = -0.322$, $r_b = 3.661$) had the largest value for betweenness. In the network for Class 2 (Movement-limitation and lymph-stasis), firmness ($r_s = 1.349$, $r_c = 1.517$, $r_b = 2.487$) had the largest values for strength, closeness, and betweenness. In the network for Class 3 (Lymph-stasis), arm-swelling ($r_s = 2.121$, $r_c = 1.809$, $r_b = 3.145$) had the largest values for strength, closeness, and betweenness. In the network for Class 4 (Mild symptoms), heaviness ($r_s = 1.338$, $r_c = 0.777$, $r_b = 1.106$) had the largest value for strength; arm-swelling ($r_s = 0.532$, $r_c = 1.429$, $r_b = 2.548$) had the largest values for closeness and betweenness (Fig. 2, Table 2). The core symptoms for Class 1 to Class 4 were tenderness, firmness, arm-swelling, and heaviness, respectively. Centrality indices of symptom networks for Class 1 to 4 are presented in Supplementary Fig. S1 and Supplementary Table S3.

Discussion

This study represents a significant advancement in understanding lymphedema symptom patterns among BCS through latent class analysis (LCA). Four distinct latent classes were identified: "Severe symptoms" group, "Movement-limitation and lymph-stasis" symptom group, "Lymph-stasis" symptom group, and "Mild symptoms" group. Factors such as ALND, radiotherapy, longer duration post-surgery, and lack of medical insurance were associated with decreased likelihood of belonging to the "Mild symptoms" group. Network analysis revealed a decrease in symptom network density from severe to mild symptom groups, with core symptoms including tenderness, firmness, arm-swelling, and heaviness. Prevalent symptoms among BCRL survivors aligned with previous findings, with swelling, heaviness, and tightness being most common.[10] The present study, targeting BCS with lymphedema, delineated specific symptom patterns, enhancing understanding for targeted interventions, such as stretch exercises for improving limb movements in the "Movement-limitation and lymph-stasis symptom group."

The identification of these latent classes provides insight into the heterogeneity of BCRL symptom experiences. Recognizing such unobserved subgroups allows for more precise and stratified approaches to symptom monitoring and intervention. For example, patients in Class 1 may require intensive, multidisciplinary symptom management, while those in Class 4 may benefit from low-intensity self-care education. Failure to identify and address latent symptom profiles could delay targeted interventions, potentially worsening long-term outcomes. Additionally, the observed decrease in symptom network density from Class 1 (Severe Symptoms) to Class 4 (Mild symptoms) suggests important clinical implications. High density in Class 1 reflects complex, mutually

Table 1
Comparison of latent class models' goodness of fit.

No. of Classes	No. of free parameters	Log(L)	AIC	BIC	aBIC	LMR(P)	BLRT(P)	Entropy	Latent class probability
Model 1	19	−4041.20	8120.41	8193.21	8132.94	–	–	–	1
Model 2	39	−3458.93	6995.86	7145.31	7021.59	< 0.001	< 0.001	0.903	0.642/0.358
Model 3	59	−3262.60	6643.20	6869.27	6682.12	< 0.001	< 0.001	0.918	0.390/0.317/0.293
Model 4	79	−3188.43	6534.87	6837.58	6586.98	0.013	< 0.001	0.930	0.094/0.246/0.375/0.284
Model 5	99	−3130.64	6459.28	6838.64	6524.59	0.009	< 0.001	0.943	0.387/0.097/0.038/0.243/0.235
Model 6	119	−3094.23	6426.45	6882.45	6504.95	0.364	< 0.001	0.923	0.311/0.240/0.088/0.088/0.223/0.050

AIC, Akaike information criterion; BIC, Bayesian information criterion; aBIC, Adjusted Bayesian information criterion; Log (L), log-likelihood; LMR, Lo-Mendell-Rubin; BLRT, Bootstrap likelihood ratio test.

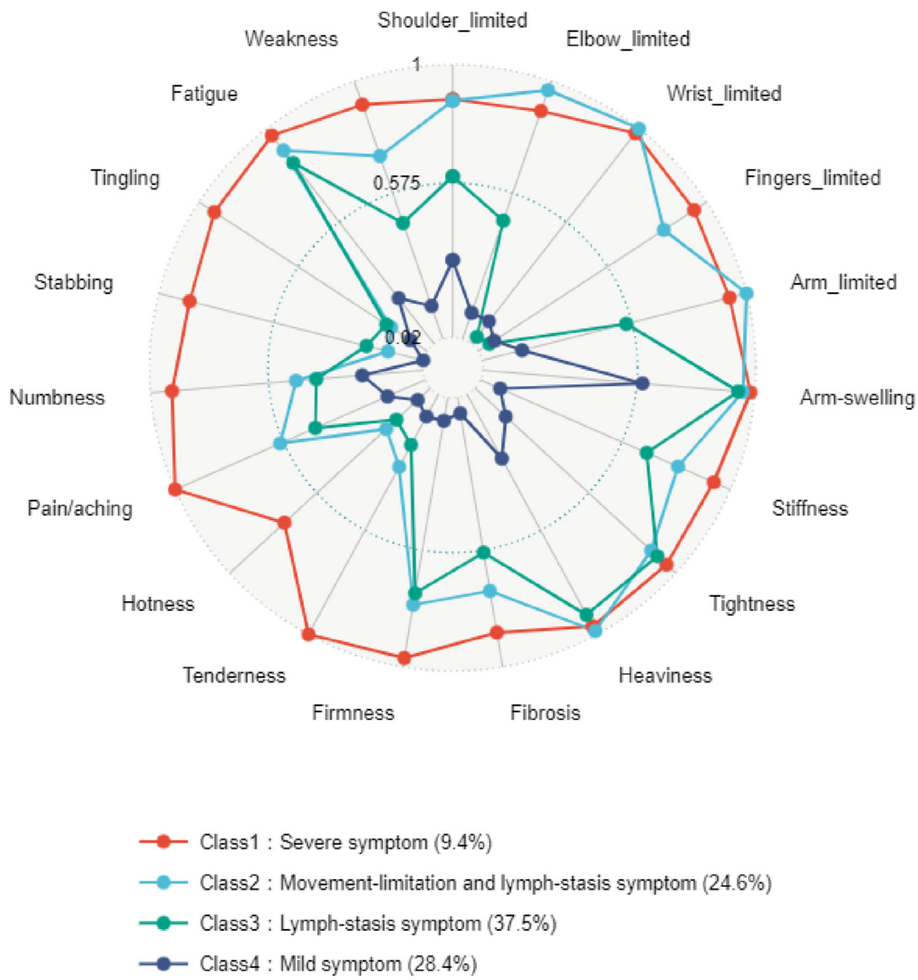

Fig. 1. Four latent classes for upper-limb symptoms of breast cancer-related lymphedema.

Table 2
Potential predictors of latent class analysis group.

Characteristics	Class 1 Severe symptom group			Class 2 Movement-limitation and lymph-stasis symptom group			Class 3 Lymph-stasis symptom group		
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Insurance									
Yes	0.141	0.034–0.588	0.007	1.325	0.253–6.932	0.739	1.085	0.257–4.584	0.911
No	ref			ref			ref		
Post-surgery years									
< 1 year	0.284	0.102–0.789	0.016	0.252	0.109–0.583	0.001	0.575	0.300–1.100	0.094
1–3 year	0.460	0.174–1.215	0.117	1.165	0.585–2.321	0.663	1.261	0.661–2.407	0.482
3–5 year	0.361	0.128–1.020	0.055	0.971	0.484–1.951	0.935	1.224	0.645–2.321	0.537
≥ 5 year	ref			ref			ref		
Type of axillary surgery									
ALND	1.910	0.665–5.481	0.229	4.296	1.768–10.438	0.001	4.447	2.110–9.370	< 0.001
SLNB	ref			ref			ref		
Radiotherapy									
Yes	1.430	0.680–3.006	0.345	2.262	1.312–3.899	0.003	1.974	1.226–3.179	0.005
No	ref			ref			ref		

SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; OR, odds ratio; CI, confidence interval.

reinforcing symptom interactions, indicating greater burden and functional impairment that may require comprehensive, multi-symptom interventions. As network density declined across Classes 2 to 4, symptoms appear more independent, potentially reflecting milder clinical states, effective management, or patient adaptation. This trend may be influenced by physiological improvements (e.g., reduced lymphatic dysfunction) or behavioral factors (e.g., enhanced self-care). Clinically, lower-density networks imply that targeted, symptom-specific interventions could effectively manage symptoms in patients with less severe presentations, whereas high-density networks in severe cases likely require integrated, multidimensional approaches.

Consistent with a previous study,[25] we observed a gradual increase in both the overall symptom severity and the average number of symptoms across classes 1 to 4. Despite common assumptions associating lymphedema symptoms with its severity, our findings showed no significant differences in lymphedema stage (Mild-to-moderate stage vs. Severe

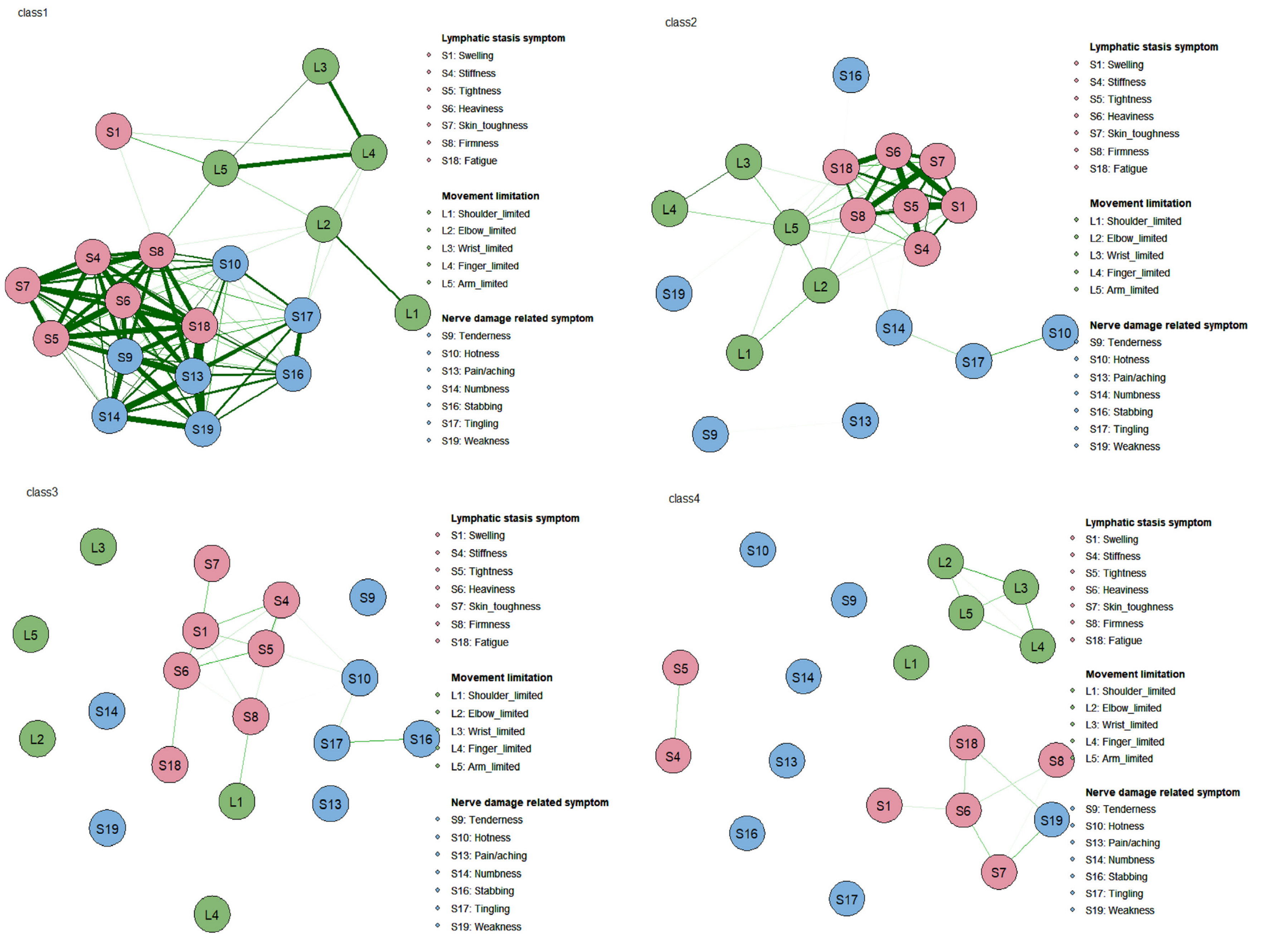

Fig. 2. Symptom networks of the four latent class groups. (a) Class 1 - Severe symptom group (30.2%); (b) Class 2 - Movement-limitation and lymph-stasis symptom group (40.2%); (c) Class 3 - Lymph-stasis symptom group (5.0%); (d) Class 4 - Mild symptom group (24.6%).

stage) among various symptom classes. This suggests that categorizing lymphedema patients solely based on symptom prevalence may not accurately reflect the progression of lymphedema. While assessing self-reported symptoms is widely accepted as a practical method for evaluating lymphedema, it is essential to recognize that symptoms are subjective experiences that include both the number of occurrences and the severity.

Our findings support the role of demographic and clinical factors in determining membership within latent symptom classes. Specifically, we observed that radiotherapy and ALND, recognized as risk factors for "Movement-limitation and lymph-stasis" symptom group (class 2) and "Lymph-stasis" symptom group (class 3), were associated with more invasive treatments that can lead to extensive tissue, nerve, vessel, and lymphatic damage, consequently exacerbating lymphedema symptoms. Additionally, participants in the first-year post-surgery were more likely to be in the "Mild symptom" group, possibly due to the predominant manifestation of BCRL within the initial two to three years following surgery.[26] Medical insurance emerged as a protective factor for the "Severe symptom" group, highlighting the role of socioeconomic disparities in symptom burden. Individuals with limited insurance coverage or lower socioeconomic status may experience restricted access to timely diagnosis, effective rehabilitation services, symptom management resources, and adequate social support, which can contribute to greater symptom severity and persistence in BCRL. However, further demonstration is required as no similar reports were found.

Symptom networks provide a novel approach to understanding lymphedema symptomatology, allowing visualization and comprehension of microlevel interactions among lymphedema symptoms.[27] Network density is a predictive factor for identifying populations prone to comorbidities, and individuals with denser networks may exhibit lower treatment responsiveness.[28] Our study revealed a decreasing trend in network density from the "Severe symptom" group to the "Mild symptom" group. This suggests that the "Severe Symptom" group may experience less favorable outcomes with standard symptom management strategies, highlighting the need for heightened attention and intensive interventions for survivors in this group. Results from network analysis identified tenderness, firmness, swelling, and heaviness as core symptoms for Class 1 to Class 4, respectively. These core symptoms exert the most significant influence on the entire network, making them potential targets for focused intervention.[29] Identifying high-risk populations within each lymphedema symptom subgroup allows efficient targeting for symptom management, aiding in the development of tailored interventions.[27] We recommend addressing upper limb symptoms alongside lymphedema treatments, and exploring effective strategies for specific core symptoms. For instance, some complementary therapies such as acupuncture or moxibustion have demonstrated efficacy in alleviating upper arm symptoms.[30,31] Future research should focus on developing interventions to improve these specific core symptoms.

Strengths and limitations

While our study contributes novel insights into the dynamics of upper limb symptoms in BCS with lymphedema through the innovative use of latent class analysis (LCA) and network analysis, several limitations must be acknowledged. First, our study's reliance on secondary data analysis constrained the inclusion of additional variables such as tumor stage or body mass index, potentially impacting the differentiation of latent classes. Additionally, restricted sample sizes within specific groups, such as non-insured individuals, may have compromised the statistical power of our analyses. Moreover, limitations within the original dataset hindered the conversion of interlimb circumference differences into limb volume, potentially affecting the accuracy of lymphedema diagnosis. Second, potential biases inherent in the parent studies from which the data were derived could have influenced the reliability and validity of our findings. The lack of control over the original data collection process introduces the possibility of biases or inconsistencies that could have affected subsequent analyses. These limitations underscore the need for further research with larger sample sizes and controlled designs to validate and build upon our findings.

Conclusions

In conclusion, our study identified four distinct upper limb symptom subgroups among breast cancer survivors with lymphedema: the severe symptom group, movement-limitation and lymph-stasis symptom group, lymph-stasis symptom group, and mild symptom group. Additionally, significant associations were uncovered between radiotherapy, ALND, insurance status, post-surgery duration, and these unique symptom subgroups. Moreover, tenderness, firmness, swelling, and heaviness were identified as core symptoms for each respective subgroup. These findings underscore the importance of heightened attention to assessing and managing lymphedema-related upper limb symptoms among BCS. The identified symptom profiles and core symptoms offer valuable insights that can aid health care providers in efficiently evaluating patients' symptom patterns and directing interventions toward addressing these core symptoms, ultimately improving paticent care and quality of life.

CRediT authorship contribution statement

Aomei Shen: Conceptualization, Methodology, Data analysis Writing – Original Draft. **Qian Lu**: Conceptualization, Supervision, Funding Acquisition. **Nada Lukkahatai**: Supervision, Writing – Review & Editing. **Zijuan Zhang**: Software, Validation. **Hongmeng Zhao**: Writing – Review & Editing. **Nezar Ahmed Salim**: Writing – Review & Editing. **Gyumin Han**: Writing – Review & Editing. **Wanmin Qiang**: Supervision. All authors contributed to reviewing and providing comments on earlier manuscript versions. The final manuscript was reviewed, read, and approved by all authors.

Ethics statement

Ethics statement is not required for the current secondary study. The protocols of the three parent studies were approved by the Biomedical Ethics Committee of Peking University (Approval Nos. IRB00001052-11051, IRB00001052-15073, and IRB00001052-21123). All procedures were in accordance with the Helsinki Declaration. Informed consents were obtained from all participants.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author, QL. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

Declaration of generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

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role in considering the study design or in the collection, analysis, interpretation of data, writing of the report, or decision to submit the article for publication.

Declaration of competing interest

The authors declare no conflict of interest. The corresponding author, Prof. Qian Lu, is an editorial board member of *Asia–Pacific Journal of Oncology Nursing*. The article was subject to the journal's standard procedures, with peer review handled independently of Prof. Lu and their research groups.

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Appendix A. Supplementary data

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