Latent Class Analysis of Lymphedema Symptoms and Phenotypic Characterization

Mei R. Fu, PhD, RN, FAAN
Rory Meyers College of Nursing, New York University, New York, NY, USA

Purpose:

Attaining the best health possible after breast cancer treatment remains an ongoing challenge since more than 50% of breast cancer survivors suffer from daily distressing symptoms related to lymphedema [hereafter, lymphedema symptoms] even years after cancer treatment. Lymphedema, a chronic abnormal accumulation of lymph fluid in the ipsilateral body area or upper limb, is a chronic condition for more than 40% of 3.1 million breast cancer survivors in the United States. Currently, no surgical or medical interventions at present can cure lymphedema. Lymphedema has been linked to detrimental patient-centered outcomes, such as disability and psychological distress. Lymphedema symptoms are complex in multitude that encompasses more than 20 symptom of arm/hand swelling, breast swelling, chest wall swelling, heaviness, firmness, tightness, stiffness, pain/aching/soreness, tenderness, fibrosis, hotness, redness, numbness, burning, stabbing, tingling, arm fatigue, arm weakness, and limited movement in shoulder, arm, elbow, wrist/fingers. Little is known about lymphedema symptoms and their association with phenotypic characterization of demographics and clinical factors, physiological outcomes of limb volume and lymph fluid level, and patient-centered outcomes of daily function, social, and affective wellbeing. The purpose of this study was to determine whether latent class analysis (LCA) would aid in the identification of lymphedema symptom patterns and associations with phenotypic characterization of demographics and clinical factors, physiological outcomes of limb volume and lymph fluid level, and patient-centered outcomes of daily function, social, and affective wellbeing.

Methods

A prospective, descriptive and repeated-measure design was used to enroll 140 women at pre-surgery and followed at 4-8 weeks and 12 months post-surgery. Lymphedema symptoms and patient-centered outcomes of daily function, social, and affective wellbeing were evaluated using a reliable and valid instrument. Limb volume was measured by a perometer and lymph fluid by a bioimpedance device.

Latent class analysis (LCA) was used to identify classes of lymphedema symptoms to better understand patterns of lymphedema symptoms and associations with phenotypic characterization of demographics and clinical factors, physiological outcomes of limb volume and lymph fluid level, and patient-centered outcomes of daily function, social, and affective wellbeing. Logistic regressions were used to explore the association of latent class of lymphedema symptoms with categorical demographic and clinical variables. ANOVAs and post-hoc pairwise comparison test with a Bonferroni correction for multiple comparisons at the 5% alpha level were used to explore the association of latent class of lymphedema symptoms with limb volume and lymph fluid level as well as patient-centered outcomes of daily function, social, and affective wellbeing.

Results

LCA identified three distinct lymphedema symptom classes at 12-month post-surgery: (1) a low symptom class (mean 1.2 symptoms) consisting primarily of numbness (29%) and tingling (28%); (2) a moderate symptom class (mean 5.9 symptoms), with higher than average prevalence of the arm tightness (58%) and the arm heaviness (44%); and (3) a severe symptom class (mean 14.0 symptoms), with a higher than average prevalence of the limited limb mobility, fluid accumulation and the pain/discomfort symptom factors. The moderate symptom class was the largest (44%), followed by the low symptom class (39%) and the severe symptom class (16%).
Lower level of education, having chemotherapy and radiation therapy were associated with moderate and severe symptom class. The moderate and severe symptom classes were associated with clinical phenotypes of higher lymph volume change and higher bioimpedance ratio (L-Dex). Patients in the severe symptom class are more likely to have a greater than 5% lymph volume increase (a criterion for a diagnosis of lymphedema) between post-surgery and pre-surgery (p = 0.024) and between 12-month follow-up and pre-surgery (p < 0.001). In terms of lymph fluid levels, patients in the severe symptom class are more likely to have a greater than 7.1 L-Dex bioimpedance ratio (a criterion for a diagnosis of lymphedema) at post-surgery (p = 0.037) and 12-month follow-up (p < 0.001).

Poor daily living, social and affective wellbeing are associated with moderate and severe symptom classes in terms of daily living, affective wellbeing, self-perception, sleep disturbance, working outside the home and days absent from work. While patients in the severe symptom class had severe impairment of patient-centered outcomes, it is important to note that the moderate symptom group had significant impairment in comparison with low symptom group in terms of patient-centered outcomes: daily living, affective wellbeing, self-perception, sleep disturbance, working outside the home and days absent from work.

Conclusion

LCA incorporating an overall count of different lymphedema symptoms detected three distinct lymphedema symptom profiles. The data illustrates that the complexity of lymphedema symptom factors that must be accounted for, both in advancing the symptom science in understanding the complexity and heterogeneity of lymphedema symptomatology to predict patient subtypes for impaired physiological outcomes of limb volume and lymph fluid level as well as impaired patient-centered outcomes of daily function, social and affective wellbeing. Early intervention for lymphedema symptoms are needed for prevent patients in the moderate symptom class from progressing into severe symptom class since even the moderate symptom class has significant impairment in terms of patient-centered outcomes of daily living, emotional wellbeing, self-perception, sleep disturbance, working outside the home and days absent from work.

Title:
Latent Class Analysis of Lymphedema Symptoms and Phenotypic Characterization

Symposium

Keywords:
breast cancer, latent class analysis and symptoms

References:


Abstract Summary:
Latent class analysis is able to identify three distinct lymphedema symptom classes with lower, moderate and severe symptom class. Identification of symptom classes is a priority to predict high-risk populations for physiologic outcomes of limb volume and lymph fluid level as well as daily function, social and affective wellbeing.

Content Outline:
1. Objectives
   1. Obtain knowledge about the complex cancer-related symptoms and phenotypic characterization.
   2. Obtain knowledge about latent class analysis for identifying symptom classes.
2. Background and Significance
   1. Attaining the best health possible after breast cancer treatment remains an ongoing challenge since more than 50% of breast cancer survivors suffer from daily distressing symptoms related to lymphedema [hereafter, lymphedema symptoms] even years after cancer treatment.
   2. Lymphedema, a chronic abnormal accumulation of lymph fluid in the ipsilateral body area or upper limb, is a chronic condition for more than 40% of 3.1 million breast cancer survivors in the United States.
   3. Currently, no surgical or medical interventions at present can cure lymphedema. Lymphedema has been linked to detrimental patient-centered outcomes, such as disability and psychological distress.
   4. Lymphedema symptoms are complex in multitude that encompasses more than 20 symptom of arm/hand swelling, breast swelling, chest wall swelling, heaviness, firmness, tightness, stiffness, pain/aching/soreness, tenderness, fibrosis, hotness, redness, numbness, burning, stabbing, tingling, arm fatigue, arm weakness, and limited movement in shoulder, arm, elbow, wrist/fingers.
   5. Little is known about lymphedema symptoms and their association with phenotypic characterization of demographics and clinical factors, physiologic outcomes of limb volume and lymph fluid level, and patient-centered outcomes of daily function, social, and affective wellbeing.
3. Purpose of the Study and Conceptual Framework
1. The purpose of this study was to determine whether latent class analysis (LCA) would aid in the identification of lymphedema symptom patterns and associations with phenotypic characterization of demographics and clinical factors, physiological outcomes of limb volume and lymph fluid level, and patient-centered outcomes of daily function, social, and affective wellbeing.

4. Setting/Sample
   1. 140 women with breast cancer.

5. Design/Methods
   1. A prospective, descriptive and repeated-measure design.
   2. Assess pre-surgery and followed at 4-8 weeks and 12 months post-surgery.
   3. Latent class analysis (LCA) was used to identify classes of lymphedema symptoms
   4. Logistic regressions were used to explore the association of latent class of lymphedema symptoms with categorical demographic and clinical variables.

6. Findings/Results
   1. LCA identified three distinct lymphedema symptom classes at 12-month post-surgery.
   2. Lower level of education, having chemotherapy and radiation therapy were associated with moderate and severe symptom class.
   3. Poor daily living, social and affective wellbeing are associated with moderate and severe symptom classes in terms of daily living, affective wellbeing, self-perception, sleep disturbance, working outside the home and days absent from work.

7. Conclusion
   1. LCA incorporating an overall count of different lymphedema symptoms detected three distinct lymphedema symptom profiles.
   2. The data illustrates that the complexity of lymphedema symptom factors that must be accounted for.

First Primary Presenting Author

**Primary Presenting Author**
Mei R. Fu, PhD, RN, FAAN
New York University
Rory Meyers College of Nursing
Tenured Associate Professor
New York NY
USA

**Professional Experience:** Dr. Mei R. Fu’s scientific focus has been on symptoms and management of chronic illnesses. Her research incorporates qualitative and quantitative methods, genomic and biomarker approaches and cutting edge measurement technology as well as mHealth and innovative behavioral interventions. Her research has been supported by National Institute of Health (NIH), the Oncology Nursing Society (ONS), the Hartford Institute of Geriatric Nursing, the Avon Foundation, the Vital Fund, Judges and Lawyers for Breast Cancer Alert, Pfizer Independent Learning and Change grant and Association of Chinese American Physicians. cutting edge measurement technology as well as innovative behavioral interventions. Her research has been supported by National Institute of Health (NIH), the Oncology Nursing Society (ONS), the Hartford Institute of Geriatric Nursing, the Avon Foundation, the Vital Fund, Judges and Lawyers for Breast Cancer Alert, Pfizer Independent Learning and Change grant.

**Author Summary:** Dr. Mei R. Fu is an internationally and nationally well-known nurse scientist and outstanding researcher and educator. She is a Tenured Associate Professor of Nursing at New York University. She has over 100 high quality publications in peer-reviewed journals, book chapters, and professional publications and her work has been cited more than 1,250 times. She has over 200 invited or peer reviewed keynote and podium presentations at international, national, regional, and local conferences.