Original Article

Distinct Patterns of Conjoint Symptom Distress and Functional Impairment in the Last Year of Life Predict Terminally Ill Cancer Patients' Survival

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Abstract

Context/Objectives. Our study addressed important knowledge gaps about trajectories of distinct conjoint symptom-functional states, that is, patterns for different levels of combined symptom distress and functional impairment, over cancer patients' last year and their ability to predict survival.

Methods. We identified distinct symptom-functional states and explored their changes over 317 terminally ill cancer patients' last year by a transition model using hidden Markov modeling. These distinct symptom-functional states' ability to predict current survival probability, measured in the previous assessment, was evaluated by multivariate Cox regression models.

Results. We identified five worsening, conjoint symptom-functional states: 1) mild symptom distress with high functioning, 2) moderate symptom distress with mild functional impairment, 3) severe symptom distress with moderate functional impairment, 4) moderate symptom distress with severe functional impairment, and 5) profound symptom distress and functional impairment. Trajectories of these five states differed substantially by direction (downward vs. upward) and speed. Participants in States 1−4 had substantially lower risk of subsequent death than those in State 5 (adjusted hazard ratios [95% CI] ranged from 0.048 [0.028−0.081] to 0.434 [0.316−0.579]). The risk of subsequent death differed significantly between patients in any two distinct symptom-functional states, except between those in States 3 and 4.

Conclusion. Our identification of five distinct symptom-functional states and their unique transition patterns and prediction of mortality provides all stakeholders with guides for end-of-life care. Goals of end-of-life care should change toward palliative care and effective symptom management for patients with at least moderate symptom distress and substantial functional impairment. J Pain Symptom Manage 2018;■:■−■. © *2018 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.*

Key Words

Symptom distress, functional impairment, survival, terminally ill cancer, end-of-life care

Introduction

Symptom distress and functional impairment, which are common manifestations of terminal illness for cancer patients,[1,2] each contribute significantly and meaningfully to patients' well-being at end of life (EOL). Symptom distress and functional impairment are associated with increased mortality,[2−6] hospice admissions,[7] and use of home care services,[8] resulting in enormous emotional, quality of life, and financial burdens to terminally ill cancer patients,[1,9,10] their

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families,[11,12] and society at large.[13,14] These stakeholders and health care providers would benefit greatly from understanding the trajectories of symptom distress and functional impairment over the dying process and how they are associated with survival. Indeed, promptly identifying physical deterioration as a sign of approaching death can inform decisions about choosing/providing value-based EOL care, for example, changing the goal of care from curative to palliative and referring patients to hospice earlier in the dying process.

A well-defined trajectory toward death, marked by increasing symptom distress and steady functional decline, has long been identified for cancer patients.[1,7,15–17] However, for a sizable minority of cancer patients, the course of increasing symptom distress and functional decline at EOL does not follow a predictable pattern, with considerable heterogeneity observed.[3,7,17,18] Rather than examining differences in patterns of symptom distress and functional impairment as death approaches, most research has instead focused on average ratings of symptom distress[1,3,7] or functional impairment[1,3,7,16,19] at EOL, which oversimplifies complex growth patterns of change. Furthermore, the few studies on patterns of symptom distress[17] and functional impairment[4,20,21] have examined individual trajectories of increasing symptom distress and functional decline before cancer patients' death despite evidence that symptom distress and functional decline do not necessarily increase in parallel at EOL.[2,18,22] However, patterns of symptom distress and functional impairment have not been studied conjointly over time for adult patients at EOL, but only for pediatric cancer patients.[22] Longitudinally examining the distinct patterns of conjoint symptom distress and functional impairment allows us to address the heterogeneity in changes of both. Furthermore, longitudinally evaluating the prognostic value of symptom distress or functional impairment increases precision in survival prediction more than traditional prognostic estimates based only on a single assessment,[23,24] but this conclusion warrants validation for distinct patterns of conjoint symptom distress and functional impairment. Therefore, the purposes of this study were to identify distinct patterns of conjoint symptom distress and functional impairment and their courses over terminally ill cancer patients' last year and to longitudinally evaluate the predictive ability of these distinct symptom-functional states on cancer patients' survival since their terminal illness was first recognized.

Methods

Design and Sample

This secondary analysis used data from a longitudinal study on the quality of EOL care in a convenience sample of terminally ill Taiwanese cancer patients recruited in 2009–2012 and followed through 2015. Methodological details are available elsewhere.[25] Briefly, adult cancer patients were referred by their oncologist when he/she recognized their disease at a terminal stage, that is, progressive and unresponsive to curative treatments. Participants were interviewed by experienced oncology nurses approximately every two weeks when they were hospitalized or returned for clinic visits until they declined to participate or died. Our report is consistent with the STROBE reporting guidelines.

Measurements

Physical symptom distress was measured by the 13-item Symptom Distress Scale (SDS).[26] SDS measures common symptoms of cancer patients, that is, pain, dyspnea, nausea/vomiting, anorexia, constipation, and insomnia. Scores range from 13 to 65, with higher scores indicating greater symptom distress.

Functional impairment was measured by the 10-item Enforced Social Dependency Scale (ESDS).[27] Total ESDS scores range from 10 to 51. Higher ESDS scores reflect greater dependence on help for personal and social functioning.

Sociodemographics and disease characteristics were collected from medical records and supplemented with patient reports, if necessary. Comorbidity was calculated by the Deyo-Charlson comorbidity index,[28] categorized as 0, 1, 2, or ≥3 comorbid conditions.

Statistical Analysis

Descriptive statistics were used to characterize study participants at baseline. Chi-square and independent t-tests were used to compare baseline characteristics of the study sample and participants not included in the analysis.

Distinct symptom-functional states and their changes between consecutive time points were identified and examined, respectively, using a transition model[29] by hidden Markov modeling (HMM).[30] HMM simultaneously examined symptom distress and functional impairment as conjoint symptom-functional patterns/states, estimated transition probabilities between states (probabilities of shifting from one state to another between consecutive time points), and described dynamic changes in patients' conjoint symptom-functional states in the last year. Data were analyzed using Latent GOLD 5.0 (Statistical Innovations Inc., Belmont, MA).[31]

HMM first assigned participants to a finite number of mutually exclusive conjoint symptom-functional states based on shared characteristics that discriminate among members of each state. Estimating conjoint symptom-functional states permits simultaneous examination of the linkage between these two important