Original Article

Repeated Assessments of Symptom Severity Improve Predictions for Risk of Death Among Patients With Cancer

Rinku Sutradhar, PhD, Clare Atzema, MD, Hsien Seow, PhD, Craig Earle, MD, Joan Porter, MSc, and Lisa Barbera, MD

Institute for Clinical Evaluative Sciences (R.S., C.A., H.S., C.E., J.P., L.B.), Toronto; Department of Biostatistics (R.S.), Dalla Lana School of Public Health, University of Toronto, Toronto; Department of Oncology (H.S.) and Supportive Cancer Care Research Unit (H.S.), McMaster University, Hamilton; and Department of Medicine (C.A., C.E.), Department of Radiation Oncology (L.B.), and Institute of Health Policy, Management and Evaluation (R.S., L.B.), University of Toronto, Toronto, Ontario, Canada

Abstract

Context. Although prior studies show the importance of self-reported symptom scores as predictors of cancer survival, most are based on scores recorded at a single point in time.

Objectives. To show that information on repeated assessments of symptom severity improves predictions for risk of death and to use updated symptom information for determining whether worsening of symptom scores is associated with a higher hazard of death.

Methods. This was a province-based longitudinal study of adult outpatients who had a cancer diagnosis and had assessments of symptom severity. We implemented a time-to-death Cox model with a time-varying covariate for each symptom to account for changing symptom scores over time. This model was compared with that using only a time-fixed (baseline) covariate for each symptom. The regression coefficients of each model were derived based on a randomly selected 60% of patients, and then, the predictive performance of each model was assessed via concordance probabilities when applied to the remaining 40% of patients.

Results. This study had 66,112 patients diagnosed with cancer and more than 310,000 assessments of symptoms. The use of repeated assessments of symptom scores improved predictions for risk of death compared with using only baseline symptom scores. Increased pain and fatigue and reduced appetite were the strongest predictors for death.

Conclusion. If available, researchers should consider including changing information on symptom scores, as opposed to only baseline information on symptom scores, when examining hazard of death among patients with cancer. Worsening of pain, fatigue, and appetite may be a flag for impending

Address correspondence to: Rinku Sutradhar, PhD, Institute for Clinical Evaluative Sciences, 2075 Bayview Avenue, Toronto, ON M4N 3M5, Canada. E-mail: rinku.sutradhar@ices.on.ca

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Key Words
Symptom scores, longitudinal data, Cox model, time-varying covariates, concordance probability

Introduction

Symptom severity is an important measure for patients with cancer and plays an essential role when monitoring the quality of cancer care. Self-reported symptom measures can document the patient experience, and symptom management across the disease trajectory can improve quality of life.[1,2] Symptom measures also have been shown to be predictors of cancer survival;[3,4] however, most studies examining survival have only used symptom scores recorded at a baseline time, such as at diagnosis, at hospice admission, or at enrollment in a clinical trial.[4,5] Other studies using symptom scores are limited by their focus on only palliative inpatient populations[6–8] or disadvantaged by small sample sizes or cross-sectional designs.[5,9]

As symptom severity changes over time and is known to deteriorate rapidly as patients approach death,[3,10] our first aim is to show that incorporating symptom scores from repeated assessments via time-varying covariates in a survival model improves the ability to predict risk of death compared with incorporating only fixed symptom scores taken at baseline (time of cancer diagnosis). To our knowledge, this has never been shown in the clinical literature and should serve as a guide when including symptom information for modeling hazard of death. The second aim is to use the survival model with time-varying symptom scores to understand the association between symptom severity and hazard of death, overall and for specific cancer types. As the survival model will update information on symptom severity over time, we would expect that symptoms that deteriorated over time would be associated with hazard of death. If large associations are seen in our province-wide cohort, it may indicate that certain symptoms could be targets for both improving quality of life and prolonging life, or it may indicate that worsening of certain symptoms is unavoidable and is a flag for impending death, which in turn can help facilitate earlier identification of patients in need of palliative care services.[5,6]

The Edmonton Symptom Assessment System (ESAS) is a patient-reported, validated, and reliable tool for assessing symptom severity in cancer populations.[11,12] Starting January 1, 2007, all cancer centers across Ontario systematically collected ESAS scores in outpatients with cancer.[13] This initiative reflects the increasing importance of the patient's voice in cancer care and offers a unique research opportunity to examine symptom scores in a population-based cancer cohort. Our work takes advantage of this rich longitudinal data (data with repeated measures over time). The examination of outpatient cancer populations makes this research relevant to oncologists practicing in a typical cancer clinic.

Methods

Study Population and Variables

This study examined a province-wide cohort of patients who were diagnosed with cancer after January 1, 2007 and had at least one ESAS assessment during their observation period. Patients eligible for ESAS assessments included those living in all regions of Ontario, with any cancer diagnoses, of any adult age, from ambulatory settings, and any treatment intent. The scheduling of assessments was made depending on how each cancer center implemented the ESAS recording initiative within the patient's region. The actual assessment dates and the corresponding ESAS scores were recorded for each patient.

The outcome of interest was time from cancer diagnosis to death. Diagnosis date was retrieved from the Ontario Cancer Registry, a comprehensive population-based cancer registry created to capture all incident cases of cancer in the province.[14,15] Date of death was