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Weighted Versus Unweighted Charlson Score to Predict Long-term Other-cause Mortality in Men with Early-stage Prostate Cancer

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Abstract

Background: Clinicians need a simple yet accurate method to predict other-cause mortality to inform medical decision making for men with prostate cancer (PCa).
Objective: To compare weighted and unweighted Charlson Comorbidity Index scores in predicting long-term, other-cause mortality in men with early-stage PCa.
Design, setting, and participants: A retrospective cohort study of 1482 men with early-stage PCa diagnosed in 1998–2004 at two Southern California Veterans Affairs medical centers.
Outcome measurements and statistical analysis: Subhazard ratios and cumulative incidence of other-cause mortality associated with weighted and unweighted Charlson scores, calculated by competing-risks regression accounting for cancer mortality, along with Harrell concordance index (C-index) values.
Results and limitations: Weighted and unweighted Charlson scores were identical in 88.6% of subjects (1313 of 1482 men) across all scores and in 91.7% of subjects (1359 of 1482 men) across scores of 0, 1, 2, and ≥3. In competing-risks analysis, hazards of other-cause mortality were similar when comparing weighted and unweighted scores. Men with weighted scores of 1, 2, and ≥3 (vs 0) had subhazard ratios of 2.3 (95% confidence interval [CI], 1.6–3.2), 4.1 (95% CI, 2.9–5.8), and 8.3 (95% CI, 5.9–11.5), respectively. Men with unweighted scores of 1, 2, and ≥3 (vs 0) had subhazard ratios of 2.5 (95% CI, 1.8–3.5), 4.5 (95% CI, 3.2–6.3), and 10.3 (95% CI, 7.2–14.7), respectively. The C-indexes for prediction of other-cause mortality were nearly identical for weighted scores (0.759 [95% CI, 0.715–0.780]) and unweighted scores (0.756 [95% CI, 0.717–0.780]). The difference in C-index between the two methods was −0.003 (95% CI, −0.01 to 0.004).
Conclusions: An unweighted Charlson score yields similar strength of association and variance in predicting long-term, other-cause mortality compared with a weighted Charlson score.
Patient summary: A simple count of major comorbidities provides similar accuracy to a weighted index in predicting death from other causes in men with early-stage prostate cancer.

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1. Introduction

Accurate estimation of long-term, other-cause mortality is critical for physicians who counsel men regarding treatment of early-stage prostate cancer (PCa). Because PCa is an indolent disease affecting older men, many who are diagnosed will not live long enough to realize a survival benefit from aggressive treatment, which takes 8–10 yr to accrue [1]. The decision of whether to pursue aggressive treatment is a particularly important one given the significant morbidities of aggressive treatment [2–4]. However, in practice, physicians do a poor job of determining who will have sufficient longevity to benefit from aggressive treatment [5], as demonstrated by frequent overtreatment of older and sicker men [6].

Recent data have shown that comorbidity burden at diagnosis is a strong predictor of long-term, other-cause mortality [7–12] and have validated the use of the Charlson Comorbidity Index to predict 10-yr mortality in men with PCa [7,10]. The Charlson index calculates a weighted score that predicts mortality based on the presence of certain comorbidities [13]. However, a disadvantage of the Charlson index is that it is cumbersome to use in the clinical setting, since it generally requires the use of a calculator to determine the weighted score. This is also a limitation of the manifold nomograms available for prediction of survival, which has led some thought leaders to question the practical worth of these nomograms [14].

Recent work from the Prostate Cancer Outcomes Study (PCOS) showed that a parsimonious model for risk stratification, including only age and a count of comorbidities, was strongly predictive of long-term, other-cause mortality [15]. At 10 yr after diagnosis, 55-, 65-, and 75-yr-old men with comorbidity counts of $\geq$3 had cumulative incidences of other-cause mortality of 28%, 40%, and 71%, respectively. An advantage of this simple risk stratification method is its potential for easy translation to the clinical setting. However, a reasonable concern is that using a raw comorbidity count compromises accuracy compared with an index that individually weights comorbidities according to risk of mortality.

We sought to determine whether the strength of prediction and variance associated with mortality estimates differ between weighted and unweighted Charlson scores. We used observational data from 1482 men with early-stage PCa diagnosed between 1998 and 2004 in two Southern California Veterans Affairs (VA) medical centers to compare the ability of weighted and unweighted Charlson scores to predict long-term, other-cause mortality. We hypothesized that unweighted scores would offer predictive accuracy similar to that of weighted Charlson scores.

2. Methods

2.1. Data sources and study participants

We used the California Cancer Registry to identify men newly diagnosed with PCa at the Greater Los Angeles and Long Beach VA medical centers between 1997 and 2004 (n = 1914). We reviewed medical records to obtain sociodemographic, tumor risk, and survival data. We excluded men with histology other than adenocarcinoma (n = 86), locally advanced or metastatic disease (n = 115), and cancer diagnosed incidentally at cystoprostatectomy (n = 25), as well as men with insufficient data to determine comorbidities or treatment (n = 206). We identified 1482 men who satisfied the inclusion and exclusion criteria. Institutional review board approval was granted at University of California, Los Angeles, and both VA medical centers.

2.2. Variables

2.2.1. Comorbidity

We assessed comorbidity using the age-unadjusted Charlson Comorbidity Index [13] versus a simple count of the Charlson comorbidities. The Charlson index estimates life expectancy based on the presence of specific comorbidities; each comorbidity is weighted by its risk of mortality, and weights are summed into a total score that is proportional to mortality risk. Comorbidities are weighted as follows: metastatic solid tumor (6), HIV/AIDS (6), moderate to severe liver disease (3), hemiplegia (2), moderate to severe renal disease (2), diabetes with end-organ damage (2), solid tumor (2), leukemia/lymphoma (2), myocardial infarction (1), congestive heart failure (1), peripheral vascular disease (1), cerebrovascular disease (1), dementia (1), chronic pulmonary disease (1), connective tissue disease (1), peptic ulcer disease (1), mild liver disease (1), and diabetes (1). PCa was not included in comorbidity scoring. We collected comorbidities at diagnosis by review of the interdisciplinary medical record within 12 mo of diagnosis, using methods previously described [16]. An exploratory analysis was also conducted using the age-adjusted Charlson index, which involves adding an additional point for each decade of age, starting with age 50 [17].

2.2.2. Tumor risk

Tumors were classified using the D'Amico risk criteria as low risk (prostate-specific antigen [PSA] $\leq$10, clinical stage $\leq$T2a, and Gleason score $\leq$6), intermediate risk (PSA 10–20, clinical stage T2b, or Gleason score 7), or high risk (PSA >20, clinical stage $\geq$T2c, or Gleason score $\geq$8) [18,19].

2.2.3. Type of primary treatment

Type of primary treatment was coded as surgery, radiation therapy/brachytherapy, watchful waiting, and androgen deprivation therapy.

2.2.4. Mortality

Survival was measured from date of treatment until date of death. We determined the date of death using a combination of the medical record and the Social Security Death Index. Cause of death was determined using the medical record with an algorithm that has been previously described [6].

2.3. Statistical analysis

We compared sample characteristics by weighted and unweighted Charlson groups using χ^2 tests for categorical variables and analysis of variance tests for continuous variables. We then determined tabular frequencies and Spearman correlation of weighted and unweighted Charlson scores across subjects.

We estimated the cumulative incidence of other-cause mortality and its associated confidence intervals (CIs) for weighted and unweighted Charlson scores using a competing-risks regression model as described by Coviello and Boggess [20]. This univariate method allows for direct calculation of standard error estimates and transformed confidence bounds for the cumulative incidence function.

We then estimated the relative subhazards and cumulative incidence of other-cause mortality for both comorbidity assessment methods