

Association of a Claims-Based Marker of Functional Impairment with Treatment Patterns and Cost in Metastatic Squamous Cell Carcinoma of the Head and Neck (mSCCHN)

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ABSTRACT

Objective: Information on patients' performance status (PS) is important to characterizing treatments and healthcare costs in the real world setting; however this information cannot be directly ascertained from administrative claims data. The objective of this analysis was to evaluate the JEN Frailty Index (JFI), a marker of functional impairment that can be derived from claims data and potentially used as proxy for PS in order to describe outcomes among mSCCHN patients.

Methods: The JFI has been found to be significantly related to concurrent and future need for long-term care services; it has been utilized by CMS and has been evaluated in studies of multiple sclerosis and Alzheimer's disease. In the current study, treatment patterns data for patients with mSCCHN were evaluated using categories of low, medium, and high JFI, with high JFI corresponding to high impairment and by extrapolation, to poor PS. The associations between JFI and treatment patterns as well as monthly total Medicare costs were assessed. This study population was derived from the 2005-2009 Surveillance, Epidemiology and End Results (SEER) cancer registry, linked to Medicare claims for 2002-2010. SCCHN was categorized as metastatic based on either determination of stage IVC disease at diagnosis or the existence of secondary or distant cancer diagnoses in Medicare claims.

Results: A total of 4,616 patients with mSCCHN were eligible for study inclusion. Approximately 60%, 40%, and 41% of the total population received radiation, surgery, or systemic therapy, respectively. Twenty-nine percent of the total population had high JFI scores at 3 months post-metastatic diagnosis. The percentage of patients with high JFI scores fluctuated over time: 5% one year prior to diagnosis, 34% 0-8 months after diagnosis, and 16% at 18 months post-diagnosis. In patients with observed deaths, the proportion with high JFI expanded in the 36 months prior to death, rising from 22% to 51% during the last observation month. Of the 1,302 patients who received systemic therapy, only 16% had high JFI scores at the time of treatment initiation. There was a trend toward administering cetuximab monotherapy rather than platinum-containing regimens in first- and second-line treatment for patients with high JFI scores. Multivariate regression analyses found a cost impact associated with high JFI score during the observation period (9.13-fold increased cost relative to low JFI, p < 0.0001).

Conclusions: The JFI was used as a proxy for PS. Patterns of systemic therapy use and cost of care varied according to JFI strata in mSCCHN patients. This study supports the opportunity and need for further validation of the JFI as a proxy for PS in observational claims-based oncology research.

BACKGROUND

- Head and neck cancer (HNC) accounts for 3% of new cancer cases in the United States each year and includes epithelial malignancies that arise in the oral cavity, pharynx, larynx, nasal cavity, and paranasal sinuses.¹ Almost all (85% to 95%) are squamous cell carcinomas of the head and neck (SCCHN).^{1,3}
- Among US patients with newly diagnosed SCCHN, 10% to 18% have distant metastatic disease at initial clinical presentation.^{4,5} Distant metastases can also develop in 10% to 40% of patients after initial treatment of non-metastatic disease depending on population, risk factors, cancer stage at presentation, duration of follow-up, and initial treatment response.⁶ Initial therapies for metastatic SCCHN (mSCCHN) have been studied in a number of randomized and observational studies.^{7,9} However, there is limited information concerning disease management and outcomes in patients with mSCCHN who have received successive systemic treatment regimens.
- Existing literature does not characterize treatments and outcomes on the basis of patients' performance status (PS), a critical measure routinely used in oncology clinical practice to assess function and guide treatment decisions for patients.
- The JEN Frailty Index (JFI), a claims-based measure, has been found to be significantly related to concurrent and future need for long-term care services; it has been studied by the Veterans Health Administration and used to evaluate outcomes in frail populations.^{10,11}

OBJECTIVE

- To characterize treatment patterns and cost in the real-world setting for patients receiving sequential systemic therapy for mSCCHN.
- To describe results according to the JFI, a marker of functional impairment that can be derived from claims data and potentially used as a proxy for PS to describe outcomes among patients with mSCCHN.

METHODS

Population

- The study population was derived from the 2005-2009 SEER cancer registry, linked to Medicare claims for 2002-2010.
- Patients included criteria:
 - SCCHN listed in SEER as a patient's first and only primary cancer
 - Initially diagnosed with stage IVC mSCCHN or an earlier stage, with a record in Medicare claims denoting later progression to metastatic disease (155.xx, 162.xx, 170.xx, 191.xx, 197.xx, 198.xx)
 - Enrollment in traditional Medicare Fee-for-Service plan at least 12 months prior to diagnosis and during follow-up. Patients were censored if they changed to a Medicare managed care plan.

METHODS (CONTINUED)

JEN Frailty Index (JFI)

- The JFI is based on 13 condition categories found to be significantly related to concurrent and future need for long-term care services.
 - Minor ambulatory limitations
 - Severe ambulatory limitations
 - Cognitive/developmental disability
 - Chronic mental illness
 - Dementia
 - Sensory disorders
 - Self-care limitations
 - Chronic medical disease
 - Pneumonia
 - Renal disorders
 - Systemic disorders (E.G., Septicemia)
 - Cancer
- Ambulatory and self-care limitations are indicated in Medicare claims records by diagnoses related to falls and other trauma, poor nutrition, skin ulcers, and urinary tract infections.
- The magnitude of the index is calculated through a simple summation of the above diagnostic categories in the previous 12 months of a patient's healthcare claims.
 - Patients in this study were given a monthly JFI score stratified as high (JFI 7-13), medium (JFI 4-6), or low (JFI 0-3) impairment; high JFI corresponded to high impairment and, by extrapolation, to poor PS.

Treatment Patterns

- Systemic anticancer treatment evaluation in this study was informed by previous research, treatment recommendations in the National Comprehensive Network Head and Neck Guidelines,¹ and common regimens appearing in the claims records of the national Medicare 5% sample population.
- Each evaluated drug was identified by Healthcare Common Procedure Coding System (HCPCS) and National Drug Codes (NDC) in the Medicare claims of the study population.
- An episode algorithm was created evaluating the frequency of treatment, length of treatment interruptions between administration, and number of cycles.

Statistics

- Treatment pattern data were evaluated descriptively, using categories of low, medium, and high JFI.
- The associations between JFI and either survival¹² or monthly total Medicare costs¹³ were assessed utilizing multivariate regression models.
- The log-transformed cost models met accepted standards.¹³
- * Survival was assessed using a proportional hazards model that utilized a stepwise selection of model covariates. A significance level of 0.15 was required for covariates to enter and remain in the model.
- † Costs were assessed utilizing a multivariate linear regression model using a person-month categorization of log¹⁺¹ transformed total Medicare costs during the follow-up period.

RESULTS

Table 1. Baseline Characteristics

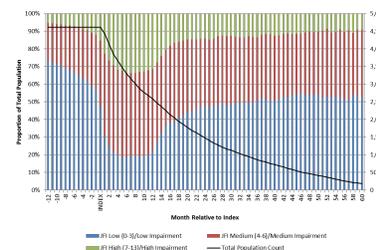
Total study population	4,616
Diagnosed at stage IVC	8.7%
Male	68.6%
White/black	82.5%/10.9%
Age, Mean (SD)	72 (10.13)
Urban residence at mSCCHN detection	80.3%
LTC status in year prior to mSCCHN	
Community or other	87.1%
Community LTC	7.2%
Nursing home or other institutional LTC	5.7%
JFI at mSCCHN detection	
Low JFI (0-3)/low impairment	47.7%
Medium JFI (4-6)/medium impairment	37.1%
High JFI (7-13)/high impairment	15.3%
JFI, Mean (SD)	4 (2.37)
CCI at mSCCHN Detection	
Low CCI (0)	56%
Medium CCI (1-2)	33%
High CCI (≥3)	10%
CCI, Mean (SD)	1 (1.35)

Abbreviations: CCI= Charlson Comorbidity Index; JFI = JEN Frailty Index; LTC= long-term care; mSCCHN = metastatic squamous cell carcinoma of the head and neck

- There were 64,340 patients with primary HNC documented in SEER between 2005-2009. The final study population was 4,616 (7.2%) after applying exclusion criteria.
- Major exclusions: previous primary cancer (8,877), initial HNC diagnosis outside 2005-2009 (7,620), primary HNC not within designated study sites (15,404), and insufficient fee-for-service Medicare history (11,496).

RESULTS (CONTINUED)

Figure 1. Monthly JFI Status



- The JFI distribution was marked by increases in high JFI after mSCCHN diagnosis.
- The greatest proportion of high JFI occurred in the first year after metastatic diagnosis, when the study population decreased by 55% largely as a result of mortality.

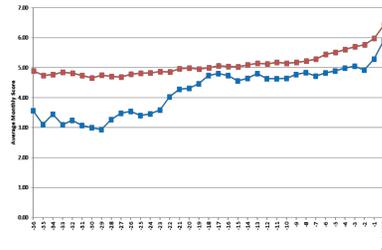
Table 2. Significant Mortality and Cost Risk Factors in the Total Study Population

Model Inputs	Baseline Survival Model ¹²	Monthly Cost Model ¹³
Mean/median K-M survival, months (95% CI)	29.7/17 (16-19)	
Observed deaths, N (%)	2,854 (61.8%)	
Censored, N (%)	1,762 (38.2%)	
Mortality Covariates	HR (95% CI)	Fold Change for a Given Month (p-value)
Demographics		
Age 80+	1.50 (1.37-1.64)	1.23 (<.001)
Age 75-79	1.29 (1.17-1.43)	1.28 (<.001)
Age 70-74	(Included in Reference Level*)	1.16 (<.001)
Male	1.09 (1.00-1.18)	0.96 (0.023)
Black	1.15 (1.02-1.29)	1.22 (<.001)
Other/unknown race/ethnicity	(Not Significant)	0.87 (<.001)
Urban county residence at mSCCHN	0.90 (0.82-0.99)	1.10 (<.001)
Health Status		
Stage IVC at initial diagnosis	2.05 (1.82-2.31)	1.54 (<.001)
Pre-metastasis nursing home residency	1.82 (1.58-2.11)	1.41 (<.001)
JFI at mSCCHN Detection		
Low JFI (0-3)/low impairment	0.90 (0.82-0.99)	(Reference Level)†
Medium JFI (4-6)/medium impairment	(Reference Level*)	3.63 (<.001)
High JFI (7-13)/high impairment	1.52 (1.36-1.70)	9.13 (<.001)
CCI at mSCCHN Detection		
Low CCI (0)	0.90 (0.81-0.99)	(Reference Level)†
Medium CCI (1-2)	(Reference Level*)	1.46 (<.001)
High CCI (≥3)	1.19 (1.04-1.36)	1.87 (<.001)
Systemic Treatment during the month	(Not a baseline variable*)	
Pre-Metastasis Systemic Therapy		0.90 (.003)
1 st -Line Systemic Therapy		23.87 (<.001)
2 nd -Line Systemic Therapy Line		15.38 (<.001)
3 rd -Line Systemic Therapy		15.69 (<.001)
4 th -Line Systemic Therapy		21.63 (<.001)

* Stepwise regression model for baseline variables. Reference levels: white race, age <75 years, JFI 4-6; CCI 1-2. † Cost impact in each month. Reference levels: white race, age 60-69 years, JFI 0-3, CCI 0, treatment = none

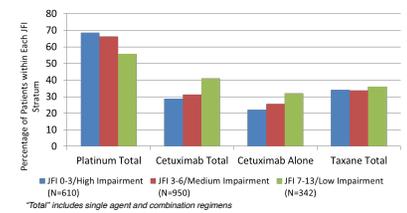
- Abbreviations: CCI= Charlson Comorbidity Index; JFI = JEN Frailty Index; K-M = Kaplan Meier; mSCCHN = metastatic squamous cell carcinoma of the head and neck
- Baseline JFI is highly associated with survival and costs even after controlling for baseline CCI.

Figure 2. Mean Monthly JFI Prior to Death



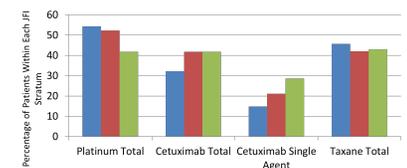
- Mean JFI gradually increased in the months preceding death, regardless of the disease stage at which the initial SCCHN diagnosis occurred.

Figure 3. First-Line Treatment Patterns vs. JFI at Treatment Initiation



- 1,902 (41%) patients received any systemic therapy, with the high JFI stratum underrepresented in the treated population.
- Patients with high JFI appear more likely to receive cetuximab-containing regimens.

Figure 4. Second-Line Treatment Patterns vs. JFI at Treatment Initiation



- 486 patients (26% of first-line recipients) received second-line therapy.

DISCUSSION

Limitations

- Although informed by other research,¹⁴⁻¹⁵ this study used new algorithms to characterize treatment episodes and the JFI as a proxy for PS. Additional validation of both approaches is needed.
 - The JFI stratification cut points have an empirical basis in previous studies.^{10,11} Validating them through further medical record reviews is suggested.
- Registry and Medicare claims information through 2009 and 2010, respectively, were available for evaluation in this study; therefore, more recent treatment pattern and cost information was not captured.
- The results of this study are most applicable to patients with mSCCHN who are covered by Fee-for-Service Medicare and may not be generalizable to patients with mSCCHN not covered by Fee-for-Service Medicare.

CONCLUSIONS

- The JFI was used as a proxy for PS. The current study is the first to characterize treatment and cost information in this manner, in patients with mSCCHN. It supports the opportunity and need for further validation of the JFI as a proxy for PS in observational claims-based oncology research.
- JFI adds explanatory value to survival and cost modeling beyond that of CCI, demonstrating that functional impairment plays a role beyond considerations of comorbidity.
- Patterns of systemic therapy use varied according to JFI strata in patients with mSCCHN.
 - There was a trend toward administering cetuximab-containing regimens rather than platinum-containing regimens in first- and second-line treatment for patients with medium to high JFIs.

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