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Comparison of Comorbidity Collection Methods

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Abstract

Background—Multiple valid comorbidity indices exist to quantify the presence and role of comorbidities in cancer patient survival. Our goal was to compare chart-based Adult Comorbidity Evaluation-27 index (ACE-27), and claims-based Charlson Comorbidity Index (CCI) methods of identifying comorbid ailments, and their prognostic ability.

Study Design—Prospective cohort study of 6138 newly-diagnosed cancer patients at 12 different institutions. Participating registrars were trained to collect comorbidities from the abstracted chart using the ACE-27 method. ACE-27 assessment was compared with comorbidities captured through hospital discharge face-sheets using ICD-coding. The prognostic accomplishments of each comorbidity method was examined using follow-up data assessed at 24 months after data abstraction.

Results—Distribution of the ACE-27 scores was: “None” for 1453 (24%) of the patients; “Mild” for 2388 (39%); “Moderate” for 1344 (22%) and “Severe” for 950 (15%) of the patients. Deyo’s adaption of the Charlson Comorbidity Index (CCI) identified 4265 (69%) patients with a CCI score of 0, and the remaining 31% had CCI scores of 1 (n=1341, 22%), 2 (n=365, 6%), or 3 or more (n=167, 3%). Of the 4265 patients with a CCI score of 0, 394 (9%) were coded with severe comorbidities based on ACE-27 method. A higher comorbidity score was significantly associated with higher risk of death for both comorbidity indices. The multivariable Cox model including both comorbidity indices had the best performance (Nagelkerke’s R-square=0.37) and the best discrimination (c-index=0.827).

Conclusion—The number, type, and overall severity of comorbid ailments identified by chart- and claims-based approaches in newly-diagnosed cancer patients were notably different. Both indices were prognostically significant and able to provide unique prognostic information.

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Keywords

Comorbidity; comorbid ailment; newly diagnosed; cancer patients; prognostic; survival

Introduction

When first diagnosed with cancer, many cancer patients have additional, non-neoplastic diseases, illnesses, and conditions, which are referred to as comorbidities. (1,2) For the patient with significant comorbidities, the aggressiveness of a cancer and treatment intensity must be weighed against the presence of pre-existing comorbidities. In the growing climate of individualized and personalized medicine and concern about preserving quality of life after treatment of cancer patients, the prognostic and therapeutic consequences of comorbidities are widely recognized by patients and health care professionals.

Multiple valid comorbidity indices exist to quantify the presence and role of comorbidities in survival. The various comorbidity instruments can be grouped into three distinct categories according to the source of the comorbid health information: 1) the patient is the primary source of the comorbid health information(3–5), 2) medical record review(6–10), where the comorbid health information is obtained through a review of the medical record, or 3) a claims-based approach (11–13), where the sources of comorbidity data are the primary and secondary diagnosis code fields using the International Classification of Diseases 9th Revision (ICD-9-CM) codes for hospitalization or outpatient visit. While the patient-based approach allows for the collection of more information on the functional impact of comorbid ailments than the other methods, there are concerns of inaccuracy and underreporting with this approach. Medical record review, also known as the chart-based approach, improves the quality of the data abstraction relative to claims-based approach, but requires additional staff and staff education. Our previous research findings (9,10,14,15) suggest that cancer registrars can be trained to review the medical record and identify the cogent comorbid conditions in a time-efficient and valid fashion. The claims-based approach requires all accredited cancer registries to collect comorbid health information using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes from the hospital discharge face-sheet at the time of initial cancer hospitalization. The advantage of the claims-based approach is its simplicity and straightforward nature; however, it is systematically less accurate and complete than the chart-based approach. (10,16–20)

The goal of this research project was to compare chart-based Adult Comorbidity Evaluation-27 index (ACE-27) and claims-based Charlson Comorbidity Index (CCI) methods of identifying comorbid ailments and prognostic ability.

Methods

Registrar Training and Abstraction of Comorbidity Information

The on-line training program (<http://otooutcomes.wustl.edu/research/topics/cancer/Pages/Cancer-Comorbidities.aspx>) for coding comorbidities using the chart-based ACE-27 (21)

comorbidity method was successfully completed by 39 cancer registrars from 13 different hospitals or health care systems in seven states. The ACE-27 comorbidity index includes a variety of individual comorbid ailments grouped under the following body systems: cardiovascular, respiratory, gastrointestinal, renal, endocrine, neurological, psychiatric, rheumatologic, immunological, malignancy, substance abuse, and obesity. There are four severity grades for each comorbid condition, except obesity: *No comorbidity (Grade 0)*, *Mild (Grade 1)*, *Moderate (Grade 2)*, and *Severe (Grade 3)*. Obesity has only 2 severity grades: “*Grade 0*” if the body mass index (BMI) is less than 38, and “*Grade 2*”, if the BMI is greater than or equal to 38. Since cancer patients can have more than one comorbid ailment, an overall comorbidity severity score is determined based on the grade of the highest-ranked single ailment or if two comorbid ailments of different body systems are graded as *Moderate (Grade 2)* then the overall score is *Severe (Grade 3)*.

All new cancer cases diagnosed and/or receiving part of the first course of treatment at a given institution are defined as analytical cases for the specific institution.(9) Participating cancer registrars completed the on-line ACE-27 form [<http://cancercomorbidity.wustl.edu/ElectronicACE27.aspx>] for all new analytical cases abstracted in the first six months after training. The online ACE-27 form offers the advantage of automatically calculating the overall comorbidity score based on the individual comorbid ailments identified (by check box option) from the cancer registrars. Accession and sequence numbers were used to identify each case.

The registrars collected claims-based comorbid health information using the American College of Surgeons Commission on Cancer guidelines.(22) Participating cancer registrars abstracted comorbid ailments from the patient’s hospital discharge attestation or “face sheet”. A maximum of ten comorbid conditions were abstracted. Deyo’s adaption (23) of Charlson’s Comorbidity Index (CCI) (7) was used to calculate an overall score using the ICD-9 codes obtained by the registrars.

There were 6138 adult cases abstracted from registrars at 12 registries between May 2007 and March 2011. The number of cases from each registry ranged from 124 to 1770 cases. One registry submitted only 48 cases online and, due to staff changes, did not continue with the comorbidity data collection part of the study. For this reason, cases from this registry were excluded from analysis. Data elements provided from each registry included demographic, clinical, and tumor characteristics, as well as comorbid ailments collected from the medical record as part of routine chart abstraction using the ACE-27 and from the hospital discharge face-sheet.

To allow for comparison of the prognostic accomplishments between the chart-based and claims-based approaches, each registry provided follow-up cancer and survival status information 2 years after the last reported case was included in the study. Date of cancer diagnosis was defined as “zero-time” for study entry and survival analysis. For patients who died, the date of death was considered date of last follow-up.

All data were de-identified. Accession and sequence numbers were used to merge the information from the cancer registry with the comorbidity information entered on-line from

registrars of the same registry. This study was approved by Washington University Human Research Protection Office (HRPO).

Statistical Analysis

Standard descriptive statistics were used to describe the distribution of demographic and clinical characteristics, presence of comorbid ailments, and overall severity score for all new analytical adult cancer cases submitted from cancer registries. Frequency distributions of ICD-9 claims-based comorbidity information were compared to the ACE-27-defined comorbidity information. The kappa statistic (24) was used to quantify the agreement between the two methods. Acknowledging that kappa is a prevalence-dependent statistic (25), we calculated Yule's Y. (26) The prognostic performance of each comorbidity coding method was evaluated using the Kaplan-Meier product limit method (KM) and Cox Proportional Hazards (Cox PH) survival analyses. The prognostic performance of the two comorbidity collection methods was further assessed based on Likelihood Ratio (LR) Chi square statistic, Nagelkerke's R square, Schwarz's Bayesian information criterion (BIC), c-statistic as a measure of model discrimination, and model calibration as a measure of models' accuracy. (27) Predictive accuracy was assessed using generalizations of variance explained by Nagelkerke's R-square. (28) BIC (29) was used for evaluating the models after penalizing for number of parameters in the model.

Discrimination refers to the ability to distinguish high-risk from low-risk patients. Discrimination of the two different methods of comorbidity capture were measured using the area under the receiver-operating characteristic curve (ROC) and quantified by the c-statistic. (30) A c-statistic equal to one corresponds to perfect discrimination and a c-statistic equal to 0.5 corresponds to no discrimination. In predicting the time until death, *c* is calculated by considering all possible pairs, at least one of whom has died. If one patient has died and the other is known to have survived at least until the death of the first, the second patient is assumed to have outlived the first. The c-index from the model with no comorbidity was compared to the c-indices of the models with comorbidity coded based on the ACE-27 chart-based comorbidity coding, ICD-9 Charlson Index, and, finally, to the c-index of the model incorporating both comorbidity indices. Since the models were fitted from the same patients, a bootstrapping technique with clustering based on center registry was used to compute the standard error for the difference in the c- statistics from any pair of models being compared and to correct for optimism. (27) Bootstrapping with clustering on center also controls for the prediction role of cancer center in both survival estimates and c-index calculations.

Calibration is a measure of accuracy of the predicted probabilities of outcome from the model analyzed. For each patient, the predicted probability of death and the observed value was determined. To quantify the misclassification associated with each of the two different methods of comorbidity capture, calibration curves were generated using a generalization of the methods described by Harrell. (31) A curve fitting close to the 45-degree line shows a model with good calibration.

The proportional hazards assumption was tested using log(-log) survival plots for all variables included in Cox regression analyses. All statistical tests were evaluated at the two-

sided alpha level of 0.05. Statistical analyses were performed in SAS, STATA, and R version 2.14.2.

Results

The description of characteristics for the 6138 adult cases with cancer submitted from 12 cancer registries is presented in Table 1. The average age of the patients was 62.5 years (SD 14.1) and 74% of the patients were 55 years of age or older. There was an approximately equal distribution between genders and the majority of the patients were white (n=5358; 87%). There were 392 (6%) patients with in situ tumors, 2628 (47%) local, 1698 (28%) regional, and 1136 (19%) distant tumor stage. The frequency distributions for each cancer site are shown in Table 1. The “other site” category included: unspecified site in abdomen, adrenal gland, aorta, blood, lymph node, musculoskeletal, parathyroid, other male, ophthalmology, unknown primary, not specified site in pelvis, pleura, and thymus. The majority (n=4174, 68%) received surgery, 2122 (35%) received chemotherapy, 1977 (32%) received radiotherapy, and 571 (9%) did not receive any form of treatment.

The distribution of overall ACE-27 scores was: 1453 (24%) with *None*, 2388 (39%) with *Mild*, 1344 (22%) with *Moderate*, and 950 (15%) with *Severe*. The overall ACE-27 score was not available for 3 patients. The number of ICD-9 coded comorbidities per patient varied from 0 (no comorbidity) for 1808 (29%) of the patients to 10 for 387 (6%) of the patients. The majority of the patients (71%) had at least one ICD-9-coded comorbid condition. Deyo's adaption of the Charlson Comorbidity Index (CCI) was used to calculate CCI comorbidity scores using ICD-9 codes in the 10 claim-based comorbidity fields. There were 4265 (69%) patients coded as 0, or without comorbidity. The remaining patients had a CCI score of 1 (n=1341, 22%), 2 (n=365, 6%), or 3 or greater (n=167, 3%). As can be seen in Figure 1, the distribution of scores within each of the two indices was quite different and the agreement poor. As compared with ACE-27, there were a greater number of patients scored as no comorbidity and a much smaller number scored as severe comorbidity with CCI.

The distribution of comorbidity scores for each patient according to the ACE-27 and CCI is shown in Table 2. As can be seen, of the 4262 patients with CCI score of 0, only 1386 (33%) were identified as without comorbidities using the chart-based ACE-27 method. Of the remaining, 1704 (40%) were coded with a mild comorbidity score, 778 (18%) with moderate comorbidity, and 394 (9%) with severe comorbidities, based on ACE-27 method. From the 1453 patients with ACE-27 score of 0, the majority (n=1386, 95.3%) were coded as without comorbidities from the CCI index, and the remaining 5% were distributed as: CCI comorbidity score of 1 (n=56, 4%); CCI comorbidity score 2 (n=6, 0.4%); and CCI comorbidity score 3 (n=5, 0.3%).

A comparison of the prevalence of comorbid conditions identified as important and captured by both methods was performed. As shown in Table 3, for every condition, except paralysis, the number of patients detected by chart review was greater than those detected through the ICD-9 claims-based approach. The detection rate for the ACE-27 was significantly higher than expected by chance alone for all but one condition (AIDS). The Kappa statistic ranged

from 0.73 for diabetes to 0.002 for malignancy. The Yule's Y statistic showed a range of agreement between the two comorbidity indices from as high as 0.87 for AIDS to as low as 0.12 for malignancy.

The secondary goal of the study was to compare the prognostic performance of the two different comorbidity collection methods. The median follow-up for all patients was 22 months and interquartile range (IQR) was 10–31 months. For survivors the median follow-up time was 27 months and IQR was 19–33 months. There were 2803 (46%) patients alive at the two-year follow-up and 1753 (29%) dead within the first two years post-cancer diagnosis. For 1582 (26%) of the patients who were recorded as alive at the time of last follow-up, follow-up time was shorter than two years. The results of univariate Cox regression analysis are presented in Table 1.

Kaplan-Meier survival analyses showed that there is a significant difference in survival between different levels of comorbidity, independent of their coding methods (ACE-27 – Figure 2/A; CCI-Figure 2/B). Interestingly, among the patients coded as CCI=0, but identified as having different levels of comorbidity severity using ACE-27, there was a clear survival gradient across ACE-27-defined groups (Figure 2/C). Among patients coded as ACE-27 = 0, the survival gradient according to CCI group was statistically significant but not as clear as it was for patients coded as CCI=0 (Figure 2/D). This difference in the appearance of survival gradients may be due to the much smaller number of patients with comorbidity score of none according to ACE-27 (n=1453) as compared to CCI (n= 4265).

Multivariable Cox Proportional Hazard regression analyses was used to evaluate the prognostic role of each comorbidity measure individually and then in combination on overall survival. In Table 4 the adjusted Hazard Ratios (HRs) and corresponding 95% confidence intervals (95% CI) show that for each comorbidity measure increasing levels of comorbidity severity are significantly associated with higher risk of death, even after adjusting for other important predictors of survival. This also remains true for the model incorporating both comorbidity indices.

The performance of the model with no comorbidities was compared to the performance of the models with ACE-27 only, CCI only, and finally, the model including both indices (Table 5). All models yielded overall statistically significant results in predicting survival. The multivariable model including both comorbidity indices had the best performance, as evidenced by the fact that it produced the highest value of Nagelkerke's R^2 (0.37), lowest value of BIC (30749), and best discrimination, shown by a c-index = 0.827. The multivariable Cox PH model with ACE-27 is the second best performer based on the same parameters ($R^2=0.367$; BIC=30755; c-index=0.825), and is followed closely by the model with CCI only ($R^2=0.364$; BIC=30784; c-index=0.824). The model without comorbidities was the worst performer. Comparison of c-indices showed that each of the two models including the individual comorbidity assessments and the model that includes both comorbidity indices had significantly better discrimination power than the model without comorbidities. There was no statistically significant difference in the discrimination of the model with ACE-27 chart-based comorbidity versus the CCI claims-based model, but the model including both indices was superior to all models. Figure 3 shows the calibration

curves for all four models. The calibration lines for all four models roughly follow the 45-degree angle and thus demonstrated adequate calibration.

Discussion

In this study, we found that the number, type, and overall severity of individual comorbid ailments identified by a chart- and claims-based approach in newly-diagnosed cancer patients were notably different. The chart-based review identified a greater number of cogent comorbid ailments than the claims-based approach.

Our finding that a large majority of cases from claims were coded as not having comorbid conditions is consistent with Deyo's previous work. (32) However, our data also showed that at least one comorbid condition, as defined by the ICD-9, was found in approximately 70% of cancer patients. Thus, only a small number of the ICD-9 codes were used in defining a comorbidity score according to Deyo's adaption of the Charlson's index. The relatively small percentage of patients we identified as having no comorbid conditions using the chart-based ACE-27 method is consistent with percentages reported by others. (10,33,34)

The two systems performed nearly equally well in predicting two-year overall survival, despite the significant differences in the identification and grading of comorbid ailments. Both systems identified unique prognostic subgroups within categories of comorbidity severity even after controlling for other significant prognostic factors. For each comorbidity method, patients with higher levels of overall comorbidity severity demonstrated worse survival. Interestingly, both systems seem to combine independent prognostic information as both remained in the multivariable prognostic model.

This study incorporates the experiences of many newly-diagnosed cancer patients as represented by the cancer coding performed by cancer registrars from multiple institutions. The data used for all analyses were collected prospectively from trained cancer registrars. While the ICD-9 coding is consistently provided through the hospital discharge face sheet at all institutions, the mandatory online training program and post-program assessment enabled reliable and consistent coding of comorbidities through the ACE-27 method. Though a relatively large sample size was used for analysis, the acquisition of follow-up survival information was limited due to constraints of the study duration.

Unlike other studies (34,35), we did not find a statistically significant benefit of the chart-based ACE-27 comorbidity method when compared to the ICD-9 claim-based Charlson's method for prediction of survival. However, our study did demonstrate that the chart-based method identified comorbidities in a larger number of patients (76%) in comparison to the claims-based method (31%) and the claims-based method identified many comorbidities that are not germane to treatment decision-making and survival. The chart-based ACE-27 method captures additional pancreatic, neuromuscular, psychiatric, alcohol and illicit drug use, and obesity comorbidity information not captured by Charlson. In addition, a wider range of cardiovascular diseases are captured by ACE-27. We believe the differences in the number of patients identified with comorbidities between the two methods are a reflection of both the ascertainment method and the kinds of comorbid ailments captured.

The ability of the ACE-27 chart-based approach to be adapted to a claims-based method for breast and prostate cancer patients was assessed by Fleming et al.(36) In that study, the authors found that the claims-based ACE-27 method had a sensitivity of 80% when compared to the chart-based ACE-27 approach. Furthermore, the number of patients identified with the claims-based ACE-27 approach as having no comorbidities was approximately 30%. This percentage of patients identified as having no comorbidities with the claims-based ACE-27 is considerably different from the value of 69% we observed using the claims-based Charlson. This difference in the percentage of patients identified as having no comorbidities likely reflects the difference in the comorbid ailments and description of organ decompensation between the ACE-27 and the Charlson. The claims-based ACE-27 proposed by Fleming and colleagues is a tool that uses the advantage of the ailments of ACE-27 and the relatively low cost of a claims-based approach.

As can be seen in Table 3, the ACE-27 chart-based method identifies a higher prevalence of the individual comorbid conditions coded by both methods. We believe another reason for this discrepancy in the number of patients with comorbid conditions identified through the two different systems is the increasing role of outpatient cancer care and thus the large number of cases that did not have an inpatient hospital discharge sheet to abstract the ICD-9 code. For cancer patients treated as outpatients without hospital admission, comorbidity information may still be obtained through the chart-based approach. While the patient's history, physical examination, consult notes, and laboratory data may be available in the outpatient record, the ICD-9 codes from a non-existent hospital discharge record will be unavailable. Since the care of the cancer patient is not a one day/one episode event, but rather extends to weeks and months, patients' involvement can be helpful. One solution is to include the cancer patient in the completion of the comorbidity evaluation. The authors worked with the National Health Service of the United Kingdom to develop a patient version of the ACE-27 and we think a patient-based approach would work well in North America.

Our findings support previous research that demonstrated comorbidity information may be incomplete or lack sufficient detail when a claims-based approach using ICD-9 codes is utilized. (13,17,37–39) As Elixhauser et al. (17) concluded, "Administrative data are never complete or detailed enough to provide a clinically precise method for identifying comorbidities". Klabunde et al. (39) found that the comorbidity information currently collected from the hospital discharge face-sheet is incomplete. Furthermore, the ICD-9 system does not allow for the patho-physiological descriptions of the severity of individual comorbid ailments. Another disadvantage of the ICD-9 system is the potential for misclassification of complications as preexisting chronic comorbid conditions. (18) It is unclear if the ICD-10 code sets, which include greater detail, changes in terminology, and expanded concepts for injuries, laterality, and other related factors, will automatically result in improved comorbidity assessment when compared to ICD-9.

While evaluating the ICD-9 codes recorded from cancer registrars, certain conditions were identified that seem uninformative for inclusion in a cancer patient registry. These conditions, such as hypercholesterolemia, esophageal reflux, gout, urinary tract infection, diarrhea, nausea and vomiting, constipation, and backache, are unlikely to impact on

treatment selection or patient outcome. Since registrar time is spent collecting and recording comorbidity information, it is important that the captured comorbid health data are relevant to cancer statistics and the patient experience. When the captured comorbid information is unhelpful with respect to the quantification and evaluation of the overall comorbid status of the patient, minimal prognostic benefit is realized.

In conclusion, chart- and claims-based comorbidity collection methods identify different number, type, and overall severity of comorbid ailments in newly-diagnosed cancer patients. Independent of the method used, the presence of comorbidities greatly impacts the survival of newly-diagnosed cancer patients. We acknowledge that each of the comorbidity collection methods features various strengths and limitations and we did not find any significant difference between methods in survival prediction. A model including both indices produced a better overall predictive model, suggesting that the models, in combination, are able to compensate for the limitations of the other. The combined model, however, features its own disadvantages, including costliness. Our primary conclusion is in support of the quantification of comorbidity and its incorporation into survival prediction models. The choice of collection method should be based on availability of data sources and other administrative issues rather than the expected superior performance of one collection method over another.

In summary, the large-scale collection of cogent comorbid health information for newly-diagnosed cancer patients is important to ensure high-quality and meaningful cancer statistics. The inclusion of comorbidities in cancer predictive models is a necessity, given their far-reaching implications in clinical applications. We believe the inclusion of comorbid health information is critical for informed patient treatment decisions and quality of life considerations.

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Figure 1.
Distribution of comorbidity scores for each comorbidity index. Black bar, Adult Comorbidity Evaluation-27; gray bar, Charlson Comorbidity Index. Kappa=0.12

Figure 2.

(A) Comparison of Kaplan-Meier overall survival curves stratified by Adult Comorbidity Evaluation-27 (ACE-27) categories. (B) Comparison of Kaplan-Meier overall survival curves stratified by Charlson Comorbidity Index (CCI). (C) Comparison of Kaplan-Meier overall survival curves stratified by ACE-27 categories for patients identified as CCI=0. (D) Comparison of Kaplan-Meier overall survival curves stratified by CCI categories for patients identified as ACE-27=0.

Figure 3.

Multivariable Cox Regression calibrations curves for the model with (A) no comorbidities; (B) Adult Comorbidity Evaluation-27 (ACE-27) only; (C) Charlson Comorbidity Index (CCI) only, and (D) both ACE-27 And CCI. The calibration lines for all 4 models roughly follow the 45-degree angle showing agreement between predicted (x-axis) and observed (y-axis) survival at 2 years and thus demonstrate adequate calibration.

Table 1

Description of Characteristics of 6,138 Newly Diagnosed Cancer Patients Diagnosed Between 2006–2009, and the Role of Each Characteristic in Overall Survival

	n	%	Unadjusted Hazard Ratio (HR)	95% Hazard Ratio Confidence Limits	p Value
Age at diagnosis groups, y					
18–29	139	2	1.0(Ref)	—	—
30–34	120	2	1.32	0.72–2.42	0.374
35–39	134	2	1.19	0.64–2.21	0.598
40–44	232	4	1.43	0.83–2.45	0.19
45–49	394	6	1.42	0.86–2.36	0.17
50–54	613	10	2.20	1.37–3.53	0.001
55–59	816	13	2.30	1.44–3.68	<0.001
60–64	835	14	2.38	1.49–3.79	<0.001
65–69	863	14	2.56	1.61–4.08	<0.001
70–74	712	12	3.29	2.06–5.24	<0.001
75–79	594	10	4.35	2.73–6.93	<0.001
80–84	412	7	5.05	3.16–8.08	<0.001
85	274	4	7.03	4.37–11.30	<0.001
Sex					
Female	3,112	49	Ref	—	—
Male	3,026	51	1.29	1.18–1.41	<0.001
Race					
Caucasian	5,358	87	Ref	—	—
African-American	659	11	1.35	1.19–1.54	<0.001
Other	115	2	0.90	0.64–1.27	0.55
ACE-27 Score					
None	1,453	24	Ref	—	—
Mild	2,388	39	1.46	1.28–1.67	<0.001
Moderate	1,344	22	1.98	1.72–2.29	<0.001
Severe	950	15	3.31	2.87–3.81	<0.001
Charlson Score					

	n	%	Unadjusted Hazard Ratio (HR)	95% Hazard Ratio Confidence Limits	p Value
0	4,265	69	Ref	—	<0.001
1	1,341	22	1.72	1.55–1.90	<0.001
2	365	6	2.30	1.97–2.68	<0.001
>=3	167	3	3.10	2.53–3.81	<0.001
SEER Tumor staging					
In situ	392	6	Ref	—	—
Local	2,628	47	0.59	0.49–0.71	<0.001
Regional	1,698	28	1.66	1.39–1.98	<0.001
Distant	1,136	19	3.97	3.33–4.73	<0.001
Main cancer diagnosis *					
Breast	894	15	0.19	0.15–0.24	<0.001
Colorectal	501	8	1.08	0.93–1.26	0.332
Digestive	598	10	3.45	3.09–3.85	<0.001
Gynecological	477	8	0.57	0.47–0.69	<0.001
Head and Neck	428	7	0.71	0.58–0.86	<0.001
Lung	784	13	3.61	3.27–3.99	<0.001
Prostate	700	11	0.12	0.09–0.17	<0.001
Skin	345	6	0.31	2.23–0.42	<0.001
Urinary	435	7	0.79	0.66–0.95	0.012
Other	975	15	1.45	1.30–1.62	<0.001
Treatment †					
None	571	9	--		
Surgery	4,174	68	0.24	0.22–0.27	<0.001
Chemotherapy	2,122	35	1.83	1.68–2.00	<0.001
Radiation	1,977	32	0.97	0.88–1.06	0.514
Hormones	824	13	0.33	0.27–0.39	<0.001
Immuno	63	1	0.38	0.21–0.71	0.002
Other	89	1	3.16	2.47–4.04	<0.001

* The HR for each site is relative to all the other sites together (e.g. lung cancer vs. non-lung cancer).

† Treatment categories are not mutually exclusive.

Table 2
Distribution of Patients According to Level and Grade of Adult Comorbidity Evaluation-27 and Charlson Comorbidity Index

Adult Comorbidity Evaluation-27	Charlson Comorbidity Index			
	None, 0	Mild, 1	Moderate, 2	Severe, 3
None, 0, n (%)	1,386 (33)	56 (4)	6 (2)	5 (3)
Mild, 1, n (%)	1,704 (40)	571 (43)	87 (24)	26 (16)
Moderate, 2, n (%)	778 (18)	381 (28)	132 (36)	53 (32)
Severe, 3, n (%)	394 (9)	333 (25)	140 (38)	83 (50)
Total, n	4,262	1,341	365	167
				6,135*

* Three patients with Charlson Comorbidity Index = 0 were missing the Adult Comorbidity Evaluation-27 data.

Table 3

Comparison of Prevalence of Comorbid Conditions Coded from Both Indices

	Condition	Chart-based ACE-27	Claims-based CCI	p Value*	Kappa [†]	Yule's Y [‡]	95% CI for Yule's Y
1	MI	317 (5%)	176 (3%)	<0.001	0.55	0.84	0.81–0.87
3	CHF	261 (4%)	219 (4%)	0.0033	0.56	0.80	0.77–0.83
6	Venous+PAD	270 (4%)	96 (2%)	<0.001	0.25	0.68	0.62–0.74
7	PAD	141 (2%)	96 (2%)	0.0002	0.37	0.76	0.71–0.81
8	Respiratory	834 (14%)	722 (12%)	<0.001	0.63	0.74	0.72–0.76
9	Hepatic	129 (2%)	65 (1%)	<0.001	0.44	0.84	0.80–0.88
10	Stomach	63 (1%)	39 (0.6%)	0.015	0.03	0.40	0.09–0.70
12	Renal	189 (3%)	17 (0.3%)	<0.001	0.10	0.77	0.67–0.87
13	Diabetes	1051 (17%)	884 (14%)	<0.001	0.73	0.81	0.79–0.83
14	Stroke	241 (4%)	63 (1%)	<0.001	0.12	0.56	0.46–0.65
15	Dementia	88 (1%)	2 (0.03%)	<0.001	0.02	0.79	0.52–1.00
16	Paralysis	150.2%	18 (0.3%)	0.59	0.06	0.67	0.38–0.96
19	Rheumatologic	155 (3%)	60 (1%)	<0.001	0.316	0.79	0.73–0.84
20	AIDS	32 (0.5%)	18(0.3%)	0.016	0.32	0.87	0.81–0.93
22	Malignancy	1046 (17%)	16 (0.3%)	<0.001	0.002	0.12	–0.16–0.40

* McNemar's test p value.

[†] Kappa statistic is a measure of agreement that ranges from an expected value of 0 in case of agreement no more than expected by chance to a value of 1 in case of perfect agreement.

[‡] Yule's Y is a measure of association independent of the prevalence that ranges from –1 to 1. Values of Yule's Y close to 0 indicate poor agreement and values of Yule's Y closer to 1 indicate strong agreement.

ACE-27, Adult Comorbidity Evaluation-27; CCI-Charlson Comorbidity Index; MI, myocardial infarction; CHF, congestive heart failure; PAD, peripheral arterial disease; AIDS, acquired immunodeficiency syndrome.

Table 4

Summary of Adjusted* Hazard Ratios for Each Comorbidity Index from Multivariable Cox Proportional Hazards Model Predicting Mortality

Comorbidity index	ACE-27 model only, HR (95% CI)	CCI model only, HR (95% CI)	Model with both indices, HR (95% CI)
ACE-27			
None	--	--	--
Mild	1.08 (0.94–1.24)	--	1.04 (0.90–1.20)
Moderate	1.25 (1.08–1.45)	--	1.16 (0.99–1.35)
Severe	1.80 (1.55–2.09)	--	1.60 (1.37–1.88)
CCI			
0	--	--	--
1	--	1.23 (1.11–1.36)	1.15 (1.03–1.27)
2	--	1.44 (1.23–1.68)	1.26 (1.07–1.49)
>=3	--	2.09 (1.70–2.58)	1.75 (1.41–2.17)

* Hazard ratios from each model for each comorbidity index are adjusted for age, sex, race, tumor site, tumor stage, and treatment (as described in Table 1).

ACE-27, Adult Comorbidity Evaluation-27; CCI-Charlson Comorbidity Index.

Table 5

Performance of the Multivariable Cox Proportional Hazards Regression Models Adjusted for Age, Sex, Race, Tumor Site, Tumor Stage, Treatment and Comorbidity

	Df [*]	LR χ^2 [†]	R ² [‡]	BIC [§]	c-index
No comorbidity	33	2687.11	0.358	30820.72	0.820
ACE-27	36	2773.71	0.367	30755.38	0.825
CCI	36	2746.61	0.364	30784.03	0.824
CCI+ACE-27	39	2802.41	0.370	30749.50	0.827

^{*} Degrees of freedom.

[†] Likelihood ratio Chi square.

[‡] Nagelkerke's R square.

[§] Bayesian information criterion.