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Short-Form Charlson Comorbidity Index for Assessment of Perioperative Mortality After Radical Cystectomy

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Abstract

Background: The Deyo adaptation of the Charlson comorbidity index (DaCCI), which relies on 17 comorbid condition groupings, represents one of the most frequently used baseline comorbidity assessment tools in retrospective database studies. However, this index is not specific for patients with bladder cancer (BCa) treated with radical cystectomy (RC). The goal of this study was to develop a short-form of the original DaCCI (DaCCI-SF) that may specifically predict 90-day mortality after RC, with equal or better accuracy. **Patients and Methods:** Between 2000 and 2009, we identified 7,076 patients in the SEER-Medicare database with stage T1 through T4 nonmetastatic BCa treated with RC. We randomly divided the population into development (n=6,076) and validation (n=1,000) cohorts. Within the development cohort, logistic regression models tested the ability to predict 90-day mortality with various iterations of the DaCCI-SF, wherein <17 original comorbid condition groupings were included after adjusting for age, sex, race, T stage, and N stage. We relied on the Akaike information criterion to identify the most parsimonious and informative set of comorbid condition groupings. Accuracy of the DaCCI and the DaCCI-SF was tested in the external validation cohort. **Results:** Within the development cohort, the most parsimonious and informative model resulted in the inclusion of 3 of the 17 (17.6%) original comorbid condition groupings: congestive heart failure, cerebrovascular disease, and chronic pulmonary disease. Within the validation cohort, the accuracy was 68.4% for the DaCCI versus 69.7% for the DaCCI-SF. Higher accuracy of the DaCCI-SF was confirmed in subgroup analyses performed according to age (≤75 vs >75 years), stage (organ-confined vs non–organ-confined), type of diversion (ileal-conduit vs non–ileal-conduit), and treatment period. **Conclusions:** DaCCI-SF relies on 17.6% of the original comorbid condition groupings and provides higher accuracy for predicting 90-day mortality after RC compared with the original DaCCI, especially in most contemporary patients.

J Natl Compr Canc Netw 2017;15(3):327–333

Background

Radical cystectomy (RC) is one of the most invasive surgeries in urologic oncology, with an elevated perioperative mortality that can reach 14.8% in elderly patients, according to the SEER-Medicare database.[1] SEER-Medicare represents one of the most widely used population-based repositories of urologic oncology data. Within SEER-Medicare–based analyses, including those focusing on perioperative mortality, the Deyo adaptation of the Charlson comorbidity index (DaCCI) is

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Submitted June 11, 2016; accepted for publication November 28, 2016.

The authors have disclosed that they have no financial interests, arrangements, affiliations, or commercial interests with the manufacturers of any products discussed in this article or their competitors.

Author contributions: *Study conception and design:* Dell'Oglio, Tian, Karakiewicz. *Acquisition of data:* Dell'Oglio, Tian. *Analysis and interpretation of data:* Dell'Oglio, Tian, Karakiewicz. *Drafting of manuscript:* Dell'Oglio, Tian, Karakiewicz. *Critical revision:* Dell'Oglio, Tian, Leyh-Bannurah, Trudeau, Larcher, Moschini, Di Trapani, Capitanio, Briganti, Montorsi, Saad, Karakiewicz. *Statistical analysis:* Dell'Oglio, Tian. *Study supervision:* Karakiewicz.

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customarily used.[2,3] This index was originally developed[3] with the intent of predicting 1-year mortality in admitted medical patients. Several investigators[4,5] suggested the development of a comorbidity index specific to patients with bladder cancer (BCa) treated with RC for specific prediction of various mortality end points, including perioperative mortality. To address this unmet need, we attempted to identify a short-form of the original DaCCI (DaCCI-SF), using the most parsimonious and informative set of predictors of 90-day mortality after RC. Specifically, we hypothesized that a simplified comorbidity index, which rests on a fraction of the 17 original comorbid condition groupings that form the original DaCCI, may be developed with equal or better accuracy.

Patients and Methods

Data Source

A SEER-Medicare–specific approval was obtained through the NCI. The current study relied on the SEER-Medicare linked database. The SEER registries identify 28% of all cancer cases in the United States, and Medicare insures approximately 97% of all Americans aged ≥65 years. Linkage to the SEER database is complete for approximately 93% of cases.[6]

Study Population

In the SEER-Medicare–linked database, we identified 10,522 patients with nonmetastatic (cM0) urothelial carcinoma of the urinary bladder (UCUB) treated with RC between 2000 and 2009. Patients not enrolled in Medicare Parts A or B for a minimum of 12 months before their first recorded diagnosis and for a minimum of 3 months after RC were not considered. Patients who had health maintenance organization enrollment in the year before or for any period after diagnosis were also excluded. To ensure that all subjects had ≥1 year of claims from which comorbidities were derived, only those aged ≥66 years were considered. This resulted in a final population of 7,076 assessable patients with UCUB treated with RC.

Variable Definition

Patient characteristics included age at diagnosis, sex, race (white vs black vs other), and the 17 comorbid condition groupings contributing to the original DaCCI[2] (myocardial infarction, congestive heart failure [CHF], peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, mild liver disease, diabetes, diabetes with chronic complications, hemiplegia or paraplegia, renal disease, leukemia/lymphoma, moderate or severe liver disease, metastatic solid tumor, AIDS). All ICD-9-CM diagnostic codes that identified these 17 comorbid condition groupings were established by classifying inpatient and outpatient claims and physicians billing claims for the 12-month interval preceding RC. Tumor characteristics included pathologic stage (T1, T2, T3, and T4) and lymph node stage (N0, N+, Nx).

Outcomes

The end point our study was to identify the most parsimonious and informative set of comorbid conditions among the 17 original comorbid condition groupings included in the original DaCCI in order to predict 90-day mortality after RC, which was defined as overall mortality.

Statistical Analyses

Our analyses consisted of 5 steps. First, we randomly divided the population into development (n=6,076) and validation (n=1,000) cohorts. Second, within the development cohort, we relied on logistic regression models to test the ability of the 17 original comorbid condition groupings included in the original DaCCI to predict 90-day mortality after adjusting for age, sex, race, pathologic T stage, and N stage. Subsequently, the same analyses were performed to test the ability to predict 90-day mortality with various iterations of the DaCCI-SF, which included <17 of the original comorbid condition groupings. We relied on the Akaike information criterion (AIC)[7,8] to identify the most parsimonious and informative set of comorbid condition groupings for inclusion in the DaCCI-SF.

Third, within the validation cohort we tested the accuracy of the original DaCCI to predict 90-day mortality after RC, after adjusting for age, sex, race, pathologic T stage, and N stage. Subsequently, we tested the accuracy of the DaCCI-SF that was identified within the development cohort as the most parsimonious and informative. To further illustrate the DaCCI-SF's performance, receiver operating characteristic (ROC) curves were generated to compare models using the DaCCI-SF, the DaCCI, and no adjustment for comorbidity.

Finally, as a way to perform sensitivity analyses and to confirm the robustness of our findings, within the external validation cohort we tested the ability to predict 90-day mortality for the original DaCCI and the DaCCI-SF in specific patient subgroups, which included age (≤75 vs >75), stage (organ-confined vs non–organ-confined), type of diversion (ileal-conduit vs non–ileal-conduit), and treatment period (2005–2009).

All statistical tests were performed using the RStudio graphical interface v.0.98 for R software environment v.3.0.2 (R Foundation, Vienna, Austria). All tests were 2-sided with a significance level set at $P<.05$.

Results

Testing Population

The median age in the development and validation cohorts was 75 years. Most patients were male (71.4% and 71.9%), white (90.2% and 89.6%), and had pathologic T2 BCa (35.9% and 34.7%) and pN0 stage (64.5% and 63.0%; Table 1). Overall, 90-day mortality rates after RC were 10.7% and 11.2%, respectively, within development and validation cohorts (Table 2). Within the 17 comorbid-condition groupings of the original DaCCI, chronic pulmonary disease was the most frequent, followed by diabetes and cerebrovascular disease (Table 1). Conversely, virtually no patient was identified with dementia, leukemia/lymphoma, AIDS, or metastatic solid tumors of origin other than BCa, all of which represent DaCCI groupings.

In multivariable analyses performed in the development cohort, of 17 comorbid condition groupings, 5 were independent predictors of 90-day mortality after RC: CHF (odds ratio [OR], 1.49; $P<.001$), cerebrovascular disease (OR, 1.40; $P=.001$), chronic pulmonary disease (OR, 1.40; $P<.001$), rheumatologic disease (OR, 1.52; $P=.04$), and renal disease (OR, 1.47; $P=.003$; Table 3). Conversely, myocardial infarction, peripheral vascular disease, dementia, peptic ulcer disease, diabetes, diabetes with chronic complications, hemiplegia or paraplegia, moderate or severe liver disease, AIDS, and leukemia/lymphoma failed to reach the independent predictors status.

Analyses performed in the development cohort, aimed at identifying the most parsimonious and informative DaCCI-SF, resulted in inclusion of 3 of the 17 (17.6%) original comorbid condition groupings includ-

Table 1. Overall Patient Characteristics of Development and Validation Cohorts

Variables	Development Cohort (N=6,076)	Validation Cohort (N=1,000)	*P* Value
Age at diagnosis, y			.5
Median	75	75	
IQR	70.2–79.8	70.4–80.1	
Sex, n (%)			.8
Male	4,341 (71.4)	719 (71.9)	
Female	1,735 (28.6)	281 (28.1)	
Race, n (%)			.6
Other	302 (5)	57 (5.7)	
White	5,483 (90.2)	896 (89.6)	
Black	291 (4.8)	47 (4.7)	
Pathologic T stage, n (%)			.02
T1	1,586 (26.1)	271 (27.1)	
T2	2,181 (35.9)	347 (34.7)	
T3	1,563 (25.7)	228 (22.8)	
T4	746 (12.3)	154 (15.4)	
N status, n (%)			.6
N0	3,917 (64.5)	630 (63)	
Nx	1,340 (22.1)	227 (22.7)	
N+	819 (13.5)	143 (14.3)	
Myocardial infarction	534 (8.8)	90 (9)	.7
Congestive heart failure	790 (13)	127 (12.7)	.9
Peripheral vascular disease	554 (9.1)	78 (7.8)	.2
Cerebrovascular disease	1,108 (18.2)	176 (17.6)	.7
Dementia	*	*	.4
Chronic pulmonary disease	1,911 (31.5)	325 (32.5)	.5
Rheumatologic disease	179 (2.9)	33 (3.3)	.6
Peptic ulcer disease	156 (2.6)	25 (2.5)	.9
Mild liver disease	35 (0.6)	*	.5
Diabetes	1,622 (26.7)	252 (25.2)	.3
Diabetes with chronic complications	345 (5.7)	43 (4.3)	.09
Hemiplegia or paraplegia	54 (0.9)	*	.9
Renal disease	548 (9)	94 (9.4)	.7
Leukemia/lymphoma	*	*	.9
Moderate or severe liver disease	13 (0.2)	*	.9
AIDS	*	*	.9

Comorbidities are presented according to comorbid condition groupings of the Deyo adaptation of the Charlson comorbidity index.

Abbreviation: IQR, interquartile range.

*Masked for protection of patient confidentiality reasons, as per NCI regulations.

Table 2. 90-Day Mortality Development and Validation Cohort

Variables	Development Cohort n=649 (10.7%)	Validation Cohort n=112 (11.2%)
Age at diagnosis, y		
Median	77.7	78.5
IQR	72.6–81.9	73.2–83.1
Sex, n (%)		
Male	438 (67.5)	73 (65.2)
Female	211 (32.5)	39 (34.8)
Race, n (%)		
Other	29 (4.5)	*
White	581 (89.5)	101 (90.2)
Black	39 (6)	*
Pathologic T stage, n (%)		
T1	130 (20)	20 (17.9)
T2	184 (28.4)	32 (28.6)
T3	193 (29.7)	37 (33)
T4	142 (21.9)	23 (20.5)
N status, n (%)		
N0	361 (55.6)	59 (52.7)
Nx	165 (25.4)	31 (27.7)
N+	123 (19)	22 (19.6)
Myocardial infarction	70 (10.8)	14 (12.5)
Congestive heart failure	145 (22.3)	23 (20.5)
Peripheral vascular disease	80 (12.3)	12 (10.7)
Cerebrovascular disease	170 (26.2)	28 (25)
Dementia	*	*
Chronic pulmonary disease	256 (39.4)	43 (38.4)
Rheumatologic disease	31 (4.8)	*
Peptic ulcer disease	25 (3.9)	*
Mild liver disease	*	*
Diabetes	207 (31.9)	35 (31.2)
Diabetes with chronic complications	51 (7.9)	*
Hemiplegia or paraplegia	*	*
Renal disease	96 (14.8)	14 (12.5)
Leukemia/lymphoma	*	*
Moderate or severe liver disease	*	*
AIDS	*	*

Comorbidities are presented according to comorbid condition groupings of the Deyo adaptation of the Charlson comorbidity index.

Abbreviation: IQR, interquartile range.

*Masked for protection of patient confidentiality reasons, as per NCI regulations.

ed in the original DaCCI: CHF (OR, 1.65; $P<.001$), cerebrovascular disease (OR, 1.45; $P<.001$), and chronic pulmonary disease (OR, 1.43; $P<.001$; Table 3)

External Validation

Within the validation cohort, the individual accuracy figures for predicting 90-day mortality after RC for the 3 comorbid condition groupings were 68.5% for CHF, 67.9% for cerebrovascular disease, and 67.3% for chronic pulmonary disease. The combination of these 3 comorbid condition groupings that formed the DaCCI-SF yielded an accuracy of 69.7% versus 68.4% for the original DaCCI (Table 4). ROC curves for the comparison of these models are shown in supplemental eFigure 1 (available with this article at JNCCN.org).

Subgroup Analyses

Lastly, we tested the accuracy of the DaCCI-SF for predicting 90-day mortality after RC relative to the original DaCCI in specific patient subgroups. In brief, the DaCCI-SF predicted 90-day mortality after RC with higher accuracy relative to the original DaCCI in all subgroups, without exception (Table 4).

Discussion

The study objective was to devise a short-form of the original DaCCI (DaCCI-SF) with equal or better accuracy for predicting 90-day mortality after RC. The rationale for such analysis stems from the absence of a contemporary, validated tool in the specific setting of patients with BCa treated with RC.[5]

Our analyses demonstrated several important findings. First, 1 out of 10 patients treated with RC died within 90 days. This observation validates the importance of perioperative mortality as an important clinical concept. Moreover, it calls for a contemporary, validated tool for analyses of 90-day mortality after RC that is ideally simpler than the relatively cumbersome DaCCI,[2] but offers same or better accuracy.

Second, of 17 tested comorbid condition groupings that contribute to the original DaCCI, only 5 achieved independent predictor status in models aimed at predicting 90-day mortality after RC (CHF, cerebrovascular disease, chronic pulmonary disease, rheumatologic disease, and renal disease). Several of

Table 3. Logistic Regression Models Quantifying Ability to Predict 90-Day Mortality After Radical Cystectomy[a]

	DaCCI		DaCCI-SF	
	Multivariable OR (95% CI)	*P* Value	Multivariable OR (95% CI)	*P* Value
Myocardial infarction	1.04 (0.78–1.37)	.8	–	–
Congestive heart failure	1.49 (1.19–1.86)	<.001	1.65 (1.33–2.05)	<.001
Peripheral vascular disease	1.04 (0.79–1.36)	.8	–	–
Cerebrovascular disease	1.4 (1.14–1.71)	.001	1.45 (1.19–1.77)	<.001
Dementia	0.8 (0.07–9.43)	.9	–	–
Chronic pulmonary disease	1.4 (1.17–1.67)	<.001	1.43 (1.2–1.7)	<.001
Rheumatologic disease	1.52 (1.01–2.3)	.04	–	–
Peptic ulcer disease	1.31 (0.83–2.07)	.2	–	–
Mild liver disease	0.28 (0.04–2.06)	.2	–	–
Diabetes	1.2 (0.98–1.46)	.08	–	–
Diabetes with chronic complications	1.15 (0.81–1.64)	.4	–	–
Hemiplegia or paraplegia	0.99 (0.43–2.27)	.9	–	–
Renal disease	1.47 (1.14–1.89)	.003	–	–
Leukemia/ lymphoma	3.26 (0.33–32.49)	.3	–	–
Moderate or severe liver disease	0.52 (0.06–4.24)	.5	–	–
AIDS	1.0 (0.1–9.1)	.9	–	–

Abbreviations: DaCCI, Deyo adaptation of the Charlson comorbidity index; DaCCI-SF, a short-form of the original DaCCI; OR, odds ratio.
[a]The models were adjusted for age, sex, race (white vs black vs others), pathologic T stage (T1 vs T2 vs T3 vs T4), and pathologic N stage (N0 vs N+ vs Nx).

these entities have an established role in potentially predicting perioperative mortality.[9–13] However, it is also noteworthy that 12 of the 17 comorbid condition groupings failed to achieve independent predictor status. Of these, several noteworthy entities, such as myocardial infarction, diabetes, or diabetes with chronic complications, failed to make the cut. This observation indicates that even though some entities predict overall mortality,[14–20] they may not be capable of accurately predicting 90-day mortality in the specific setting of RC for BCa. It is also important to note that, based on their low or even marginal prevalence among patients with BCa treated with RC (Table 1), some of the original comorbid condition groupings, such as AIDS and leukemia/lymphoma, were not expected to accurately predict 90-day mortality. This observation validates the need for the development of a contemporary and validated tool for predicting 90-day mortality after RC, as was done in the current study.

Third, to the best of our knowledge, we are the first to devise and test a DaCCI-SF for predicting 90-day mortality after RC. Our results showed that the DaCCI-SF performs better and is substantially simpler than the original DaCCI. Specifically, the DaCCI-SF relies on only 3 comorbid condition groupings and achieved 69.7% accuracy compared with 68.4% with the original DaCCI, which relies on 17 comorbid condition groupings. Higher accuracy of the DaCCI-SF was invariably confirmed in all subgroup analyses performed according to age (≤75 vs >75 years), stage (organ-confined vs non–organ-confined), type of diversion (ileal-conduit vs non–ileal-conduit), and treatment period. The increase in accuracy of the DaCCI-SF relative to the original DaCCI was not overwhelming, except in the most contemporary patients, namely those treated between 2005 and 2009. This was expected considering the fact that we are proposing a simplification of the DaCCI that was originally developed in admitted medical patients and not in the specific setting of patients with BCa treated with RC.

Fourth, we performed a detailed assessment of individual groupings of specific comorbid conditions to identify the most and least informative one based on individual consideration. These analyses revealed that the accuracy was 68.5% for CHF, 67.9% for cerebrovascular disease, and 67.3% for chronic pulmonary disease.

Previous studies proposed a simplification of the CCI[21,22] or developed a new comorbidity score[23–29] in a specific disease setting. However, in all of these studies, the focus did not represent patients with BCa treated with RC, and therefore these indexes are not applicable in the BCa setting. This is important to underline, because comorbidity profiles differ depending on the disease.

Clinical implications of our findings are severalfold. First, we demonstrated that the original DaCCI can be shortened without loss of accuracy when prediction of 90-day mortality after RC represents the end point. It may be replaced with a DaCCI-SF that relies on only 3 comorbid condition groupings, instead of 17; this applies to the specific population of patients with BCa treated with RC. Therefore, we

Table 4. Externally Validated Accuracy Estimates

	DaCCI	DaCCI-SF
Overall population	68.4%	69.7%
Age		
≤75 y	65.0%	66.8%
>75 y	63.3%	64.0%
Stage		
Organ-confined	65.5%	65.8%
Non–organ-confined	73.4%	76.0%
Type of diversion		
Ileal-conduit	66.6%	66.8%
Non–ileal-conduit	72.7%	76.8%
Most contemporary patients (2005–2009)	60.3%	68.0%

Abbreviations: DaCCI, Deyo adaptation of the Charlson comorbidity index; DaCCI-SF, a short-form of the original DaCCI.

proposed a more user-friendly, less labor-intensive and time-consuming comorbidity index that is intended for use in retrospective analyses performed using large-scale BCa databases, in which ICD-9-CM diagnostic codes are found. Moreover, one comorbidity grouping, CHF, was equally as accurate as with the original DaCCI. Therefore, investigators searching for adjustment for comorbidity in small cohorts, in which the number of degrees of freedom is restricted, may rely on this single variable. Conversely, in larger database analyses, use of the DaCCI-SF, which relies on the 3 comorbid condition groupings, should be encouraged if sample size permits.

Other approaches are recommended in retrospective databases in which American Society of Anesthesiologists[30] or other coding schemes[31,32] are used, because such methods were shown to result in higher accuracy in predicting 90-day mortality after RC than the CCI.[33] However, such coding schemes are not widely accepted[5] and cannot be applied in administrative databases, such as SEER-Medicare, which uses ICD-9-CM codes.

Despite the strengths of our study, it is not devoid of limitations. First, our findings are not generalizable, because they originated from the SEER-Medicare setting. Second, our tools may not be applicable to younger patients, given the fact that SEER-Medicare relies on patients aged ≥66 years. Third, despite the fact that we devised the first DaCCI-SF for predicting 90-day mortality in contemporary patients with BCa treated with RC, there might be some comorbid conditions[34,35] that are not included in this index because of the nature of the original CCI, that are more represented among patients with BCa, and that might be more strictly related to perioperative mortality after RC. Future studies are needed to develop a new comorbidity score for the specific prediction of 90-day mortality in patients who have undergone RC, analyzing all possible individual comorbid conditions to identify those that satisfy the criteria of maximal accuracy and parsimony for predicting perioperative mortality after RC.

Conclusions

In the current study, we devised the first short-form version of the DaCCI for predicting 90-day mortality in patients with BCa treated with RC. The DaCCI-SF relies on only 3 (17.6%) of the 17 original comorbid condition groupings and provides higher accuracy for predicting 90-day mortality after RC compared with the original DaCCI, especially in most contemporary patients.

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