Validation and Recalibration of Charlson and Elixhauser Comorbidity Indices to Predict In-hospital Mortality in Hospitalized Patients in a Japanese Hospital-Based Administrative Database

Tomomi KIMURA*, Toshifumi SUGITANI*, Takuya NISHIMURA*, Masanori ITO*

Objective: To validate and recalibrate Charlson and Elixhauser comorbidity indices (CCI and ECI, respectively) in a Japanese hospital-based administrative database.

Methods: In this retrospective, cohort study, derivation and validation cohorts were developed to include all hospitalizations for patients aged ≥18 years at admission and discharged in 2015 or 2016, respectively, from an administrative database based on 287 hospitals. Seventeen CCI and 30 ECI conditions were identified using the International Classification of Diseases (ICD)-10 codes at admission or during the stay. Predictability for hospital death was evaluated using C statistics from multivariable logistic regression models including age, sex, and individual CCI/ECI conditions or the CCI/ECI score in the derivation cohort. After stepwise selection, weighted risk scores were re-assigned to each condition based on the odds ratios (CCI) or beta-coefficient (ECI), and these modified models were evaluated in the validation cohort.

Results: The original CCI/ECI had good predictive abilities for hospital death: C statistics (95% confidence interval) for individual comorbidities and score models were 0.764 (0.762-0.765) and 0.731 (0.729-0.733) for CCI and 0.783 (0.781-0.784) and 0.750 (0.748-0.752) for ECI, respectively. Modified CCI and ECI had 13 and 27 conditions, respectively, but maintained comparable predictive abilities: C statistics for modified individual comorbidities and score models were 0.761 (0.759-0.763) and 0.759 (0.757-0.760) for CCI, and 0.784 (0.782-0.785) and 0.783 (0.781-0.785) for ECI, respectively.

Conclusions: The original and modified CCI/ECI models, with reduced numbers of conditions, had sufficient and comparable predictive abilities for hospital death and can be used in future studies using this administrative database.

Keywords: comorbidity, database, hospital mortality, Japan

Introduction

Charlson¹ and Elixhauser² Comorbidity Indices (CCI and ECI, respectively) are established, validated tools and widely used to quantify comorbidity burden.³⁻¹⁵

The CCI was developed in the United States based on statistical modeling of raw medical chart data from hospitalized patients more than 30 years ago.¹ The presence of 17 conditions at admission and the sum of weighted scores for prevalent conditions were used to predict 1-year mortality. Over the years, attempts have been made to validate and/or modify the CCI to better account for variabilities in countries, diagnoses, and data sources.¹⁶⁻²⁴ Thus, the Elixhauser

* Advanced Informatics & Analytics, Astellas Pharma Inc., Tokyo, Japan
Address for correspondence: Tomomi KIMURA, Advanced Informatics & Analytics, Astellas Pharma Inc., 2-5-1 Nihonbashi Honcho, Chuo-ku, Tokyo 103-8411, Japan
Phone: +81-80-1004-0648, E-mail: tomomikimura@astellas.com
classification system was developed as a more comprehensive measure of comorbidity for hospitalized patients using data from an administrative claims database. The initial list of 41 comorbidities was refined to include 30 conditions in the final list. This was later modified into the ECI scoring system that has been validated and widely used for predicting outcomes in hospitalized patients.

Quan and colleagues developed coding algorithms to define each condition listed in the CCI/ECI using the International Classification of Diseases (ICD) 9th revision, its Clinical Modification (ICD-9-CM), and its 10th revision (ICD-10). In this study, they evaluated the performance of these coding algorithms in predicting hospital mortality. They further updated the Charlson Index and score and validated it in six countries, including Japan. The Japanese data were derived from national data for 2008 and showed nominally lower C statistics compared to the other five countries, probably due to having no more than 10 fields for diagnosis.

A recent study that used an insurance claims dataset from the Japan Medical Data Center (JMDC) demonstrated that the discriminatory ability of both the original and modified CCI/ECI models for hospital deaths and readmissions was comparable. To the best of our knowledge, the applicability of the CCI/ECI in the commercially accessible Japanese administrative databases has not yet been evaluated. It is important to determine if the original CCI/ECI remains an appropriate and optimal approach to study comorbid conditions in the present-day patient population in Japan, and if reevaluation of the indices and reassignment of the weighted risk score can improve the performance, especially when administrative databases are used.

In this study, we evaluated the applicability of the original CCI/ECI in predicting hospital death using a Japanese hospital-based administrative database. We also developed and assessed modified versions of these indices and descriptively compared the predictive ability with the original indices.

Methods

This was a retrospective cohort study using a nationwide Japanese hospital-based administrative database.

Data source

The database included >17 million inpatients and outpatients from 287 Diagnosis Procedure Combination (DPC) hospitals as of March 2017 (approximately 17% of DPC hospitals or 4% of total hospitals [DPC and non-DPC hospitals] in Japan). The authors purchased the data from Medical Data Vision as Anonymously Processed Information.

DPC is a uniquely Japanese payment system that first emerged in the year 2003 amidst growing concerns over healthcare costs, length of hospital stays, and the healthcare needs associated with the growing aging population. The goal of DPC is to support improvement in healthcare standards and transparency. Through the collection of objective treatment information made accessible through a database, this system strives to not only help hospital administrators and providers better understand the outcomes related to the care they are delivering, but also to improve quality of care and address disparities between hospitals. Patients also have access to data-based care standards as well as pricing information. DPC was also designed to shorten the average hospital stay length. As of 2015, this payment system was estimated to cover nearly 54% of general hospital beds in Japan. All the DPC hospitals were acute care hospitals in the period 2015-2016 and provided discharge summaries in the DPC format (DPC data), in addition to monthly medical claims. The DPC data in the years 2015 and 2016 contained 12 and 25 fields for diagnosis, respectively, which included primary diagnosis that triggered the hospitalization, diagnosis with the highest resource use, diagnosis with the second highest resource use, diagnoses at admission, and post-admission complications. The database also includes the medical claims data. Unlike the DPC data, medical claims do not
have a limit on the number of diagnoses to be reported. In addition, the Treatment Initiation Date at the medical institution is included in medical claims data.

**Study population**

All hospitalization records for patients ≥18 years old at admission were extracted and allocated either to the derivation cohort (with discharge date between January 1 and December 31, 2015) or the validation cohort (with discharge date between January 1 and December 31, 2016). Maternal hospitalizations (ICD-10 = O00–O99), hospitalizations with discharge on admission date, and hospitalizations with ambiguous records, such as those for patients having any records after death, with overlapping hospitalization (hospitalized before discharge from previous hospitalization), or with more than one discharge date for one admission date, were excluded. The unit of analysis was hospitalization. Therefore, if a patient had multiple hospitalizations, we treated them as statistically independent in the following analyses.

**Defining CCI and ECI conditions and outcomes**

CCI- and ECI-listed conditions were defined using the ICD-10 codes according to the definitions developed by Quan and colleagues. Two pilot assessments were performed before determining the definitions for the primary analysis. The first assessment was to determine the lookback period. Using both DPC data and medical claims, we looked back 6 or 12 months (180 or 365 days, respectively) from the admission date to collect CCI- and ECI-listed conditions, in addition to the diagnoses during the stay. We excluded diagnoses with a suspicion flag in the medical claims. The second pilot assessment was to determine if we should exclude post-admission complications from the analysis. By using the DPC data diagnosis category, we compared the results with and without including post-admission complications.

Based on the findings from the pilot assessments, the ascertainment period was defined as either at admission or during the stay, ie, no lookback period was applied to the primary analysis, and post-admission diagnoses to be included. As a data source for diagnosis, we used the discharge summary (DPC data) but not medical claims, although the latter would have potentially captured more diagnoses.

Hospital death was obtained as an outcome of hospitalization. Direct cost during the stay was obtained from hospitalization with valid cost data.

**Statistical analyses**

The predictive ability was assessed using C statistics and their 95% confidence interval (CI) derived from logistic regression models that included hospital death as a dependent variable, and age (<65 versus ≥65 years at admission), sex, and either all CCI/ECI conditions ("individual comorbidity model") or score (ie, the sum of weighted scores assigned to individual comorbidities; "score model") as explanatory variables. Pearson chi-square statistic was used to correct possible over-dispersion in the logistic regression models. Validation cohort was used to test C-statistic in the original CCI and ECI models.

Modified versions of CCI/ECI were developed in the derivation cohort by using the stepwise variable selection method, including all CCI- or ECI-listed conditions (but not age and sex). In the modified CCI conditions with an odds ratio (OR) <1.0 were excluded. Weighted scores were reassigned to individual conditions based on OR for modified CCI score model (0 for OR <1.2 : 1 for ≥1.2 and <1.5 : 2 for ≥1.5 and <2.5 : 3 for ≥2.5 and <3.5 : 4 for ≥3.5 and <4.5 : 5 for ≥4.5 and <6 : 6 for ≥6) or on beta-coefficient for modified ECI score model, respectively. The predictive abilities of the modified CCI/ECI models and the scores were assessed in the validation cohort and the C statistics were descriptively compared with that of the original CCI/ECI models.

The association of the modified CCI/ECI scores with length of hospital stay and cost during the hospital stay was assessed in the validation cohort using a box-whisker plot. Whiskers
showed the nearest values within 1.5 times the interquartile range. The hospitalizations included in the validation cohort were divided into four groups according to the order of the CCI/ECI scores.

All statistical analyses were performed using SAS Studio 3.5 (SAS Institute, Cary, NC, USA.).

**Ethical approval**

The protocol was approved under the auspices of the Astellas Project Review Board and Ethics and Compliance Review Committee.

**Results**

The derivation cohort included 1,577,897 hospitalizations from 1,168,935 patients and the validation cohort included 1,258,934 patients. The patient flow in the derivation and validation cohorts is shown in Figure 1.

**Figure 1** Patient flow

Table 1 shows the summary of the baseline characteristics and summary of the main outcome measures. CCI/ECI scores and the prevalence of individual comorbidity conditions were similar in the derivation and validation cohorts. Two-thirds of patients were ≥65 years old at admission and 55% were male. Nearly 70% of patients, and 76% of patients, had at least one CCI and ECI condition, respectively, at admission or during the stay and a quarter of them had malignancy without metastasis. Hospital deaths in the derivation and validation cohorts were 71,987 (4.6%) and 75,783 (4.5%), respectively. The median hospital stay was 8 days, and the median cost was approximately 500,000 JPY (4,800 USD).

Age- and sex-adjusted logistic regression showed the highest OR for metastatic solid tumor followed by moderate or severe liver disease and congestive heart failure (Table 2A). By stepwise selection, acquired immunodeficiency syndrome/human immunodeficiency virus (AIDS/HIV) was not selected. Peptic ulcer disease and diabetes (with and without complications) were negatively (ie, protectively) associated with hospital death and manually excluded. This resulted in the inclusion of 13 instead of 17 CCI comorbidities in the modified model. Further, only 9 out of 17 conditions had an OR ≥1.2 and were given positive weights. As per the modified model, peripheral vascular disorders were not associated with hospital death in this study setting. Similar-
| Parameter | Derivation cohort | Validation cohort | Absolute standardized mean difference$^a$ |
|-----------|-------------------|-------------------|------------------------------------------|
| Number of patients | 1,168,935 | 1,258,934 | 0.016 |
| Number of hospitalizations | 1,577,897 | 1,702,464 | |
| **Age, years** | | | 0.016 |
| Mean (SD) | 68.3 (15.96) | 68.6 (15.98) | |
| Median (Q1–Q3) | 71.0 (60.0–80.0) | 71.0 (61.0–80.0) | |
| Range | 18–111 | 18–111 | |
| **Age group, n (%)** | | | 0.020 |
| ≥65 years | 1,061,549 (67.3) | 1,160,929 (68.2) | |
| <65 years | 516,348 (32.7) | 541,535 (31.8) | |
| **Sex, n (%)** | | | 0.001 |
| Female | 716,264 (45.4) | 773,987 (45.5) | |
| Male | 861,633 (54.6) | 928,477 (54.5) | |
| **Prevalence of individual CCI conditions, n (%)**$^b$ | | | |
| With any CCI condition | 1,092,703 (69.3) | 1,182,074 (69.4) | 0.004 |
| Myocardial infarction | 49,845 (3.2) | 56,984 (3.3) | 0.011 |
| Congestive heart failure | 155,864 (9.9) | 178,367 (10.5) | 0.020 |
| Peripheral vascular disorders | 50,502 (3.2) | 58,996 (3.5) | 0.015 |
| Cerebrovascular disease | 173,627 (11.0) | 195,579 (11.5) | 0.015 |
| Dementia | 60,491 (3.8) | 73,583 (4.3) | 0.025 |
| Chronic pulmonary disorders | 90,495 (5.7) | 103,144 (6.1) | 0.014 |
| Rheumatoid arthritis | 30,389 (1.9) | 33,245 (2.0) | 0.002 |
| Peptic ulcer disease | 125,167 (7.9) | 140,347 (8.2) | 0.011 |
| Mild liver disease$^c$ | 71,950 (4.6) | 80,895 (4.8) | 0.009 |
| Diabetes, uncomplicated$^c$ | 228,023 (14.5) | 255,485 (15.0) | 0.016 |
| Diabetes, complicated$^c$ | 68,526 (4.3) | 74,943 (4.4) | 0.003 |
| Hemiplegia or paraplegia | 14,109 (0.9) | 14,754 (0.9) | 0.003 |
| Renal disease | 81,528 (5.2) | 91,032 (5.3) | 0.008 |
| Any malignancy$^{c,d}$ | 395,361 (25.1) | 426,889 (25.1) | 0.000 |
| Moderate or severe liver disease$^c$ | 15,085 (1.0) | 15,726 (0.9) | 0.003 |
| Metastatic solid tumor$^c$ | 124,422 (7.9) | 136,892 (8.0) | 0.006 |
| AIDS/HIV | 414 (0.0) | 454 (0.0) | 0.000 |
| **Original CCI score** | | | 0.024 |
| Mean (SD) | 1.9 (1.93) | 1.9 (1.97) | |
| Median (Q1–Q3) | 2.0 (0.0–3.0) | 2.0 (0.0–3.0) | |
| Range | 0–15 | 0–17 | |
| **Prevalence of individual ECI conditions, n (%)** | | | |
| With any ECI condition | 1,200,583 (76.1) | 1,299,414 (76.3) | 0.006 |
| Congestive heart failure | 155,864 (9.9) | 178,367 (10.5) | 0.020 |
| Cardiac arrhythmias | 136,956 (8.7) | 162,008 (9.5) | 0.029 |
| Valvular disease | 43,026 (2.7) | 48,550 (2.9) | 0.008 |
| Pulmonary circulation disorders | 9,782 (0.6) | 10,967 (0.6) | 0.003 |
| Peripheral vascular disorders | 50,502 (3.2) | 58,996 (3.5) | 0.015 |
| Hypertension | 438,345 (27.8) | 514,397 (30.2) | 0.053 |
| Paralysis | 14,109 (0.9) | 14,754 (0.9) | 0.003 |
| Neurological disorders | 54,775 (3.5) | 62,463 (3.7) | 0.011 |
| Chronic pulmonary disease | 90,495 (5.7) | 103,144 (6.1) | 0.014 |

(Continued)
### Table 1 (Continued)

| Parameter | Derivation cohort | Validation cohort | Absolute standardized mean differencea |
|-----------|------------------|-------------------|-----------------------------------------|
| Diabetes, uncomplicatedc | 213,014 (13.5) | 239,035 (14.0) | 0.016 |
| Diabetes, complicatedc | 83,535 (5.3) | 91,393 (5.4) | 0.003 |
| Hypothyroidism | 16,583 (1.1) | 21,427 (1.3) | 0.019 |
| Renal failure | 80,997 (5.1) | 90,453 (5.3) | 0.008 |
| Liver disease | 88,590 (5.6) | 98,261 (5.8) | 0.007 |
| Peptic ulcer disease, no bleeding | 97,626 (6.2) | 111,289 (6.5) | 0.014 |
| AIDS/HIV | 414 (0.0) | 454 (0.0) | 0.000 |
| Lymphoma | 28,644 (1.8) | 32,279 (1.9) | 0.006 |
| Metastatic cancerc | 124,422 (7.9) | 136,892 (8.0) | 0.006 |
| Solid tumor without metastasisc | 364,871 (23.1) | 393,477 (23.1) | 0.000 |
| Rheumatic disease/collagen vascular diseases | 35,687 (2.3) | 39,457 (2.3) | 0.004 |
| Coagulopathy | 28,112 (1.8) | 31,163 (1.8) | 0.004 |
| Obesity | 2,940 (0.2) | 3,609 (0.2) | 0.006 |
| Weight loss | 5,451 (0.3) | 6,387 (0.4) | 0.005 |
| Fluid and electrolyte disorders | 106,831 (6.8) | 121,978 (7.2) | 0.015 |
| Blood loss anemia | 17,406 (1.1) | 18,940 (1.1) | 0.001 |
| Deficiency anemia | 63,116 (4.0) | 73,184 (4.3) | 0.015 |
| Alcohol abuse | 13,926 (0.9) | 15,874 (0.9) | 0.005 |
| Drug abuse | 400 (0.0) | 412 (0.0) | 0.001 |
| Psychoses | 24,520 (1.6) | 29,345 (1.7) | 0.013 |
| Depression | 29,851 (1.9) | 36,512 (2.1) | 0.018 |
| **Original ECI score** | | | 0.030 |
| Mean (SD) | 4.8 (5.58) | 5.0 (5.78) | |
| Median (Q1–Q3) | 4.0 (0.0–8.0) | 4.0 (0.0–9.0) | |
| Range | −10 to 43 | −12 to 52 | |
| **Outcome measure** | | | |
| Hospital death, n (%) | 71,987 (4.6) | 75,783 (4.5) | 0.005 |
| LoS, days | | | 0.006 |
| Mean (SD) | 16.0 (58.68) | 15.6 (62.54) | |
| Median (Q1–Q3) | 8.0 (3.0–18.0) | 8.0 (3.0–18.0) | |
| Range | 1 to 18,902 | 1 to 22,760 | |
| Cost, 1,000 JPY | | | 0.015 |
| N | 1,564,566 | 1,688,290 | |
| Mean (SD) | 883 (1151) | 901 (1165) | |
| Median (Q1–Q3) | 526 (289–1052) | 537 (297–1072) | |
| Range | 0.010 to 84,164 | 0.006 to 75,724 | |

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a Absolute standardized mean difference ≥0.1 was considered negligible.\(^{(2,4)}\)

b Percentages for CCIIs calculated against number of hospitalizations (derivation cohort, n = 1,577,897; validation cohort, n = 1,702,464).

c Diabetes with versus without complications, mild versus moderate or severe liver diseases, and malignancy with versus without metastasis, respectively, are mutually exclusive.

d Any malignancy, including lymphoma and leukemia, except malignant neoplasm of skin.

e Summary statistics were calculated for patients with valid cost data.

AIDS/HIV, acquired immunodeficiency syndrome/human immunodeficiency virus; CCI, Charlson Comorbidity Index; ECI, Elixhauser Comorbidity Index; JPY, Japanese yen; LoS, length of hospital stay; SD, standard deviation.
ly, the modified ECI model had 27 instead of 30 conditions (Table 2B). The mean (standard deviation [SD]) for the modified CCI and ECI scores was 1.9 (2.11) and 3.9 (6.57) and the median (Q1–Q3) was 2.0 (0.0–3.0) and 2.0 (0.0–7.0), respectively.

Although the modified CCI and ECI had fewer conditions, their predictive abilities were comparable to the original CCI and ECI (Figure 2). The C statistics (95% CI) were comparable between the original (0.764 [0.762–0.765]) and modified (0.761 [0.759–0.763]) models using CCI individual conditions. The C statistics for the modified CCI score model (0.759 [0.757–0.760]) was better than the original score model (0.731 [0.729–0.733]). An increment of 1 unit in the modified score was associated with a larger increase in hospital mortality compared to the original CCI
### Table 2 Comparison of the ORs and the weights of the original and the modified CCIs and ECIs for hospital death

**B. ECI model**

| Individual comorbidity model | Original model | Condition selection and weight re-assignment | Modified model |
|------------------------------|----------------|---------------------------------------------|----------------|
|                              | OR (95% CI)    | van Walraven point                          | OR (95% CI)    | Beta coefficient | Modified weight* (risk score) | OR (95% CI) |
| Age, ≥65 years               | 3.01 (2.95-3.08) | 0.54 (0.50-0.58)                            | 2.96 (2.90-3.03) | 2.67 (2.62-2.73) |
| Sex, female                  | 0.93 (0.91-0.94) | 0.09 (0.07-0.11)                            | 0.93 (0.91-0.94) | 0.80 (0.77-0.84) |
| Congestive heart failure     | 2.66 (2.60-2.72) | 0.94 (0.92-0.96)                            | 1.12 (1.11-1.13) | 1.14 (1.11-1.17) |
| Valvular disease             | 0.78 (0.75-0.82) | 0.09 (0.07-0.11)                            | 0.80 (0.77-0.84) | 0.84 (0.80-0.89) |
| Pulmonary circulation disorders | 1.73 (1.61-1.86) | 0.09 (0.07-0.11)                            | 1.71 (1.60-1.84) | 1.03 (0.98-1.07) |
| Peripheral vascular disorders | 1.05 (1.00-1.10) | 0.09 (0.07-0.11)                            | 0.94 (0.92-0.96) | 0.91 (0.89-0.93) |
| Hypertension                 | 0.60 (0.59-0.61) | 0.09 (0.07-0.11)                            | 0.58 (0.57-0.59) | 0.51 (0.49-0.53) |
| Paralysis                    | 1.65 (1.54-1.78) | 0.09 (0.07-0.11)                            | 1.62 (1.51-1.74) | 1.61 (1.56-1.65) |
| Neurological disorders       | 2.18 (2.10-2.25) | 0.09 (0.07-0.11)                            | 2.10 (2.03-2.17) | 1.28 (1.24-1.31) |
| Chronic pulmonary disease    | 1.26 (1.22-1.30) | 0.09 (0.07-0.11)                            | 1.28 (1.24-1.31) | 1.28 (1.24-1.31) |
| Diabetes, uncomplicated^b    | 0.88 (0.86-0.90) | 0.09 (0.07-0.11)                            | 0.94 (0.92-0.97) | 0.91 (0.89-0.93) |
| Diabetes, complicated^b      | 0.80 (0.77-0.83) | 0.09 (0.07-0.11)                            | 0.81 (0.78-0.84) | 0.77 (0.74-0.80) |
| Hypothyroidism               | 0.81 (0.75-0.88) | 0.09 (0.07-0.11)                            | 0.83 (0.77-0.89) | 0.84 (0.78-0.89) |
| Renal failure                | 1.97 (1.92-2.03) | 0.09 (0.07-0.11)                            | 2.10 (2.04-2.16) | 1.87 (1.82-1.92) |
| Liver disease                | 1.67 (1.62-1.72) | 0.09 (0.07-0.11)                            | 1.65 (1.61-1.72) | 1.61 (1.56-1.65) |
| Peptic ulcer disease, no bleeding | 0.53 (0.51-0.55) | 0.09 (0.07-0.11)                            | 0.52 (0.50-0.55) | 0.51 (0.49-0.53) |
| AIDS/HIV                     | 1.11 (0.67-1.84) | 0.09 (0.07-0.11)                            | 1.12 (1.11-1.17) | 1.72 (1.64-1.80) |
| Lymphoma                     | 1.72 (1.65-1.81) | 0.09 (0.07-0.11)                            | 1.79 (1.71-1.87) | 1.72 (1.64-1.80) |
| Metastatic cancer^b           | 6.96 (6.82-7.10) | 0.09 (0.07-0.11)                            | 7.11 (6.97-7.25) | 6.82 (6.69-6.95) |
| Solid tumor without metastasis | 1.50 (1.47-1.53) | 0.09 (0.07-0.11)                            | 1.62 (1.58-1.65) | 1.50 (1.48-1.53) |
| Rheumatic disease/collagen vascular diseases | 1.02 (0.97-1.08) | 0.09 (0.07-0.11)                            | 1.02 (0.97-1.08) | 1.02 (0.97-1.08) |
| Coagulopathy                 | 5.90 (5.71-6.09) | 0.09 (0.07-0.11)                            | 5.82 (5.64-6.01) | 5.40 (5.24-5.57) |
| Obesity                      | 0.54 (0.38-0.76) | 0.09 (0.07-0.11)                            | 0.55 (0.49-0.61) | 0.50 (0.39-0.60) |
| Weight loss                  | 3.00 (2.78-3.24) | 0.09 (0.07-0.11)                            | 3.16 (2.93-3.41) | 3.05 (2.84-3.26) |
| Fluid and electrolyte disorders | 2.26 (2.21-2.31) | 0.09 (0.07-0.11)                            | 2.38 (2.33-2.44) | 2.29 (2.24-2.34) |
| Blood loss anemia            | 1.66 (1.57-1.75) | 0.09 (0.07-0.11)                            | 1.71 (1.62-1.81) | 1.57 (1.49-1.66) |
| Deficiency anemia            | 0.84 (0.81-0.88) | 0.09 (0.07-0.11)                            | 0.84 (0.81-0.87) | 0.82 (0.80-0.86) |
| Alcohol abuse                | 1.45 (1.34-1.56) | 0.09 (0.07-0.11)                            | 1.19 (1.11-1.28) | 1.29 (1.20-1.39) |
| Drug abuse                   | 0.97 (0.92-1.02) | 0.09 (0.07-0.11)                            | 1.02 (0.97-1.08) | 0.97 (0.92-1.02) |
| Psychoses                    | 1.49 (1.42-1.57) | 0.09 (0.07-0.11)                            | 1.44 (1.37-1.52) | 1.47 (1.40-1.54) |
| Depression                   | 0.93 (0.87-0.98) | 0.09 (0.07-0.11)                            | 0.93 (0.87-0.99) | 0.91 (0.86-0.96) |

**Score model**

|                              | OR (95% CI)    | Beta coefficient | Modified weight* (risk score) | OR (95% CI) |
|------------------------------|----------------|------------------|-------------------------------|-------------|
| Age, ≥65 years               | 2.67 (2.61-2.73) | 2.67 (2.62-2.73) | 2.76 (2.70-2.82) |
| Sex, female                  | 0.95 (0.94-0.97) | 0.94 (0.92-0.95) | 0.94 (0.92-0.95) |
| ECI score                    | 1.12 (1.12-1.12) | 1.12 (1.12-1.12) | 1.12 (1.12-1.12) |

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*a* Modified weights were assigned using the lowest non-negative beta coefficient as a reference category.*

*b* Diabetes with versus without complications and malignancy with versus without metastasis, respectively, are mutually exclusive.

Based on the original model analysis, condition selection and weight re-assignment were performed in the derivation cohort. The modified model was evaluated in the validation cohort.

AIDS/HIV, acquired immunodeficiency syndrome/human immunodeficiency virus; CI, confidence interval; ECI, Elixhauser Comorbidity Index; OR, odds ratio.
The ECI showed better predictive ability compared to CCI both by using individual conditions and the score. C statistics (95% CI) of the original and modified ECI models using individual conditions were comparable: 0.783 (0.781–0.784) and 0.784 (0.782–0.785), respectively, although the modified model had fewer comorbidities (27 versus 30). The modified ECI score model showed larger C statistics (0.783 [0.781–0.785]) compared to the original ECI score model (0.750 [0.748–0.752]). As the CCI score increased, the hospital mortality also increased (Figure 3). There were no clinically meaningful differences in the results with and without including post-admission complications (Supplemental Online Materials, Tables S1 and S2). By looking back 6 or 12 months (180 or 365 days, respectively), the prevalence of each condition increased but the association between each condition and hospital death was less pronounced (Supplemental Online Materials, Figures S1 and S2). Higher modified CCI and ECI scores were also associated with longer length of hospital stay and higher cost (Figure 4).

Discussion

This study demonstrated the validity of CCI and ECI to predict hospital mortality in the updated inpatient data from the hospital-based Japanese administrative database. The modified CCI/ECI required fewer conditions as independent variables while maintaining comparable predictive ability. In particular, by updating the weighted risk score, the predictive ability was...
Figure 3  Hospital deaths according to CCI (a) and ECI (b) scores
The percentage of hospital deaths by CCI score is indicated with upper limit of the 95% CIs. Light gray bars, per original CCI score; dark gray bars, per modified CCI score.
The analysis for original scores was performed using data from both the derivation and validation cohorts. The analysis for modified score was performed using data from the validation cohort.
CCI, Charlson Comorbidity Index; CI, confidence interval; ECI, Elixhauser Comorbidity Index.

Figure 4  Length of hospital stay and cost during the hospital stay by the modified CCI (a and b) and ECI (c and d) scores
Scores were calculated from the modified model in the validation cohort.
CCI, Charlson Comorbidity Index; ECI, Elixhauser Comorbidity Index.
slightly improved compared to the original scores. ECI performed better than CCI, as reported previously.\textsuperscript{27,28} Furthermore, in the present analysis, we found that the higher the risk score, the longer was the length of hospital stay for patients. Similarly, CCI/ECI scores were linearly associated with the hospitalization cost in our study.

In this study, we estimated the weights using OR(\textit{Charlson})\textsuperscript{1} or beta-coefficient (\textit{Elixhauser})\textsuperscript{25} based on the logistic model and evaluated the models using \textit{C} statistics derived from the logistic regression model, instead of Cox regression.\textsuperscript{25,26} Regarding the outcomes, the original \textit{Charlson} model\textsuperscript{1} as well as Quan et al.\textsuperscript{24} used 1-year mortality whereas we used hospital mortality in this study because this database does not have follow-up ability of the patients after discharge. The original \textit{Elixhauser} model used hospital death as the outcomes.\textsuperscript{2,25} Although direct comparisons with prior studies applying different methodologies may not be advisable, the \textit{C} statistics of the original CCI based on the individual comorbidity model and the score model were slightly better in the present study than in the previous report (0.736 and 0.723, respectively : 2008 Japanese data)\textsuperscript{24} this may be due to a) an increase in the number of diagnosis columns from April 1, 2016 and/or b) inclusion of diagnoses flagged as post-admission complications in our study. The derivation and validation cohorts in our study were developed using the data in 2015 and 2016. The mean (SD) number of CCI and ECI diagnoses was 2.0 (1.59) in the derivation cohort and 2.1 (1.73) in the validation cohort, respectively, when post-admission complications were included. On excluding post-admission complications, the mean (SD) number of CCI or ECI diagnoses was slightly decreased to 1.7 (1.39) and 1.8 (1.53), respectively. We observed a decreased prevalence of each CCI comorbidity by excluding complications after admission: however, there were no material differences in the multivariable ORs (\textit{Supplemental Online Materials}, Table S1), and the \textit{C} statistics decreased only nominally (from 0.764 to 0.753 for the CCI individual comorbidity model and from 0.759 to 0.749 for the CCI score model : \textit{Supplemental Online Materials}, Table S3). This was also true for ECI (\textit{Supplemental Online Materials}, Tables S2 and S3). We have previously shown that the diagnoses flagged at or after the hospital admission may not be categorized correctly.\textsuperscript{27} Indeed, a lower prevalence was observed for some chronic conditions (eg, diabetes and rheumatoid arthritis) by excluding post-admission diagnoses (\textit{Supplemental Online Materials}, Table S1). Because these conditions are unlikely to occur after admission, “post-admission diagnosis” fields may also be used for prevalent conditions at admission. This further supported the use of all diagnoses during the hospitalization period as explanatory variables.

\textit{C} statistics in our study were still lower compared to previously published 2004 Canadian data (CCI original models : 0.884 [individual] and 0.879 [score]).\textsuperscript{24} Patients in the Canadian study were younger (29.9% versus 67.3% were ≥65 years old), had lower mortality (3.5% versus 4.6%), and were healthier (lower prevalence of cerebrovascular disease [3.0% versus 11.0%], peptic ulcer disease [1.1% versus 7.9%], diabetes without complications [6.9% versus 14.5%], and malignancy [5.0% versus 25.1%]).\textsuperscript{24} Thus, CCI may work better in a setting where a limited number of conditions can explain the risk of mortality. Indeed, in our previous study using data mostly from a relatively young Japanese population, \textit{C} statistics for individual comorbidities (CCI, 0.845 [0.835–0.855] ; ECI, 0.839 [0.828–0.850]) and score (CCI, 0.823 [0.813–0.834] : ECI, 0.801 [0.790–0.812]) in the original CCI/ECI model were higher than that observed in the current study.\textsuperscript{30}

The original CCI model was developed using medical charts to identify diagnoses on admission,\textsuperscript{1} while our study was conducted using an administrative database which may have
lower sensitivity. Indeed, a previous study in four Japanese hospitals reported that 7 of the 17 CCI conditions in the DPC file showed sensitivity less than 50% compared to the diagnoses recorded in the medical chart. Therefore, compared to abstracting a medical chart, the prevalence of each condition may be underestimated in this study. The limited sensitivity may also be due to the limited number of diagnosis fields in DPC format (≤12 in fiscal year 2015 and ≤25 in fiscal year 2016). We might have been able to identify more diagnoses by using medical claims where no such restriction existed. When we looked back 6 or 12 months prior to admission (including admission month) to ascertain underlying conditions at admission more thoroughly, we found that the prevalence for each condition increased up to 2- or 3-fold with the length of the look-back period, but ORs for hospital death associated with individual CCI conditions decreased in 12 out of 17 CCI conditions with longer look-back periods (Supplemental Online Materials, Figure S1). Further, 23 out of 30 ECI conditions also showed higher prevalence and lower ORs with longer look-back periods (Supplemental Online Materials, Figure S2). The impact on predictive ability was again considered minimal by looking back 6 or 12 months to include more conditions in the models.

The model used in this study considered in-hospital mortality as an outcome because patients cannot be followed-up in this database after hospital discharge. Therefore, this model may not be applicable when considering other mortality outcomes (eg, 1-year mortality). Because the original model was developed a long time ago (in the 1980s), and since then, substantial progress has been made in diagnosis and treatment, some conditions (eg, HIV/AIDS) are no longer considered life threatening, which may have resulted in no increased mortality risk with some chronic conditions (eg, diabetes) any longer in our updated models. Another reason could be use of in-hospital mortality instead of 1-year mortality as the outcome in our study. If we could have followed-up patients for a year, these conditions might still be associated with increased risk of death. We only evaluated CCI/ECI and did not explore other potentially and newly associated conditions. By adding other conditions to the CCI and/or ECI or a combination of them, the predictive ability may be improved further. Although the length of hospital stays (8.0 days) in the present study was consistent with that of the Japanese national statistics for standard DPC hospitals in 2015, the mortality was higher in our dataset (4.5-4.6% versus 3.3%). Therefore, generalizability of the DPC data may be limited in comparison to “national data.” Additionally, our analysis included only DPC hospitals and may not be generalizable to other types of hospitals in Japan. We excluded maternal hospitalizations from the analysis (~4% in total) according to the previous study. In the DPC data, they are considered abnormal pregnancies and may have been associated with higher mortality than normal pregnancies; therefore, the results may not be totally generalizable for DPC hospitalizations, either. Applicability of CCI and ECI to other types of databases (eg, insurance claims) may need to be further evaluated. Additionally, we did not account for clustering data by same patients being readmitted again in the same year. In our study, peptic ulcer disease and diabetes (with and without complications) were negatively (ie, protectively) associated with hospital death and manually excluded from the CCI models: the negative association can be due to a confounder that is not accounted in the diagnosis or condition and confounder adjustment could have unmasked the association of diabetes with mortality.

Conclusions

The original CCI and ECI had a good predictive ability for hospital death in the latest and nationwide Japanese data from a hospital-based administrative database. The modified CCI and ECI models with a reduced number of conditions showed comparable predictive abilities to the original ones. The models using cumulative scores instead of including individual conditions also had sufficient predictive abilities for hospital
death. Both original and modified versions of CCI and ECI can be useful in future studies using this administrative database.

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