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An improved comorbidity index for outcome analyses among dialysis patients

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Since comorbid conditions are highly prevalent among patients with end-stage renal disease, indexes measuring them have been widely used to describe the comorbidity burden and to predict outcomes as well as adjust for their roles as confounders. The current comorbidity indexes, however, were developed for general populations or on small patient cohorts. In this study we developed a new index for mortality analyses of dialysis patients based on the 2000 US incident dialysis population, and validated this using the 1999 and 2001 incident and 2000 prevalent dialysis patient populations. Numerical weights were assigned to the comorbid conditions of atherosclerotic heart disease, congestive heart failure, cerebrovascular accident/transient ischemic attack, peripheral vascular disease, dysrhythmia, other cardiac diseases, chronic obstructive pulmonary disease, gastrointestinal bleeding, liver disease, cancer, and diabetes. A patient's comorbidity score was the sum of the weights corresponding to the individual conditions present and could be used as a continuous variable in analyses. Our index performance was almost identical to the individual comorbid conditions regarding model fit, predictive ability, and effect on inference, and it outperformed the widely used Charlson Comorbidity Index.

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Comorbid conditions are highly prevalent among end-stage renal disease (ESRD) patients, and comorbidity indexes have been widely used for describing comorbidity burden, predicting outcomes, and adjusting as a confounder in analyses involving ESRD patients.[1–4] A comorbidity index can give a single-value summary for several comorbid conditions, thereby simplifying the comparison. A comorbidity index can also reduce the dimension of model-based analysis. Too many comorbid conditions and their correlations may distort the information an analysis yields. Large numbers of variables and their correlations may also make the parameter estimation inefficient and the result difficult to interpret.[5] Reducing the dimension of the analysis and therefore reducing the correlations among variables is necessary to produce reliable and meaningful results, especially when the sample size is small.

Several comorbidity indexes have been used for analysis of ESRD patients. The Charlson Comorbidity Index (CCI)[6] is the most widely used. It was developed for mortality analysis based on 604 patients admitted to the medical services at New York Hospital-Cornell Medical Center during a 1-month period in 1984, and was validated based on 685 women with histologically proven primary carcinoma of the breast, who received their first treatment at Yale New Haven Hospital between 1 January 1962 and 31 December 1969. Khan *et al.*[7] proposed a comorbidity index for survival analysis based on 375 ESRD patients, and Davies *et al.*[8] used a different comorbidity index for analyses of 97 continuous ambulatory peritoneal dialysis patients. Van Manen *et al.*[9] compared these three indexes and showed that the CCI performs slightly better than the other two, based on *c*-statistic, a model predictive ability statistic.[10] Fried *et al.*[3] compared the CCI with the Davies comorbidity index based on 415 incident peritoneal dialysis patients. Results showed that CCI was a better predictor for mortality, but the Davies index was a better predictor for hospitalizations.

These comorbidity indexes were developed for general populations or on small samples. The effects on survival of the comorbid conditions included in the CCI are different for the general population than for ESRD patients.[11] Whether the CCI conditions can accurately describe the comorbidity burden for ESRD patients is also questionable. The Khan index did not specify which conditions should be included, and mixed chronological age with comorbid conditions

without showing clear evidence for doing so. In the Davies index, all comorbid conditions were assigned the same weight no matter how different their effects on outcome, and the definitions of the conditions were unclear.

In addition, these indexes were not formally validated or were validated based only on predictive ability or significance as a predictor. The validation of an index should be goal-driven, against a gold standard. To be used to predict mortality, a comorbidity index should have the same, or very similar, predictive ability for mortality as the individual comorbid conditions represented by the index. To be used as an adjustor in survival analyses, a comorbidity index should make the same inferences made when using individual comorbid conditions. An index validated for mortality prediction should not be used for medical cost prediction, unless it was also validated for doing so.

Increasing numbers of analyses are done using administrative data. In addition to observational studies, some clinical trials[12,13] and 'quasi-clinical trials'[14] are conducted based at least partially on the Centers for Medicare & Medicaid (CMS) ESRD database, which is the largest administrative database for ESRD patients in the United States. For those studies, most information on comorbid conditions was derived from the CMS ESRD database. A comorbidity index developed for analyses based on administrative data would be useful. Thus, we propose a new comorbidity index, including and excluding ESRD primary cause, for mortality analyses of dialysis patients, using administrative data, based on the comorbid conditions used by the United States Renal Data System (USRDS).[15] The index was developed using the 2000 US incident dialysis population and validated using the 1999 and 2001 US incident dialysis populations and the 2000 US prevalent dialysis population. The validation was based on model fit, model predictive ability, index predictive ability, and effect on inference. The new index was also checked to see if it can be used for hospitalization and medical cost analysis. Because the CCI performs better than the other indexes for mortality analyses among dialysis patients,[3,9] the new index was compared with it.

RESULTS

Description of data

A total of 102,134 incident and 142,517 prevalent dialysis patients were included in this study (Table 1). Mean follow-up time was 2.3 years per patient for incident and 2.5 years per patient for prevalent patients. Percentages of patients with atherosclerotic heart disease (ASHD), congestive heart failure (CHF), cerebrovascular accident/transient ischemic attack (CVA/TIA), chronic obstructive pulmonary disease (COPD), dysrhythmia, diabetes and liver disease increased over the incident year. Compared with the incident cohort, prevalent patients were younger, fewer were white, fewer had diabetes as primary ESRD cause, and fewer had comorbid conditions, possibly because of older patients with more comorbidity dying earlier than younger, healthier patients. The death rate was 26.36, 26.21, 25.59, and 24.55 per 100 patient-years for the 1999, 2000, 2001 incident cohorts and the 2000 prevalent cohort, respectively. It decreased slightly over time for incident patients.

Table 1 | Patient characteristics: 1999–2001 US incident dialysis patients and 2000 prevalent dialysis patients

	Cohort[a]			
Characteristics	1999 Incident *n*=33,166	2000 Incident *n*=33,077	2001 Incident *n*=35,891	2000 Prevalent *n*=142,517
Age				
Mean	65.6	65.0	66.0	61.0
Median	69.0	68.0	69.0	63.0
s.d.	14.7	15.0	15.0	16.0
Age group, years				
0–19	0.3	0.4	0.4	0.4
20–29	1.9	2.1	1.9	3.0
30–39	4.6	4.6	4.4	7.5
40–49	8.4	9.0	8.2	13.7
50–59	13.6	13.7	13.5	18.2
60–64	8.3	8.9	8.9	10.1
65–69	15.4	14.5	15.0	12.7
70–79	33.0	32.1	32.1	24.9
⩾80	14.6	14.8	15.6	9.7
Sex				
Women	48.3	48.1	48.0	48.3
Men	51.7	51.9	52.0	51.7
Race				
White	64.0	64.1	65.4	52.9
African American	30.7	30.8	29.8	41.7
Native American	1.6	1.6	1.4	1.6
Asian	2.8	2.7	2.6	3.1
Other	0.8	0.9	0.8	0.7
ESRD primary cause				
Diabetes	46.9	47.5	48.4	38.6
Hypertension	29.8	29.7	29.4	29.9
Glomerulonephritis/ cystic kidney disease	10.4	9.6	9.2	17.4
Other	12.9	13.2	13.1	14.1
Comorbid conditions				
ASHD	51.5	52.2	53.8	41.2
CHF	54.3	55.0	55.5	44.3
CVA/TIA	24.2	25.1	25.6	18.4
PVD	44.4	44.5	45.6	38.0
Other cardiac[b]	35.3	34.9	36.9	33.1
COPD	20.5	21.2	22.2	16.1
GI	10.8	10.7	10.7	9.9
Liver disease	5.3	6.8	7.1	6.8
Dysrhythmia	30.6	31.7	32.3	26.2
Cancer	12.2	12.2	12.8	9.4
Diabetes	63.6	65.3	67.2	53.4

Abbreviations: ASHD, atherosclerotic heart disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CVA/TIA, cerebrovascular accident/transient ischemic attack; ESRD, end-stage renal disease; GI, gastrointestinal bleeding; PVD, peripheral vascular disease.
[a]Values are percents unless otherwise specified.
[b]Includes pericarditis, endocarditis, myocarditis, other complications of heart disease, heart transplant, heart valve replacement, and cardiac devices.

Calculation of comorbidity score

The coefficient estimates and their *P*-values for all variables from the Cox proportional regression model for the 2000