

Identifying high-risk hospitalised chronic kidney disease patient using electronic health records for serious illness conversation

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ABSTRACT

Introduction: This study aimed to identify risk factors that are associated with increased mortality that could prompt a serious illness conversation (SIC) among patients with chronic kidney disease (CKD).

Methods: The electronic health records of adult CKD patients admitted between August 2018 and February 2020 were retrospectively reviewed to identify CKD patients with >1 hospitalisation and length of hospital stay ≥ 4 days. Outcome measures were mortality and the duration of hospitalisation. We also assessed the utility of the Cohen's model to predict 6-month mortality among CKD patients.

Results: A total of 442 patients (mean age 68.6 years) with median follow-up of 15.3 months were identified. The mean (standard deviation) Charlson Comorbidity Index [CCI] was 6.8 ± 2.0 with 48.4% on chronic dialysis. The overall mortality rate until August 2020 was 36.7%. Mortality was associated with age (hazard ratio [HR] 1.51, 95% confidence interval [CI] 1.29–1.77), CCI ≥ 7 (1.58, 1.08–2.30), lower serum albumin (1.09, 1.06–1.11), readmission within 30-day (1.96, 1.43–2.68) and CKD non-dialysis (1.52, 1.04–2.17).

Subgroup analysis of the patients within first 6-month from index admission revealed longer hospitalisation stay for those who died (CKD-non dialysis: 5.5; CKD-dialysis: 8.0 versus 4 days for those survived, $P < 0.001$). The Cohen's model demonstrated reasonable predictive ability to discriminate 6-month mortality (area under the curve 0.81, 95% CI 0.75–0.87). Only 24 (5.4%) CKD patients completed advanced care planning.

Conclusion: CCI, serum albumin and recent hospital readmission could identify CKD patients at higher risk of mortality who could benefit from a serious illness conversation.

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Keyword: Charlson comorbidity index, chronic kidney disease, dialysis, hospitalisation, mortality

INTRODUCTION

In-hospital cardiopulmonary resuscitation (CPR) for chronic kidney disease (CKD) patients is shown to have lower survival¹ and a higher proportion of survivors on maintenance haemodialysis were discharged to skilled nursing facilities.² Despite that, haemodialysis patients still preferred CPR during cardiac arrest³ and there are lower do-not-resuscitate orders for the critically ill end-stage kidney disease patients.⁴ Notably, there have been discordant views towards end-of-life care among patients, relatives and healthcare professionals locally.⁵ Timely engagement of high-risk patients and their families in serious illness conversation (SIC) would better prepare for the inevitable trajectory and outcome.

Facilitating concordance in end-of-life care and respecting patients' wishes should hence be our goal,⁶ instead of focusing on life extension associated with lower family satisfaction.⁷

Living Matters adopted from Respecting Choices model was implemented for advance care planning (ACP) in Singapore almost a decade ago.⁹ A retrospective study of ACP done between January 2011 and December 2015 in Singapore found that the median time between ACP completion and death was 7.27 months (95% confidence interval [CI] 6.35–8.18), with 63.2% of the participants completing ACP within only 3 months prior to death.⁹ In addition, among individuals with chronic illness, almost 1 in 3 opted for CPR and

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CLINICAL IMPACT

What is New

- This study highlights use of the Charlson Comorbidity Index, serum albumin and 30-day readmission to prompt serious illness conversation among chronic kidney disease patients in Singapore.

Clinical Implications

- The study supports the use of poor prognosis factors to trigger discussions with patients and family to improve their end-of-life preparedness.

life-sustaining treatment even though the likelihood of survival was low. In a semi-structured interview with CKD stage 4–5 patients, care partners and healthcare professionals had discordant views during ACP discussion.^{10,11} One of the challenges in implementing ACP is shifting the paradigm from life prolongation to maximum quality of life¹² without jeopardising care.

A population study from Singapore Eastern Regional Health System in 2016 showed that CKD was the most prevalent condition (31.9%) in healthcare utilisation.¹³ A systematic review by Tonelli et al.¹⁴ showed that CKD patients have higher mortality especially from cardiovascular cause. However, information regarding hospitalised Singapore CKD patients at high risk of mortality and utility of SIC is limited.

Using our hospital's electronic health records, we conducted a retrospective cohort study of CKD patients who were admitted from Aug 2018 to February 2020. The primary objective was to identify adverse factors associated with inpatient mortality in CKD patients. Secondary objectives were assessing the length of stay within 6-month of index admission stratified to dialysis status and mortality, and the utility of Cohen's 6-month haemodialysis mortality predictor¹⁵ for hospitalised CKD patients. The study was approved by SingHealth Centralised Institutional Review Board with waiver of informed consent (CIRB Ref 2020/2103).

METHODS

Study design and subjects

This was a retrospective cohort study of CKD patients admitted to Sengkang General Hospital from August 2018 to February 2020. All cases in the study have been followed up for at least 6 months, last follow-up date was 31 August 2020 or date of patient's death. Clinical data were extracted from SingHealth's Electronic Health

Records system, using the Electronic Health Intelligence System, which is an enterprise data repository that integrates information from multiple sources, including administrative, clinical and ancillary.

The International Classification of Disease-10 (ICD-10) codes used for identifying patients were N 185 CKD stage 5, N189 CKD unspecified, T827 AVF infection, T 828 Dialysis AVF stenosis/ thrombosis, T856 PD catheter obstruction, T8571 PD associated peritonitis and I 978 HD associated hypotension. Only admissions to our hospital were captured. Based on a retrospective study at the Singapore General Hospital, the average length of hospital stay was 4.6 days.²⁸ We hence decided to choose patients who had more than 1 admission from August 2018 to February 2020 and with any of the stays being 4 days or more. The former would serve as a trigger for SIC while the latter provided an adequate period to broach SIC while addressing the clinical issues.

Main outcome was inpatient mortality until end of follow-up. Other outcomes were length of stay within 6 months from index admission, high dependency and/or intensive care unit (HD/ICU) admission and advance care planning (ACP) documentation.

Variables noted were:

- Patient demographics and laboratory results: age, sex, ethnicity, dialysis status and serum albumin
- Medical comorbidities
- Readmission within 30 days

Medical comorbidities identified were those for Charlson Comorbidity Index (CCI) scoring. These diseases were extracted using ICD-10 codes of the discharge diagnoses and problem list compiled from all admissions. We calculated the age-adjusted CCI using MdCal.

Primary analysis was to determine the factors associated with inpatient mortality. Secondary analysis was to assess the length of stay of all hospitalisations within the 6-month from index admission stratified according to the survival outcome and dialysis status. Subsequently, we used Cohen's 6-month haemodialysis mortality predictor calculator to assess the correlation with 6-month mortality in our study cohort. The variables used for age and serum albumin were based on index admission. The diagnosis of dementia and peripheral vascular disease were based on the discharge diagnosis and problem list within 6 months from the index admission. The "surprise question" was "Would I be surprised if this patient were to die within the next 12 months?". A "no" response to the question was applied if the patients had extent of care and resuscitation status documented within 6 months from the index admission.

Statistical analysis

Continuous variables were presented as mean and standard deviation for normally distributed data and median and interquartile range (IQR) for non-normally distributed data. Categorical variables were presented as number and percentage. Univariate and multivariable Cox regression analyses were performed to evaluate the risk factors associated with mortality. Kaplan-Meier survival function was used to compare the patients with $\text{CCI} \geq 7$ versus < 7 .³⁷ Length of stay for all hospitalisations at 6-month follow-up from index admission was stratified to dialysis status and mortality using Kruskal-Wallis test. Receiver operating characteristic analysis was performed to evaluate the association with Cohen's 6-month haemodialysis mortality predictor.

RESULTS

A total of 3,301 admissions from August 2018 to February 2020 with the diagnosis of CKD were extracted from our institution's Electronic Health Records. After excluding cases with only 1 admission, hospitalisation less than 4 days and incomplete data, 442 patients were included in the analysis (Fig. 1). Inpatient mortality outcome was collected up to August 2020. Median follow-up for the whole cohort was 15.3 months (IQR 8.1–20.1). The mean age was 68.6 ± 13.6 years, 51.8 % were male, 65.6 % were Chinese, mean

CCI was 6.8 ± 2 , median serum albumin was 34g/L (IQR 30.0–37.3), 45.7% had admission to HD/ICU, 48.4% were on chronic dialysis (haemodialysis or peritoneal dialysis) and 47.3% were readmitted within 30 days (Table 1).

Overall inpatient mortality outcome

The overall inpatient mortality rate was 36.7%. Univariate Cox regression showed that increasing age, $\text{CCI} \geq 7$, lower serum albumin, readmission within 30 days and CKD non-dialysis were associated with higher risk of mortality, $P < 0.05$ (Fig. 2 and Table 2). On multivariable Cox regression, all these variables remained statistically significant factors for risk of mortality after adjustment for sex, ethnicity and HD/ICU admission. For every 10-year increase in age, the adjusted risk of mortality increases by 51%. The adjusted mortality risk for patients with $\text{CCI} \geq 7$ was 1.58 (95% CI 1.08–2.30) compared to those with $\text{CCI} < 7$. Patients in the 30-day readmission group were also observed to have a higher risk mortality (HR 1.96, 95% CI 1.43–2.68). Each 1g/L increment in serum albumin was associated with a lower mortality risk (HR 0.92, 95% CI 0.90–0.94). Chronic dialysis patients were also observed to have a lower risk of mortality (HR 0.66, 95% CI 0.46–0.96) compared to CKD non-dialysis patients (Table 2).

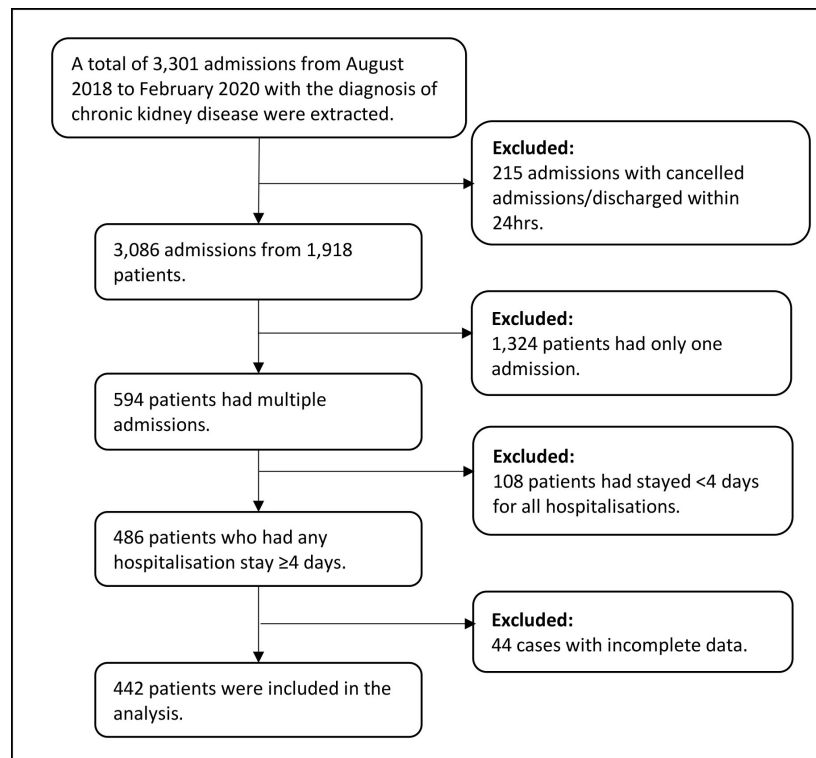


Fig. 1. Patient selection criteria.

Table 1. Characteristics of patients included in the study, stratified by survival status at the end of study period

	Overall N=442	Survived n=280	Died n=162
Age, mean (SD), years	68.6 (13.6)	65.4 (13.2)	74.2 (12.3)
Male sex, %	51.8	52.9	50.0
Chinese ethnicity, %	65.6	63.6	69.1
Charlson Comorbidity Index, mean (SD)	6.8 (2.0)	6.2 (1.8)	7.8 (2.0)
Serum albumin, g/L (IQR)	34.0 (30.0–37.3)	35.0 (32.0–38.0)	32.0 (27.0–36.0)
Chronic dialysis, %	48.4	54.6	37.7
High dependency/ICU, %	45.7	45	46.9
Readmission within 30 days, %	47.3	43.6	53.7
Follow-up, months (IQR)	15.3 (8.1–20.1)	18.8 (14.9–21.6)	6.9 (2.6–11.5)

ICU: intensive care unit IQR: interquartile range; SD: standard deviation

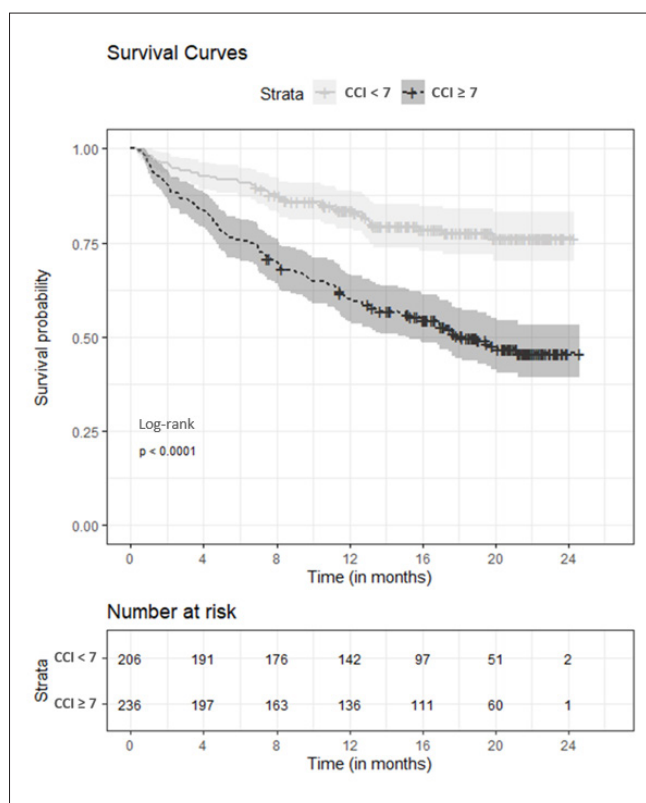


Fig. 2. Kaplan-Meier survival functions for patients with CCI < 7 and CCI ≥ 7.

ACP documentation

Only 24 out of 442 (5.4%) patients had completed ACP between August 2018 and February 2020. Among this group, mean age was 72.3 years and CCI was 7.9. Twelve (50%) were chronic dialysis patients and 10 had prior HD/ICU admission. A total of 11 (45.8%) patients who completed ACP had died by the end of August 2020, in

contrast to 151 out of 162 (93.2%) patients who died without ACP completion. We do not have the data for ACP referral and incomplete ACP.

Subgroup analysis

Length of stay and high dependency/ICU admission at 6 months

We decided to look at the length of stay for all hospitalisations at 6-month from the index admission as the median follow-up time for those who died was 6.9 months. Patients were stratified according to their dialysis status and survival outcome (Table 3). There were a total of 75 deaths (17.0%) out of the 442 patients within 6 months from the index admission.

Kruskal-Wallis test showed that there were statistically significant differences in the median length of stay between the different groups of patients, $P < 0.001$ (Table 3). Dunn's test with Bonferroni Correction showed that the length of stay for those who died at 6-month was statistically significantly longer (CKD-non dialysis: 5.5 days; CKD-dialysis: 8.0 days) as compared to those who survived (4.0 days), regardless of dialysis status (Table 3). No statistically significant differences in the median ICU/HD days were observed among groups, $P = 0.122$ (Table 3).

Utility of Cohen's 6-month haemodialysis mortality predictor

We applied Cohen's haemodialysis mortality predictor to our study cohort, correlating it to the chance of survival at 6 months from index admission. The association with predicted mortality probability was high, irrespective of their dialysis status. The C-statistic was 0.81 (95% CI 0.75–0.87) (Fig. 3).

Table 2. Univariate and multivariable Cox regression model with mortality as the outcome variable

	Univariate			Multivariable			
	P value	Unadjusted HR	95% CI Lower Upper	P value	Adjusted HR	95% CI Lower Upper	
Age (every 10-year increase)	<0.001	1.57	1.38 1.79	<0.001	1.51	1.29 1.77	
Sex							
Female	reference			reference			
Male	0.482	0.90	0.66 1.22	0.984	1.00	0.73 1.38	
Ethnicity	0.377			0.618			
Chinese	reference			reference			
Malay	0.575	0.90	0.61 1.31	0.275	1.25	0.84 1.88	
Indian	0.202	0.63	0.31 1.28	0.645	0.84	0.41 1.74	
Others	0.208	0.61	0.29 1.31	0.528	1.29	0.58 2.88	
CCI							
<7 (n=206)	reference			reference			
≥7 (n=236)	<0.001	2.71	1.91 3.85	0.018	1.58	1.08 2.30	
Serum albumin (g/L) (every unit increase)	<0.001	0.92	0.90 0.94	<0.001	0.92	0.90 0.94	
Chronic dialysis							
No	reference			reference			
Yes	0.001	0.55	0.40 0.76	0.028	0.66	0.46 0.96	
Readmission within 30 days							
No	reference			reference			
Yes	0.001	1.71	1.25 2.33	<0.001	1.96	1.43 2.68	
HD/ICU utilisation							
No	reference			reference			
Yes	0.876	1.03	0.75 1.40	0.031	1.48	1.04 2.11	

CCI: Charlson Comorbidity Index; CI: confidence interval; HD/ICU: high dependency/intensive care unit; HR: hazard ratio

Table 3. Total in-hospital stay and high dependency/ICU admission at 6-month follow-up

	Survived		Died		P value
	Non-dialysis (n=178)	Dialysis (n=189)	Non-dialysis (n=50)	Dialysis (n=25)	
Cumulative LOS, days ^a	2,891	4,754	1,317	1,117	
Total number of admissions	500	598	172	70	
Average number of admissions per index case	2.8	3.2	3.4	2.8	
LOS, mean (SD), days	5.8 (6.8)	8.0 (12.8)	7.7 (7.8)	16.0 (24.0)	
LOS, median (IQR)	4.0 (2.0–6.0)	4.0 (2.0–9.0)	5.5 (3.0–9.0)	8.0 (3.5–15.3)	
Mean rank of LOS, days	626.5	661.0	755.4	857.9	<0.001
HD/ICU admissions					
Total days	121	296	56	117	
Total number of admissions	57	113	14	28	
Average number of admissions per index case	0.3	0.6	0.3	1.1	
HD/ICU, mean (SD), days	2.1 (1.6)	2.6 (2.7)	4.0 (4.8)	4.2 (4.8)	
HD/ICU, median (IQR), days	2.0 (1.0–3.0)	2.0 (1.0–3.0)	2.0 (1.8–4.0)	2.0 (1.0–4.8)	
Mean rank of HD/ICU, days	97.8	103.9	126.4	124.7	0.122

HD/ICU: high dependency/intensive care unit; IQR: interquartile range; LOS: length of stay

^a The total length of stay in each admission within the first 6 months from index admission

DISCUSSION

CKD has a significant impact on global health with regards to morbidity and mortality.¹⁶ Data from the chronic renal insufficiency cohort demonstrated that high hospital utilisation was associated with a trajectory towards mortality among CKD patients.¹⁷ Risk of fatal hospitalisation is known to be higher in dialysis and CKD compared to non-CKD admissions.¹⁸ With all this in mind, timely discussion to explore the goals of care with patients and families is important since shared decision making is crucial to align the subsequent care plans. Achieving concordance in goals of care will reduce decisional burden when confronting uncertainties, while honouring the patients' wishes.

End-stage kidney disease patients were more likely to receive active treatment and ICU admission compared to patients with other major organ diseases.⁴ Such dissociation between the intensity of care despite high mortality among CKD patients occurs because of overly optimistic outcome prognostication¹⁹ and higher perceived life expectancy²⁰ by dialysis patients. A substantial proportion of patients (45.7%) required HD/ICU utilisation in our cohort. However, this might be an over-representation because dialysis patients who need vasopressor support or non-invasive ventilation are admitted to our HD unit for dialysis.

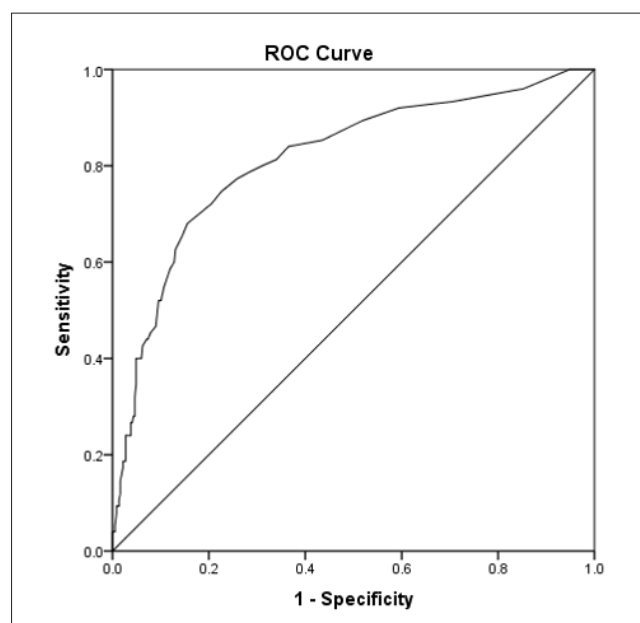


Fig. 3. ROC curve to evaluate the performance of the Cohen's haemodialysis mortality predictor.^a

ROC: receiver operating characteristic

^a Diagonal segments are produced by ties

Despite significant mortality (36.7%) in our cohort study of hospitalised CKD patients, completion of ACP was low (5.4%). However, a survey conducted among

community-dwelling Singaporeans revealed willingness to discuss ACP in particular those of older age, with life-threatening illness and with ACP knowledge.³⁸ The dissonance between expectation and reality prompted us to study factors associated with mortality. If we were able to identify patients at high risk of early mortality, we could then initiate SIC such as ACP as part of clinical care. Local experience has shown that 90% of ACP was completed in the acute hospital setting,⁹ hence our choice of studying an inpatient cohort. We looked at well-established mortality factors such as age, CCI,²¹⁻²³ serum albumin,^{24,25} readmission^{17,18} and ICU admission.^{26,27}

Based on our hospital's electronic health records, we found that higher CCI, hypoalbuminemia, readmission within 30 days, and CKD non-dialysis patients had higher in-patient mortality. There have been conflicting studies on CCI and mortality outcome in CKD patients, some reporting an association^{21,22} but others not.²⁹ The heterogeneity in study populations, setting and duration of follow-up could explain the different findings. Nonetheless, a study from Korea demonstrated that for maintenance haemodialysis patients, CCI predicted mortality, especially for scores ≥ 7 .³⁸ The CCI score in our study was based on the cumulative diagnoses made throughout the study period, and therefore reflected cumulative burden of disease. In this context, we found a parallel between CCI score and mortality, in particular when comparing the score of ≥ 7 to lower. We felt that the cumulative CCI calculation when the patients were admitted with new events had better prognostic value than a single time point for the CCI score. We also noted that median serum albumin was low for our cohort at 34.0 g/L (IQR 30.0–37.3). Nonetheless, the degree of hypoalbuminemia remained significantly associated with mortality, which was consistent with other studies.²⁴

Readmission within 30 days has been widely used to assess quality of healthcare delivery and cost. In our study, we also found an association with mortality. A study from Alberta, Canada shown that chronic dialysis patients had longer hospitalisation stays and were more likely to receive HD/ICU care.³⁰ In our cohort, the median follow-up for those who died was 6.9 months (IQR 2.6–11.5). In order to standardise the comparison for hospitalisation stay and survival, we decided to assess total in-hospital stay and death within 6 months from index admission. In this sub-group, mortality rate was 17%. Patients who died, regardless of dialysis status, had longer length of stay than those who survived. However, HD/ICU utilisation was not significantly different between the groups. Given these patients with

higher mortality risk, timely discussion on goals and end-of-life care is critical.

Various risk stratification tools^{29,31} have been studied to predict survival in CKD patients. One of the readily accessible online calculators is the Cohen's 6-month mortality on haemodialysis derived from prevalent community dialysis patients.¹⁵ Our population included non-dialysis CKD in an acute hospital setting, while the calculator was derived from an ambulatory chronic haemodialysis setting. Nonetheless, our study demonstrated Cohen's model has reasonable predictive ability to discriminate 6-month mortality in CKD patients. The variables used in the calculator were age, serum albumin, whether the patient had dementia, and whether he/she had peripheral vascular disease. Compared to the cohorts used in Cohen's study,¹⁵ our population was older (mean age 68 compared to 61) and a high proportion had low serum albumin <35 g/L (normal range 40–51 g/L). There was significant deviation in the survival estimate for those >80 years old and those with albumin <30 g/L (data not shown). The calculator also has a question asking if the clinician would be surprised if the patient died in the next 12 months. There might be a bias since we entered a "no" in response to the "surprise question" for those with documented resuscitation and extent of care plan. Establishment of such plans presumably may indicate anticipation of deterioration in a critically ill patient. The "surprise question" itself to identify patients near end-of-life should not be used in isolation.³² Despite that, 6-month mortality on haemodialysis predictor¹⁵ has shown its applicability in hospitalised CKD patients in our study. The utility has to be contextualised and further validation studies are required.

There were many limitations to our study. Data were retrieved only from our hospital's electronic health records, with no case note review to validate the information retrieved from the system. Since medical comorbidities were based on discharge diagnoses and problem lists, CCI could be incomplete. CKD patients may also have been missed out if the diagnosis was not coded. All events (death and admissions) were limited to those that occurred within our hospital. In addition, for the mortality outcomes, it was not possible to follow up all participants for the same amount of time after index admission. Information such as functional status³³ and frailty,³⁴⁻³⁶ which are important factors and can enhance accuracy of mortality prediction, was not included due to incomplete data entry.

In conclusion, use of electronic health records might serve as a readily accessible tool to trigger SIC such as ACP. Hospitalised CKD patients who have readmission

within 30 days, CCI $\geq$ 7 and lower serum albumin are at higher risk of mortality. The CCI score derived from the medical history and admitting diagnosis has better reflection on the cumulative burden of disease, therefore providing more precise information for the disease trajectory than the baseline CCI. Further studies have to be done to validate the utility of Cohen's 6-month mortality predictor in the acutely hospitalised CKD/dialysis population.

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