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Quality indicators and clinical outcomes: the role of care quality in nondiabetic chronic kidney disease management

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ABSTRACT

Quality indicators (QIs) are essential for evaluating healthcare quality, but their validation for nondiabetic chronic kidney disease (CKD) populations is limited. We aimed to assess the association between QIs and outcomes in nondiabetic CKD patients. Using Taiwan's National Health Insurance claims data and death registries, we analyzed 27,842 nondiabetic adults with stage 3B-5 CKD from 2016 to 2019. Three QIs were assessed: renin–angiotensin system (RAS) inhibitor prescription, proteinuria testing, and nonsteroidal anti-inflammatory drug (NSAID) avoidance. Each patient received an overall QI score (range: 0–3) based on the sum of the individual QI scores. Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for associations between QI scores and outcomes, including long-term dialysis, all-cause death, hospitalization for acute kidney injury (AKI), hyperkalemia, and acidosis. The study population had a mean age of 68.7 years and a female prevalence of 41.7%. Only 33.5% of patients received the highest QI score. During a median follow-up period of 23 months, higher overall QI scores were associated with lower risks of long-term dialysis (HR 0.891, 95% CI 0.846–0.938), all-cause death (HR 0.900, 95% CI 0.864–0.939), and acidosis (HR 0.882, 95% CI 0.799–0.972). Notably, the prescription of RAS inhibitors was consistently correlated with better outcomes. These findings underscore the importance of quality indicators, particularly the continued use of RAS inhibitors, in improving outcomes for nondiabetic CKD patients. Future research should focus on refining existing QIs and expanding their validation to broader populations and healthcare settings.

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Introduction

Chronic kidney disease (CKD) has become one of the leading noncommunicable causes of death globally [1–3]. The prevalence of CKD is on the rise, with an estimated global rate of 9.1%, affecting approximately 700 million individuals worldwide and resulting in a growing financial strain on healthcare systems globally [4,5]. In 2017, CKD accounted for 35.8 million disability-adjusted life-years (DALYs), with nondiabetic CKD contributing to more than two-thirds of these DALYs and diabetic kidney disease accounting for the remaining one-third [6]. Taiwan has one of the highest incidence and prevalence rates of end-stage renal disease (ESRD) worldwide, with a prevalence of dialysis being 3,546 per million people in 2021 [7]. Therefore, in order to effectively monitor and control the severity of CKD, it is crucial to assess the quality of renal care.

Quality indicators (QIs) are tools developed to assess the quality of care provided by healthcare professionals or medical facilities. These QIs are commonly utilized by researchers in public health and health authorities to monitor and improve the quality of healthcare services and their management infrastructure [8]. QIs developed for renal care have predominantly focused on the dialysis population [9]. A systematic review of process-based QIs in non-dialysis CKD identified 31 studies, of which four exclusively examined diabetic CKD patients, while the remaining 27 addressed CKD populations comprising both diabetic and non-diabetic

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individuals. However, research on QIs specifically for non-diabetic CKD patients is sparse [10]. Additionally, many QI development studies involved the use of medical charts rather than electronic medical records or administrative claims data, which limits the potential for automatic retrieval of QI information by health authorities [9,10]. In a previous study utilizing claims data from Taiwan's National Health Insurance (NHI), we validated several QIs for renal care, including the prescription of renin–angiotensin system (RAS) inhibitors, proteinuria testing, and nutritional guidance [11,12]. The study showed that higher overall quality scores were associated with lower risks of long-term dialysis and hospitalization due to acute kidney injury (AKI) in CKD patients with diabetes [12]. In a Japanese cohort study of elderly patients newly diagnosed with CKD, a higher QI score was associated with a lower risk of ESRD in diabetic patients, whereas in nondiabetic patients, a higher QI score did not demonstrate a statistically significant reduction in ESRD risk, possibly due to the lower incidence of ESRD observed during the limited follow-up period [13]. In the current study, we aimed to investigate the associations between the quality of renal care and various renal outcomes necessitating substantial hospital interventions in nondiabetic CKD patients.

Methods

Data sources

In this study, we utilized deidentified data from the NHI and the death registry of Taiwan, accessible exclusively at the Health and Welfare Data Science Center, Ministry of Health and Welfare. Launched in 1995, the NHI provides universal medical coverage to more than 99% of the population [12,14]. Its claims data encompass insured individuals' details, disease diagnoses, and information on prescriptions and treatments from both outpatient and inpatient records [15,16]. Initially, the NHI used the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) for disease coding. Since 2016, it has transitioned to the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) [17]. The national death registry offers data on the dates and causes of death [18]. The data analyzed in this study were deidentified and can only be accessed at data centers operated by the Health and Welfare Data Science Center, with approval from the Ministry of Health and Welfare, Taiwan. This study was exempted from review by the Research Ethics Review Committee of the Far Eastern Memorial Hospital because the database provides only deidentified information.

Study participants

This study enrolled nondiabetic adults with advanced CKD from 2016 to 2019. Advanced CKD was defined as participation in the pre-End Stage Renal Disease (pre-ESRD) program, a multidisciplinary care approach for patients with stages 3B-5 CKD or those with proteinuria ≥1 g/day. To avoid inconsistencies due to the shift from ICD-9-CM to ICD-10-CM coding, inclusion criteria were limited to those who had newly joined the pre-ESRD education program (treatment code: P3402C) since 2016. The exclusion criteria were age younger than 20 years or a diagnosis of diabetes. Diabetes was diagnosed if a patient met one of the following conditions: (1) had at least two outpatient diagnoses of diabetes within one year, or (2) had at least one inpatient diagnosis of diabetes. The relevant diagnosis codes for diabetes were ICD-9-CM 250 and ICD-10-CM E08-E14. The index date was defined as the 180th day following participation in the pre-ESRD program. Patients who underwent long-term dialysis or who died prior to the index date were excluded from the analysis.

QI assessment

To evaluate the quality of renal care among the study participants, we utilized QIs suitable for assessing CKD patients through claims data [11]. These QIs were developed using the RAND-modified Delphi method [11,19]. Among the eleven QIs [11], three were suitable for nondiabetic CKD patients in our claims-based study cohort: the prescription of RAS inhibitors, testing for proteinuria, and the avoidance of nonsteroidal anti-inflammatory drugs (NSAIDs), as detailed in Supplementary Table 1. Each QI was assessed over a 180-day observation period, starting from the date of participation in the pre-ESRD program until the index date. For each QI, we assigned a score of 1 (achieved) or 0 (not achieved) for each patient and then summed these individual QI scores to calculate an overall QI score, which ranged from 0 to 3 [12,20].

Potential confounders

Patient characteristics, including age, sex, comorbidities, income, occupation, residential location, and type of medical facility where pre-ESRD multidisciplinary care was administered, were extracted from the NHI claims data. Comorbid diseases were identified through inpatient or outpatient diagnosis codes within the 180-day period from the participation of the pre-ESRD program to the index date, with Charlson Comorbidity Index (CCI) scores calculated to reflect the presence and severity of these comorbid conditions [12,21]. Because CKD staging requires data on the estimated glomerular filtration rate (eGFR), we were unable to determine the CKD stage for the study participants due to the absence of laboratory results in the NHI claims data. However, the pre-ESRD program provides a bonus to the multidisciplinary care team for managing to slow the decrease in the eGFR to less than 4 mL/min/1.73 m^2/year in patients diagnosed with stage 5 CKD, as indicated by the treatment code P3407C. Therefore, we used this specific treatment code as a means to identify patients with stage 5 CKD.

Primary and secondary outcomes

The primary outcome of this study was the initiation of long-term dialysis. Secondary outcomes included all-cause death, hospitalization due to AKI, hospitalization due to hyperkalemia, and hospitalization due to acidosis. Patients were

followed from the index date until either the occurrence of the specified outcome or December 31, 2020, whichever came first. Individuals requiring long-term dialysis were registered as patients with catastrophic illness, assigned a specific diagnosis code (ICD-9-CM code: 585; ICD-10-CM code: N18.6), and thereby could qualify for copayment exemptions for dialysis under the NHI scheme [18]. The date of onset for long-term dialysis was established as the date of registration for this catastrophic illness classification [15]. The secondary outcomes of AKI, hyperkalemia, and acidosis were identified through inpatient diagnoses, which are considered more accurate than outpatient data. The date of hospitalization due to AKI, hyperkalemia, or acidosis was identified using the admission date of the first hospitalization associated with the respective ICD-10-CM codes: N17 for AKI, E87.5 for hyperkalemia, and E87.2 for acidosis.

Statistical analysis

The data are presented as the means ± standard deviations for continuous variables and as frequencies with percentages for categorical variables. To evaluate differences in continuous variables, we used the independent samples *t*-test or one-way analysis of variance (ANOVA), depending on the data's characteristics. For categorical variables, the chi-square test was applied to assess distribution differences. To analyze the impact of overall QI scores on study outcomes, Cox proportional-hazards models were utilized to calculate hazard ratios (HRs) and 95% confidence intervals (CIs). Initially, univariable Cox proportional hazards models were utilized to estimate crude HRs and 95% CIs for each outcome. Subsequently, multivariable Cox proportional hazards models were applied to estimate adjusted HRs and 95% CIs, accounting for age, sex, CCI score, stage 5 CKD status, income, occupation, residential location, and the type of facility providing pre-ESRD multidisciplinary care. Additionally, both univariable and multivariable Cox proportional hazards models were utilized to estimate HRs and 95% CIs for the achievement of individual QIs on study outcomes. To ensure the robustness of our findings, sensitivity analyses were conducted by limiting the participants to those from medical facilities that provided pre-ESRD multidisciplinary care to at least 10, 20, or 30 patients with advanced CKD. A two-sided p value of ≤0.05 was considered to indicate statistical significance. All statistical analyses were conducted using SAS software, version 9.4 (SAS Institute, Cary, NC, USA).

Results

Patient characteristics

The process of selecting patients for the study is shown in Figure 1. Among the 95,862 individuals who began participating in the pre-ESRD program between 2016 and 2019, 87,610 patients were alive and had not started dialysis before the index date. According to the exclusion criteria, 27,842 CKD patients without diabetes were enrolled in the study and followed until December 31, 2020.

The baseline characteristics of the participants are shown in Table 1. The average age of the participants in the study cohort was 68.7 years, with a 41.7% prevalence of females. The mean CCI score was 5.38, and patients with stage 5 CKD constituted 2.4% of the study population. The majority of patients received CKD care at metropolitan hospitals (47.8%) and academic medical centers (34.7%).

Distribution of the QI scores

A large portion of the patients (47.6%) obtained an overall QI score of 2, while one-third (33.5%) achieved the highest possible QI score of 3 (Table 2). The smallest number of patients (0.3%) received the lowest overall QI score of 0. Regarding the achievement of individual QIs, the majority of patients (59.8%) were prescribed RAS inhibitors, more than half (56.5%) underwent proteinuria testing, and a substantial majority (98%) avoided the use of NSAIDs.

Table 3 shows that patients with higher overall QI scores were younger and had lower CCI scores. Supplementary Table 2 shows the differences in patient characteristics for each individual QI. Patients who were prescribed RAS inhibitors tended to be younger and male, and had lower CCI scores and a lower prevalence of stage 5 CKD. Those who underwent proteinuria testing were also younger but had slightly higher CCI scores and were more likely to be female. Moreover, patients who avoided the use of NSAIDs were younger, had lower CCI scores, had a greater prevalence of stage 5 CKD, and were more likely to be male.

Associations between the QI scores and outcomes

During a median follow-up period of 23 months (first quartile 12.6 months, third quartile 35.3 months), 2,808 patients (10.1%) initiated long-term dialysis; 4,140 (14.9%) died; and 2,133 patients (7.7%) were hospitalized for AKI, 1,057 (3.8%) for hyperkalemia, and 767 (2.8%) for acidosis. The results regarding the relationships between QI scores and these outcomes are shown in Table 4, with analyses conducted *via* univariable and multivariable Cox proportional hazards models. For the primary outcome, higher overall QI scores were associated with a reduced risk of long-term dialysis initiation, as shown in both univariable (HR 0.904, 95% CI 0.859–0.951) and multivariable models (HR 0.891, 95% CI 0.846–0.938; per 1-point increase in score). Regarding secondary outcomes, multivariable models revealed that higher QI scores were associated with a lower risk of all-cause death (HR 0.900, 95% CI 0.864–0.939; per 1-point increase in score) and hospitalization due to acidosis (HR 0.882, 95% CI 0.799–0.972; per 1-point increase in score). The univariable model showed that higher overall QI scores were associated with a decreased risk of hospitalization for AKI (HR 0.932, 95% CI 0.879–0.988; per 1-point increase in score), although this association was not as evident in the multivariable model (HR 0.974, 95% CI 0.919–1.034; per 1-point increase in score). Both the univariable and multivariable Cox proportional hazards models

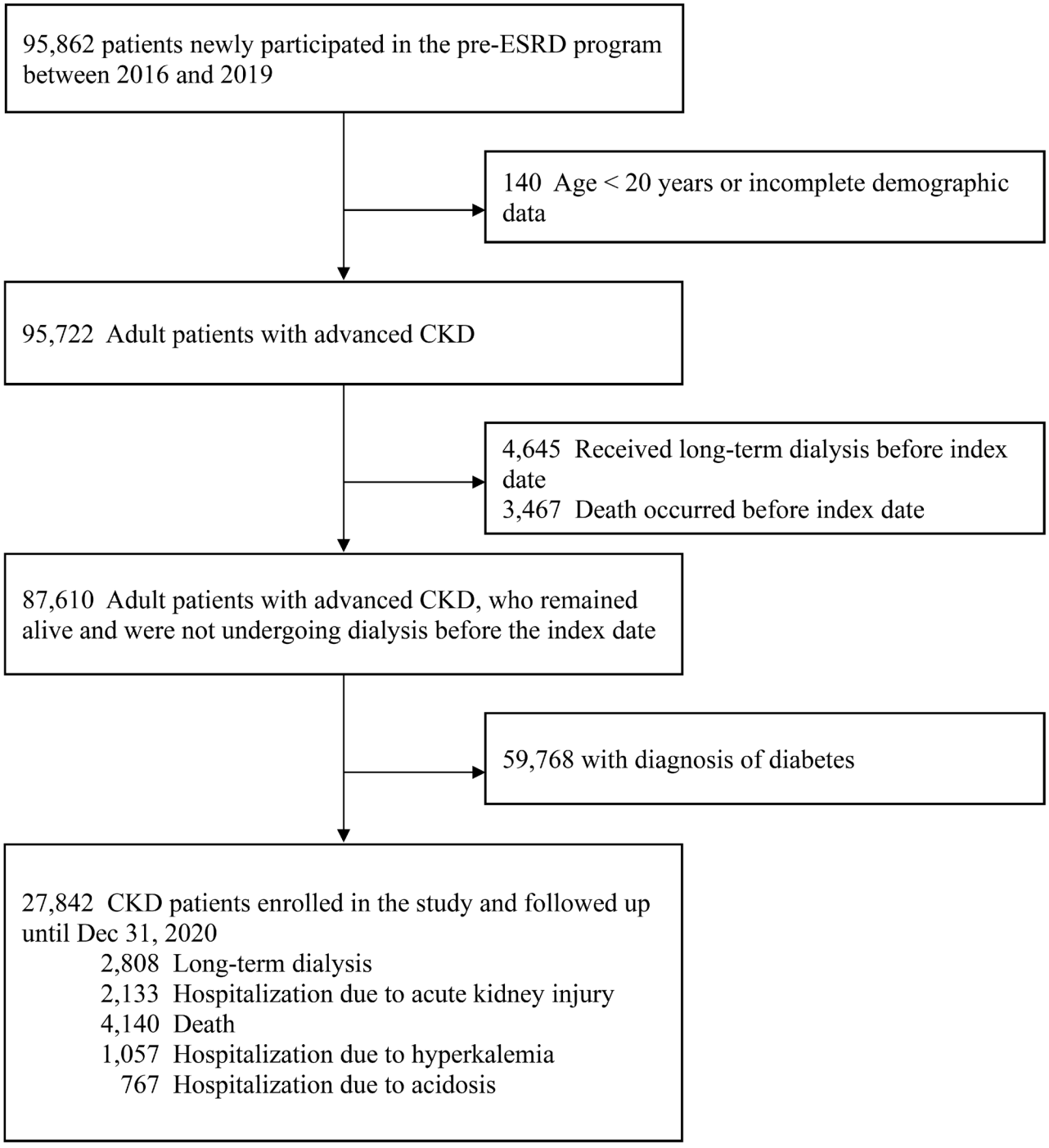

Figure 1. Summary of patient selection. CKD, chronic kidney disease.

showed no association between the overall QI score and the risk of being hospitalized for hyperkalemia.

According to the multivariable Cox proportional hazards models, the prescription of RAS inhibitors was associated with lower risks of long-term dialysis (HR 0.654, 95% CI 0.607–0.705), all-cause death (HR 0.725, 95% CI 0.682–0.770), hospitalization due to AKI (HR 0.803, 95% CI 0.737–0.875), and acidosis (HR 0.713, 95% CI 0.618–0.822). In the univariable models, a greater risk of undergoing long-term dialysis was detected in patients who were tested for proteinuria or who avoided the use of NSAIDs. However, this association gradually decreased after adjusting for multiple covariates in the model. Similarly, undergoing tests for proteinuria was associated with greater risks of all-cause death and hospitalization due to AKI in the multivariable models adjusted for age and sex, but these associations gradually attenuated in the fully adjusted model. For patients who avoided the use of NSAIDs, there was a trend toward lower risks of all-cause death and hospitalization due to AKI; nevertheless, these effects were not statistically significant according to the multivariable models.

Table 1. Baseline characteristics of the study participants.

Characteristics	Statistics	
Participant number	27,842	
Age, year	68.7 ± 15.7	
Age group, year		
<65	9,886	(35.5)
65–80	9,954	(35.8)
≥80	8,002	(28.7)
Women	11,614	(41.7)
Charlson Comorbidity Index score	5.38	(2.18)
Charlson Comorbidity Index score group		
0–3	5,589	(20.1)
4–5	8,678	(31.2)
≥6	13,575	(48.8)
Stage 5 CKD	662	(2.4)
Income, New Taiwan Dollar per month		
<20,000	7,718	(27.7)
20,000–40,000	12,272	(44.1)
≥40,000	7,852	(28.2)
Occupation		
White collar	10,449	(37.5)
Blue collar	11,099	(39.9)
Others	6,294	(22.6)
Location of residence		
Northern	10,614	(38.1)
Middle	7,113	(25.6)
Southern	8,800	(31.6)
Eastern or other islands	1,315	(4.7)
Type of facility providing CKD care		
Academic medical centers	9,671	(34.7)
Metropolitan hospitals	13,309	(47.8)
Local community hospitals	4,079	(14.7)
Physician clinics	783	(2.8)

The data are expressed as the mean ± standard deviation or number (percentage).
CKD, chronic kidney disease.

Table 2. Distribution of the quality indicators.

Quality indicators	Statistics	
Overall score of quality indicators		
0	76	(0.3)
1	5,196	(18.7)
2	13,256	(47.6)
3	9,314	(33.5)
Achievement of individual quality indicator		
Prescription of RAS inhibitors	16,642	(59.8)
Testing for proteinuria	15,725	(56.5)
Avoidance of NSAIDs	27,283	(98.0)

The data are expressed as number (percentage).
NSAIDs, nonsteroidal anti-inflammatory drugs; RAS, renin–angiotensin system.

Sensitivity analyses

Supplementary Tables 3–5 provide the results of sensitivity analyses that assessed the impact of the size of medical facilities, ranging from those managing at least 10 patients to those caring for at least 30 patients with advanced CKD. These analyses demonstrated that patients with higher overall QI scores consistently exhibited lower risks of initiating long-term dialysis, all-cause death, and hospitalization due to acidosis. There was also a borderline reduction in the risk of hospitalization due to AKI associated with higher QI scores. The prescription of RAS inhibitors was associated with lower risks of initiating long-term dialysis, all-cause death, and hospitalization due to AKI and acidosis. The findings from these sensitivity analyses were in agreement with those of the primary analyses, indicating that the associations between QI scores and patient outcomes are robust across various healthcare settings, irrespective of the size of the medical facility providing care.

Discussion

In this study, we evaluated the association between the quality of renal care and major clinical outcomes among 27,842 nondiabetic patients with stages 3B-5 CKD. Only one-third of the patients achieved the highest QI score, and nearly half received CKD care at metropolitan hospitals. A higher overall QI score was independently associated with reduced risks of initiating long-term dialysis, all-cause death, and hospitalization due to acidosis after adjusting for potential confounding factors. Among the individual QIs examined, the prescription of RAS inhibitors emerged as the strongest predictor of favorable outcomes, including lower risks of initiating long-term dialysis, all-cause death, and hospitalizations due to AKI and acidosis. These associations were consistent across univariable and multivariable analyses, as well as sensitivity tests, reinforcing the reliability of the findings.

A major strength of this study is the utilization of national claims data, with a follow-up period of up to five years. The large sample size and extended follow-up duration ensure sufficient statistical power when validating the QIs on processes and outcomes among nondiabetic CKD patients. To comprehensively validate the QIs, we examined five study outcomes using univariable and multivariable Cox proportional hazards models and conducted sensitivity analyses to ensure the robustness of the analytical results. Another strength is the accuracy of the study outcomes. Due to the high cost of long-term dialysis, the approval of copayment exemptions for dialysis requires verification by at least two senior nephrologists, ensuring high accuracy for this outcome [12]. Accurate dates of death were obtained from the national death registry. We defined the outcomes of AKI, hyperkalemia, and acidosis using inpatient data to ensure the correctness of the diagnoses.

QIs for CKD patients cover a wide range of aspects, including CKD monitoring, treatments, drug safety, adherence, and referrals to nephrologists [10]. Utilizing the RAND-modified Delphi method, Fukuma et al. developed a set of process QIs for CKD care based on electronic health data, facilitating the assessment of CKD care quality across various healthcare facilities by health authorities [11]. In our previous study, we selected three of these process QIs and assessed their predictive validity among CKD patients with diabetes [12]. Patients with higher overall QI scores had significantly lower risk of initiating long-term dialysis (HR 0.62, 95% CI 0.40–0.98) and hospitalization due to AKI (HR 0.69, 95% CI 0.50–0.96) but not all-cause death (HR 0.80, 95% CI 0.62–1.03) [12]. Additionally, only 6.6% of patients received the highest quality of CKD care, while approximately one-quarter received the lowest quality of care [12]. In the present study, we assessed the predictive validity of QIs

Table 3. Characteristics of the study participants by overall quality scores.

Characteristics	Overall quality scores								*p*
	0		1		2		3		
Participant number	76		5,196		13,256		9,314		
Age, year	76.7 ± 11.7		70.6 ± 15.3		68.9 ± 15.6		67.2 ± 15.9		<0.0001
Age group, year									<0.0001
<65	11	(14.5)	1,615	(31.1)	4,693	(35.4)	3,567	(38.3)	
65–80	27	(35.5)	1,840	(35.4)	4,717	(35.6)	3,370	(36.2)	
≥80	38	(50.0)	1,741	(33.5)	3,846	(29.0)	2,377	(25.5)	
Women	32	(42.1)	2,220	(42.7)	5,479	(41.3)	3,883	(41.7)	0.394
Charlson Comorbidity Index score	6.4 ± 1.8		5.5 ± 2.1		5.4 ± 2.2		5.3 ± 2.3		<0.0001
Charlson Comorbidity Index score group									<0.0001
0–3	3	(4.0)	858	(16.5)	2,613	(19.7)	2,115	(22.7)	
4–5	23	(30.3)	1,591	(30.6)	4,202	(31.7)	2,862	(30.7)	
≥6	50	(65.8)	2,747	(52.9)	6,441	(48.6)	4,337	(46.6)	
Stage 5 CKD	1	(1.3)	168	(3.2)	326	(2.5)	167	(1.8)	<0.0001
Income, New Taiwan Dollars per month									<0.0001
<20,000	23	(30.3)	1,556	(30.0)	3,707	(28.0)	2,432	(26.1)	
20,000–40,000	40	(52.6)	2,424	(46.7)	5,876	(44.3)	3,932	(42.2)	
≥40,000	13	(17.1)	1,216	(23.4)	3,673	(27.7)	2,950	(31.7)	
Occupation									<0.0001
White collar	15	(19.7)	1,644	(31.6)	4,957	(37.4)	3,833	(41.2)	
Blue collar	44	(57.9)	2,274	(43.8)	5,272	(39.8)	3,509	(37.7)	
Others	17	(22.4)	1,278	(24.6)	3,027	(22.8)	1,972	(21.2)	
Location of residence									<0.0001
Northern	26	(34.2)	1,904	(36.6)	4,962	(37.4)	3,722	(40.0)	
Middle	16	(21.1)	1,425	(27.4)	3,444	(26.0)	2,228	(23.9)	
Southern	25	(32.9)	1,602	(30.8)	4,218	(31.8)	2,955	(31.7)	
Eastern or other islands	9	(11.8)	265	(5.1)	632	(4.8)	409	(4.4)	
Type of facility providing CKD care									<0.0001
Academic medical centers	15	(19.7)	1,691	(32.5)	4,581	(34.6)	3,384	(36.3)	
Metropolitan hospitals	46	(60.5)	2,566	(49.4)	6,326	(47.7)	4,371	(46.9)	
Local community hospitals	13	(17.1)	812	(15.6)	1,948	(14.7)	1,306	(14.0)	
Physician clinics	2	(2.6)	127	(2.4)	401	(3.0)	253	(2.7)	

The data are expressed as the mean ± standard deviation or number (percentage).
CKD, chronic kidney disease.

among CKD patients without diabetes and found that higher overall QI scores were associated with lower risks of initiating long-term dialysis, all-cause death, and hospitalization due to acidosis. Additionally, we observed that approximately one-third of nondiabetic CKD patients received the highest quality of care. These inconsistencies reflect the differences in pathogenesis and metabolic disturbances between CKD patients with and without diabetes. Nondiabetic CKD patients often have diverse underlying etiologies, such as glomerulonephritis or hypertensive nephrosclerosis [22]. While these patients also face a risk of progression to ESRD, the pathways and rates of progression can differ from those of patients with diabetes, which influences their treatment strategies and prognosis [22].

RAS inhibitors consistently demonstrate beneficial effects on renal and cardiovascular outcomes among CKD patients. However, hyperkalemia is a major concern, and physicians frequently discontinue RAS inhibitor prescriptions when patients progress to advanced-stage CKD. In a Swedish cohort study of stages 4–5 CKD patients, Fu et al. reported that patients who discontinued RAS inhibitors had an elevated 5-year risk of mortality (risk difference [RD] 13.6%, 95% CI 7.0% to 20.3%) and major adverse cardiovascular events (RD 11.9%, 95% CI 5.7% to 18.6%) but a lower risk of initiating kidney replacement therapy (RD −8.3%, 95% CI −12.8% to −3.6%) than those who continued to use RAS inhibitors [23]. The National Kidney Foundation–Kidney Disease Outcomes Quality Initiative (NKF–KDOQI) suggested that decreases in the eGFRs or increases in serum potassium levels following RAS blockade are not associated with a greater risk for adverse renal outcomes, and the evidence is more abundant for CKD patients without diabetes [24]. The NKF–KDOQI guidelines indicate that RAS inhibitors treatment should be stopped in cases of hypotension or repeated episodes of AKI, but a definitive conclusion regarding whether RAS inhibitors should be routinely discontinued in patients with advanced CKD who experienced a decline in kidney function was not provided [24]. Similarly, the blood pressure guidelines released by the Kidney Disease: Improving Global Outcomes (KDIGO) advise against routinely discontinuing RAS inhibitors in patients with advanced CKD based on kidney function alone unless patients are experiencing uncontrolled hyperkalemia or are preparing to initiate renal replacement therapy [25]. Using data from the Chronic Kidney Disease Outcomes and Practice Patterns Study (CKDopps), an international prospective cohort study, Pecoits-Filho et al. reported that RAS inhibitors are generally underutilized in patients with advanced CKD, with prescription rates varying across countries: Germany, 80%; France, 77%; Brazil, 66%; and the United States, 52% [26]. In a cross-sectional questionnaire survey of primary care physicians in the United States, Abdel-Kader et al. reported that fewer physicians prescribed RAS inhibitors to nondiabetic patients with macroalbuminuria than to those with microalbuminuria, mainly due to concerns about adverse effects [27]. Moreover, over half of the surveyed physicians reported

Table 4. Cox proportional hazards models for the association between quality indicators and study outcomes.

	Model 1[a]		Model 2[b]		Model 3[c]	
Long-term dialysis	HR	95% CI	HR	95% CI	HR	95% CI
Overall score of quality indicators	0.904	(0.859–0.951)[d]	0.879	(0.835–0.925)[d]	0.891	(0.846–0.938)[d]
Achievement of individual quality indicator						
Prescription of RAS inhibitors	0.640	(0.594–0.689)[d]	0.629	(0.584–0.678)[d]	0.654	(0.607–0.705)[d]
Testing for proteinuria	1.187	(1.101–1.280)[d]	1.153	(1.069–1.243)[d]	1.146	(1.062–1.236)[d]
Avoidance of NSAIDs	3.762	(2.302–6.150)[d]	3.297	(2.016–5.391)[d]	3.020	(1.846–4.940)[d]
	Model 1[a]		Model 2[b]		Model 3[c]	
All-cause death	HR	95% CI	HR	95% CI	HR	95% CI
Overall score of quality indicators	0.835	(0.800–0.870)[d]	0.897	(0.860–0.935)[d]	0.900	(0.864–0.939)[d]
Achievement of individual quality indicator						
Prescription of RAS inhibitors	0.669	(0.629–0.711)[d]	0.703	(0.661–0.747)[d]	0.725	(0.682–0.770)[d]
Testing for proteinuria	1.052	(0.989–1.118)	1.139	(1.070–1.211)[d]	1.111	(1.045–1.182)[d]
Avoidance of NSAIDs	0.717	(0.596–0.863)[d]	0.911	(0.757–1.097)	0.935	(0.776–1.125)
Hospitalization due to acute kidney injury	Model 1[a]		Model 2[b]		Model 3[c]	
	HR	95% CI	HR	95% CI	HR	95% CI
Overall score of quality indicators	0.932	(0.879–0.988)[d]	0.970	(0.914–1.029)	0.974	(0.919–1.034)
Achievement of individual quality indicator						
Prescription of RAS inhibitors	0.759	(0.697–0.827)[d]	0.782	(0.718–0.852)[d]	0.803	(0.737–0.875)[d]
Testing for proteinuria	1.160	(1.064–1.265)[d]	1.211	(1.110–1.320)[d]	1.190	(1.091–1.299)[d]
Avoidance of NSAIDs	0.782	(0.597–1.024)	0.891	(0.680–1.169)	0.907	(0.692–1.190)
	Model 1[a]		Model 2[b]		Model 3[c]	
Hospitalization due to hyperkalemia	HR	95% CI	HR	95% CI	HR	95% CI
Overall score of quality indicators	0.953	(0.876–1.036)	0.982	(0.903–1.068)	1.004	(0.923–1.092)
Achievement of individual quality indicator						
Prescription of RAS inhibitors	0.894	(0.791–1.010)	0.915	(0.810–1.035)	0.949	(0.839–1.073)
Testing for proteinuria	1.012	(0.896–1.143)	1.044	(0.925–1.179)	1.053	(0.932–1.190)
Avoidance of NSAIDs	0.963	(0.632–1.469)	1.071	(0.701–1.635)	1.103	(0.723–1.685)
	Model 1[a]		Model 2[b]		Model 3[c]	
Hospitalization due to acidosis	HR	95% CI	HR	95% CI	HR	95% CI
Overall score of quality indicators	0.851	(0.772–0.939)[d]	0.857	(0.777–0.945)[d]	0.882	(0.799–0.972)[d]
Achievement of individual quality indicator						
Prescription of RAS inhibitors	0.677	(0.588–0.780)[d]	0.686	(0.595–0.790)[d]	0.713	(0.618–0.822)[d]
Testing for proteinuria	1.026	(0.889–1.183)	1.027	(0.890–1.184)	1.046	(0.906–1.207)
Avoidance of NSAIDs	1.413	(0.780–2.562)	1.451	(0.799–2.632)	1.460	(0.804–2.652)

Participant number: 27842; facility number: 244.
CI, confidence interval; HR, hazard ratio; NSAID, nonsteroidal anti-inflammatory drug; RAS, renin–angiotensin system.
[a]Model 1: Univariable Cox proportional hazards model adjusted for overall score of quality indicators or the achievement of individual quality indicator.
[b]Model 2: Multivariable Cox proportional hazards model adjusted for covariates in Model 1 and for age and sex.
[c]Model 3: Multivariable Cox proportional hazards model adjusted for all covariates in Model 2 and for Charlson Comorbidity Index scores, stage 5 chronic kidney disease, income, occupation, residential location, and the type of facility providing pre-ESRD multidisciplinary care.
[d]$p \leq 0.05$.

that they were not familiar with the NKF–KDOQI or KDIGO guidelines [27]. Similarly, our current study revealed a RAS-inhibitor prescription rate of approximately 60%, potentially attributable to concerns regarding hyperkalemia or rapid decreases in the eGFR. To prevent the discontinuation of RAS inhibitors among patients with advanced CKD, hyperkalemia can often be managed through dietary potassium restriction, potassium-binding agents, and potassium-wasting diuretics [25]. Additionally, providing continuing education to physicians regarding updated clinical practice guidelines is crucial.

Regarding the QIs of proteinuria testing and NSAID avoidance, Cox proportional hazards models showed that their attainment status was associated with a greater risk of initiating long-term dialysis. Although a trend toward lower risks of all-cause death and hospitalization due to AKI was observed in non-NSAID users, these effects were not statistically significant in the multivariable analyses. These findings could be attributed to the fact that physicians may have been more likely to order proteinuria testing or avoid NSAID prescriptions in patients with deteriorating renal function. Although the association between individual QIs and a greater risk of long-term dialysis gradually diminished after adjusting for covariates in the multivariable models, there may still be unmeasured confounding factors related to renal function in this study, such as the eGFR or the degree of albuminuria. In our study, the QI for avoiding NSAID prescriptions had a high achievement rate. Similarly, there was a significant reduction in the use of NSAIDs, with a 15% decrease from 2000 to 2018 in the proportion of patients consuming more than 30 NSAID pills per year prior to dialysis initiation among those enrolled in the pre-ESRD program in Taiwan [28]. This trend suggests improved awareness among healthcare professionals regarding the judicious use of NSAIDs in CKD patients [28]. However, only 56.5% of patients in the present study underwent proteinuria testing. It is crucial to emphasize the importance of proteinuria testing, as there are medications available to control proteinuria and postpone

CKD progression, such as RAS inhibitors, mineralocorticoid receptor antagonists, and sodium-glucose cotransporter-2 inhibitors [29,30].

This study has several limitations that should be addressed. First, as this study cohort was constructed based on claims data, information on body measurements, laboratory test results, and lifestyle behaviors could not be obtained. Consequently, several variables, such as the eGFR, severity of proteinuria, metabolic profile, body mass index, and blood pressure, could not be assessed in our study. Although the ICD-10-CM system provides specific codes for each stage of CKD, the validity might not be high enough in the present cohort because the NHI only shifted to ICD-10-CM coding in 2016. However, as this study included patients who participated in the pre-ESRD program, we were able to confirm that their CKD stages were within 3B-5. Additionally, we used specific treatment codes to identify stage 5 CKD patients with a slower rate of eGFR decline. Second, the study participants were limited to the population in Taiwan, which is mainly composed of Asian ethnic groups, and the study results might not be generalizable to other ethnicities. Future studies assessing the effects of QIs on CKD patients should be designed to include multiple ethnicities or countries from different regions. Third, we employed a complete case analysis approach, excluding individuals with missing demographic data. Because Taiwan's NHI is a single-payer, universal coverage system, the database contains very few missing values of the variables examined. Given our large sample size, the exclusion of the small number of cases with missing demographic data was expected to have a negligible impact on our findings. Finally, this was a retrospective cohort study in which causality between the QI scores and patient outcomes could not be established due to the influence of unmeasured confounding factors. Although this study revealed an association between higher overall QI scores and reduced risks of initiating long-term dialysis, all-cause death, and hospitalization due to acidosis, not all individual QIs showed associations with a better renal outcome in the multivariable Cox proportional hazards models and sensitivity analyses. A well-designed, large-scale prospective cohort study that records detailed information will be required to overcome this limitation.

Conclusion

This nationwide cohort study demonstrated a robust association between higher QI scores and decreased risks of initiating long-term dialysis, all-cause death, and hospitalization due to acidosis among nondiabetic patients with advanced CKD, after adjusting for a variety of confounding factors. Among the QIs assessed, the prescription of RAS inhibitors significantly correlated with improved clinical outcomes, while the achievement of the proteinuria testing and NSAID avoidance showed inconsistent associations with renal outcomes. The results of this study indicate a need for regular proteinuria testing and the importance of continued use of RAS inhibitors in this patient population. Continuous refinement and adaptation of these QIs will be crucial as guidelines evolve and new evidence emerges in the management of this complex chronic condition. Future prospective studies with detailed clinical information are warranted to establish a causal relationship between QI scores and patient outcomes and to explore the generalizability of these findings to other ethnic groups and healthcare settings.

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Author contributions

Y-FH, L-YH, K-LC, and H-YW conceived and designed the study. All authors were responsible for the acquisition, analysis, and interpretation of the data. Y-FH, L-YH, P-HT, and H-YW accessed and verified the data. L-YH, P-HT, and H-YW contributed to the statistical analysis. W-CT, M-JK, K-LC, and H-YW provided administrative, technical, and material support. H-YW and K-LC contributed to the acquisition of funding for the study. W-CT, K-LC, and K-YH supervised the study. Y-FH, L-YH, and H-YW drafted the manuscript. All authors read, critically revised and approved the final version of the manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Ethical approval

This study was considered to be exempted from review by the Research Ethics Review Committee of the Far Eastern Memorial Hospital because the database provided only deidentified information. All methods were carried out in accordance with relevant guidelines and regulations of the Declaration of Helsinki. The need for informed consent was waived by the Research Ethics Review Committee of the Far Eastern Memorial Hospital (No.:109202-W) due to the retrospective nature of the study, and only deidentified information was available in the database.

Data availability statement

The data that support the findings of this study are available from the Health and Welfare Data Science Center, Ministry of Health and Welfare of Taiwan, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available for researchers who meet the criteria for access to confidential data, after application to the Health and Welfare Data Science Center (https://www.mohw.gov.tw/cp-3779-39363-2.html).

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