

Effect of nephrology referrals and multidisciplinary care programs on renal replacement and medical costs on patients with advanced chronic kidney disease

A retrospective cohort study

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Abstract

Evidence-based studies have revealed outcomes in patients with chronic kidney disease that differed depending on the design of care delivery. This study compared the effects of 3 types of nephrology care: multidisciplinary care (MDC), nephrology care, and non-nephrology care. We studied their effects on the risks of requiring dialysis and the differences between these methods had on long-term medical resource utilization and costs.

We conducted a retrospective cohort study involving patients with an estimated glomerular filtration rate of (eGFR) \leq 45 mL/min/ 1.73 m² from 2005 to 2007. Patients were divided into MDC, non-MDC, and non-nephrology referral groups. Between-group differences with regard to the risk of requiring dialysis and annual medical utilization and costs were evaluated using a 5-year follow-up period.

In total, 661 patients were included. After other covariates and the competing risk of death were taken into account, we observed a significant (56%) reduction in the incidence of dialysis in both the MDC and non-MDC groups relative to the non-nephrology referral group. Costs were markedly lower in the MDC group relative to the other groups (average savings: US\$ 830 per year; 95% confidence interval: 367-1295; P < .001).

For patients without nephrology referrals, MDC can substantially reduce their risk of developing end-stage renal disease and lower their medical costs. We therefore strongly advocate that all patients with an eGFR of \leq 45 mL/min/1.73 m² should be referred to a nephrologist and receive MDC.

Abbreviations: aSDHR = adjusted subdistribution hazard ratio, BUN = blood urea nitrogen, Ca = calcium, Chol = total cholesterol, CKD = chronic kidney disease, Clinical Modification, COPD = chronic obstructive pulmonary disease, Cr = creatinine, eGFR = estimated glomerular filtration rate, ESRD = end-stage renal disease, Gluco = fasting blood glucose, HbA1c = hemoglobin A1c, I = incidence, ICD-9-CM = International Classification of Disease, IQR = interquartile range, K = potassium, MDC = multidisciplinary care, Na = sodium, Ninth Revision, NSAID = nonsteroidal anti-inflammatory drug, P = phosphate, PY = patient year, SD = standard deviation, SDHR = subdistribution hazard ratio, TG = triglyceride, U-Cr = urine creatinine, USD = United States dollar, U-TP = urine total protein.

Keywords: chronic kidney disease, costs, dialysis, multidisciplinary care, nephrology referral

Editor: Phil Phan.

All relevant data are within the paper and its supporting information files. Some of the results of this study were presented in abstract form at the Taiwan Society of Nephrology Annual Meeting 2013, and the 55th ERA-EDTA Congress. This manuscript was edited by Wallace Academic Editing.

The authors have no conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

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Medicine (2019) 98:33(e16808)

Received: 4 March 2019 / Received in final form: 9 July 2019 / Accepted: 22 July 2019

http://dx.doi.org/10.1097/MD.00000000016808

The author(s) received funding from Kaohsiung Municipal Hsiao-Kang Hospital (grant KMHK-102004), Taiwan Ministry of Science and Technology (grant 105-2314-B-037-065-), and Taiwan National Health Research Institutes (grant NHRI-EX105-10505PI) for this work.

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1. Introduction

Chronic kidney disease (CKD) is a global public health problem associated with increased morbidity, mortality, and substantial health care costs.^[1] CKD care is complex, usually requiring the knowledge, skills, and experience of various clinical professionals. Studies have demonstrated that CKD outcomes can be improved by the delivery of appropriate health care services, with timely nephrology department referral and multidisciplinary care (MDC) having the most remarkable effects in patients with advanced CKD. Some^[2–4] but not all^[5] of these studies have demonstrated that patients substantially benefit if they receive early nephrology department referrals. Singhal et al^[6] argued that the quantity of predialysis care rather than a nephrology referral alone significantly contributes to survival after dialysis. However, adequate predialysis renal care is multidimensional and thus difficult to be defined and performed by a single specialist.^[7]

MDC is a common form of care that brings together health care professionals from various disciplines. It has been widely applied in CKD treatment to manage complex therapies and deliver comprehensive health care services. Studies have demonstrated that compared with other forms of care, MDC results in more effective medication prescriptions, a lower renal progression rate, a decreased risk of temporal catheterization for dialysis, and a decreased use of medical services.^[8-12] In addition, relative to those receiving care from a nephrologist only, better survival outcomes and slower progress to end-stage renal disease (ESRD) have been observed in patients with CKD receiving MDC.^[13] Although these studies have similar results, none have compared the effects of MDC relative to those of nephrology and other types of care in a hospital-based population. It is common for patients with CKD to receive care from various specialists. A lack of information on patients who receive care from specialists other than nephrologists-such as cardiologists, endocrinologists, general practitioners, and practitioners of traditional Chinese medicine-can lead to an incomplete understanding of CKD care in the real world and lost opportunities to improve current practices.^[14] There is an urgent need to clarify healthcare gaps and formulate an optimal predialysis care model through clinical practice. This study will also be helpful in the design of a more effective care delivery system for patients with CKD.

This study aimed to investigate the proportion of patients with advanced CKD who were receiving MDC, care from nephrologists, and care from specialists other than nephrologists. In addition, the differences between groups with regard to their results from laboratory monitoring, risk of requiring dialysis, and medical service utilization were also evaluated.

2. Methods

2.1. Design and setting

We conducted a retrospective cohort study using claims and laboratory databases from 1 regional hospital. The regional hospital had 489 beds and provided acute and chronic medical services for the 150,000 residents of a region in Southern Taiwan. There were no nearby hospitals of comparable size. We first identified the patients with CKD who had received care at the hospital between 2005 and 2007. We used an approach adapted from a previous report that classified patients using codes from the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). CKD was indicated by a patient having 1 or more inpatient visits or 2 or more outpatient visits within 1 year.^[15] To ensure that we precisely identified the patients with CKD, we calculated their estimated glomerular filtration rate (eGFR) using the CKD–EPI equation and traced their first eGFR measurement after their diagnosis of CKD.^[16] Patients with a first eGFR of \leq 45 mL/min/1.73 m² were selected for our study cohort. The date of first eGFR measurement after a diagnosis of CKD was considered the index date.

The non-MDC group comprised patients who had 1 or more nephrology depart visits after the index date but received no MDC. The MDC group comprised patients who had received both nephrology referrals and MDC. The non-nephrology referral group comprised all the other patients. We followedup these patients from the index date to December 31, 2012.

This study was approved by the ethical review board of Kaohsiung Medical University (KMUH-IRB-20130072). All researchers in this study followed the directives of the Declaration of Helsinki.

2.2. Multidisciplinary care program

In our professional practice, we have conducted an MDC program since 2004. It has brought together various healthcare professionals-such as nephrologists, nurses, dieticians, pharmacists, and social workers-to deliver comprehensive CKD services. Patients with an eGFR of \leq 45 mL/min/1.73 m² and who were diagnosed as having CKD by nephrologists during outpatient or admissions visits were referred to nurses who informed them of the program. If patients agreed to join the MDC program, the nursing staff conducted a series of surveys with patients. The survey comprised questions on a patient's evaluation of medical and nursing care, their physical functions, knowledge of CKD, psychosocial status, and economic status. The patients were requested to return to the clinic every 1 to 3 months, depending on their health conditions. Routine laboratory tests and the educational programs provided by the nursing staff were conducted at least once every 3 months. Dietitian consultations and drug safety education sessions were carried out by pharmacists every 6 months. Social workers in the MDC program provided active social support when necessary.

3. Measurement of study outcomes

Differences in the risk of ESRD and annual healthcare utilization and costs between groups were the primary focuses of this study. A patient's commencement of dialysis during the period of observation was considered a study event. Patients with ESRD who require dialysis can apply to have their requirement to make copayments waived via a catastrophic illness certificate. The event date was determined using the Registry for Catastrophic Illness Patients. Information on mortality and date of death were obtained from the Registry of Death at the hospital. Death before dialysis was a competing event; those who had not received dialysis and survived to the end of the follow-up period were considered to be censored. The extent of a patient's annual utilization of medical services before dialysis was indicated by their number of outpatient visits, number of hospital admissions, and length of stay. Their annual health care expenditure was indicated by their outpatient expenses, inpatient expenses, and overall expenses. These data were assessed from claim databases. All expenses were discounted by 3% annually and reported in US dollars (where US 1=NT 30). To compare the frequency of biochemistry examinations between these groups, laboratory data on CKD control (serum albumin, blood urea nitrogen, serum creatinine, urine creatinine, and urine total protein), electrolyte control (calcium, phosphate, sodium, and potassium), and metabolic disease control (hemoglobin A1c, cholesterol, triglyceride, and fasting glucose) were obtained during the observation period.

4. Covariates of interest

We also collected data on patient characteristics-namely their age, sex, baseline eGFR, comorbidities (diabetes, hypertension, hyperlipidemia, cerebrovascular disease, and chronic obstructive pulmonary disease), Charlson comorbidity index score, and use of confounding drugs (antihypertensive, diabetic, antilipid, and nonsteroidal anti-inflammatory drugs, and analgesic drugs other than nonsteroidal anti-inflammatory drugs) as adjusted covariates. The present comorbidities were defined using ICD-9-CM codes (eTable 1 in Supplement 1, http://links.lww.com/MD/ D171) when they appeared 2 or more times in outpatient claims or 1 or more times in admission claims within 1 year before the index date. The Charlson comorbidity index score was calculated according to the weights of various diseases, as listed in a previous study.^[17] Patients who had ever used a prescribed drug during the follow-up period were defined to have been treated with these drugs.

5. Statistical analysis

The distribution of patient characteristics was expressed as mean ± standard deviation, or median (interquartile range) for continuous variables and count (percentage) for categorical variables. The differences in the characteristics and frequency of biochemistry examinations among groups were compared using the Chi-squared test for categorical variables and oneway analysis of variance or the Kruskal-Wallis test for continuous variables. We used a competing risk analysis to both estimate the 5-year cumulative ESRD incident rates and compare the statistical difference in incident rates between groups using a modified log-rank test. Fine and Gray's^[18] subdistribution hazard model with adjustments for various covariates was conducted to obtain the subdistribution hazard ratio (SDHR) and 95% confidence interval (CI). Generalized linear mixed models were used to analyze the differences in annual levels of expenditure on and utilization of medical services between the groups during the follow-up period. Because fitting a complicated model to our massive data set can be difficult, we simplified the model by assuming that the random effects had a normal distribution. This assumption is justified by studies that have demonstrated that even if the distribution of random effects is misspecified, little bias exists in the estimation of the covariates of effects.^[19,20] Coefficients were estimated using robust standard errors to correct misspecifications of the correlation structures. Results were represented as adjusted mean differences and their 95% CIs between the 3 groups. The cumulative incidence in competing risk analyses was calculated using the *cmprsk* package in R (version 3.3.4, R Foundation for Statistical Computing, Vienna, Austria).^[21] Statistical analyses were conducted using SAS 9.4 software (SAS Institute Inc, Cary, NC), and figures were created using GraphPad Prism 5.0 (GraphPad Software Inc, San Diego, CA). A 2-sided P < .05 indicated statistical significance.

6. Results

6.1. Demographic characteristics

During 2007 to 2009, 1508 patients had an eGFR of \leq 45 mL/ min/1.73 m² after CKD diagnosis. Patients who were excluded were aged <20 years (n=1), had cancer (n=18), or had no outpatient visits within the 5-year follow-up period (n=828). Thus, 661 patients were eligible for follow-up. The nonnephrology referral, non-MDC, and MDC groups comprised 26.8%, 33.2%, and 40.0% of the study cohort, respectively. In general, relative to the other groups, the MDC group had a significantly lower average eGFR, a higher average Charlson score, and higher proportions of female patients, patients with diabetes, patients with hypertension, patients with hyperlipidemia, as well as patients who used more antihypertensive and diabetes drugs (Table 1).

6.2. Quality of predialysis care

Figure 1 displays the proportions of biochemistry examinations in the observed period among the 3 groups. More than 70% of patients with an eGFR of \leq 45 mL/min/1.73 m² had ever had measurements of their blood urea nitrogen, serum creatinine, triglyceride, and fasting glucose taken. However, the proportions for serum albumin, urine creatinine, and protein, as well as the results obtained from examinations pertaining to electrolyte control, were diverse among the groups. The proportions for albumin, calcium, phosphate, as well as the urine creatinineprotein ratio were substantially higher in the non-MDC and MDC groups relative to the non-nephrology referral group. By contrast, the proportions for blood urea nitrogen and serum creatinine exhibited only slight differences between the 3 groups (Fig. 1A and B). More than 80% of the patients in the MDC group had undergone laboratory tests for electrolyte control (calcium, phosphate, sodium, and potassium). These proportions were significantly higher than those of the other 2 groups (Fig. 1B). Thorough laboratory tests for metabolic disease monitoring and control were also performed for patients in the MDC group and for patients in this group who had diabetes (Fig. 1C).

6.3. Five-year cumulative incidence rate and hazard ratios of dialysis

Figure 2 details the differences in the cumulative incident rate of dialysis of the 3 groups. During the first 3 years, the incidence of dialysis was higher in the non-nephrology referral group than the MDC and non-MDC groups (cumulative incident rate = 21.9%, 18.6%, and 13.1%, respectively). However, differences in the overall cumulative incidence of ESRD were not significant (Fig. 2). Similar results were observed in the subdistribution hazard model (both without adjustments, and with adjustments for age and sex).

After adjustments were made for age, sex, and eGFR, our multiple regression results indicated that the non-MDC group was associated with a 54% reduction in the risk of ESRD (adjusted SDHR [aSDHR]: 0.46, 95% CI: 0.29–0.72, P < .001), and the MDC group was associated with a 47% reduction in the risk of ESRD (aSDHR: 0.53, 95% CI: 0.36–0.76, P < .001) compared with the non-nephrology referral group. After potential covariates were accounted for, a similar protective

Characteristics of the study cohort.

			Nephrolog		
	Overall	Non-nephrology referral	Non-MDC	MDC	Р
	n=661	n=178	n=220	n=263	
Age, mean \pm SD, year	65.2 ± 12.6	65.5 ± 12.9	66.3 ± 12.6	64.1 ± 12.5	.15
Female sex	258 (39.0)	54 (30.3)	87 (39.6)	117 (44.5)	.01
eGFR, mL/min/1.73m ²	27.0±12.4	28.7 ± 13.2	28.3 ± 12.3	24.9±11.6	<.001
Major coexisting disease, %					
Diabetes	206 (31.2)	30 (16.9)	67 (30.5)	109 (41.4)	<.001
Hypertension	285 (43.1)	58 (32.6)	80 (36.4)	147 (55.9)	<.001
Hyperlipidemia	70 (10.6)	11 (6.2)	17 (7.7)	42 (16.0)	.001
Cerebrovascular disease	58 (8.8)	14 (7.9)	20 (9.1)	24 (9.1)	.88
COPD	27 (4.1)	6 (3.4)	5 (2.3)	16 (6.1)	.10
Confounding drugs, %					
Antihypertensive drugs	277 (41.9)	50 (28.1)	101 (45.9)	126 (47.9)	<.001
Diabetes drugs	124 (18.8)	17 (9.6)	58 (26.4)	49 (18.6)	<.001
Antilipid drugs	55 (8.3)	14 (7.9)	25 (11.4)	16 (6.1)	.11
NSAIDs	181 (27.4)	47 (26.4)	65 (30.0)	69 (26.2)	.68
Analgesic drugs other than NSAIDs	40 (6.1)	14 (7.9)	15 (6.8)	11 (4.2)	.24
Charlson score					
Mean (SD)	1.7 (1.7)	1.1 (1.4)	1.3 (1.5)	2.3 (1.8)	<.001
Median (IQR)	2 (0-3)	0 (0-2)	1 (0-2)	2 (1-3)	<.001

The differences in characteristics among groups were compared using the Chi-squared test for categorical variables and one-way analysis of variance or the Kruskal–Wallis test for continuous variables. A P value less than .05 was considered as statistically significant.

COPD = chronic obstructive pulmonary disease, eGFR = estimated glomerular filtration rate, IQR = interquartile range, MC = multidisciplinary care, NSAID = nonsteroidal anti-inflammatory drug, SD = standard deviation.

effect on ESRD risk was observed among the patients in the non-MDC and MDC groups (Table 2).

7. Healthcare utilization and expenditure

Table 3 details the differences in expenditure on, and utilization of health care services in the 3 groups. Relative to the non-nephrology referral group, patients in the non-MDC and MDC groups had significantly higher numbers of annual outpatient visits (3.33 and 3.29 times more visits per patient, respectively, P < .001). However, a shorter length of stay (1.3 less days per patient, P=.01) and lower annual inpatient expenses (a decrease of US\$ 906 per patient, P=.01) were observed in the MDC group compared with the non-nephrology referral group. The total annual health care expenditure per patient in the MDC group (95% CI=367–1295, P < .001) was lower, by US\$ 830, than for those in the non-nephrology referral group.

8. Discussion

Many healthcare delivery designs have been suggested over the past decade to provide appropriate care to patients with CKD. However, only a few evidence-based studies have observed differences in the outcomes of various forms of CKD care delivery. This study revealed that only 74% of patients with CKD stage 3b to 5 were cared for by nephrologists, among whom only approximately 55% received MDC. Relative to patients cared for by other specialists, those who had nephrology referrals or who had received MDC similarly exhibited a 56% lower ESRD risk. Relative to the non-nephrology referral group, the non-MDC and MDC groups had significantly higher frequencies of laboratory examinations, particularly examinations related to kidney disease. After tracing the data on the annual expenditure and utilization of health care services, we observed that only the MDC group had significantly lower medical costs.

The National Kidney Foundation Dialysis Outcomes Quality Initiative guidelines suggest that patients should be referred to nephrologists to deal with renal complications. Patients should also be prepared for dialysis once they have an eGFR of <30 mL/min/1.73 m².^[22] Only a few studies have reported on the prevalence of nephrology care among patients with CKD.^[23-25] Huang et al^[23] reported that 77.1% of patients who initiated dialysis from 2006 to 2008 had at least 1 nephrology-related visit during the previous 3 years. However, nephrology visit rates are usually quite low among patients with an eGFR of <60 mL/min/1.73 m². In Gasparini et al's^[24] sample, less than 10% of such patients with CKD were ever seen by a nephrologist. These differences may be attributable to automated eGFR reporting implemented in clinical routines. Such automation has been proven to increase physician awareness and improve their judgment with regard to the timing of nephrology referrals.^[26,27]

The avoidance of mortality and slowing of disease progression are the major tasks of pre-ESRD care. Our findings reinforce the importance of nephrology referrals and provide solid evidence for the need for appropriate intensive care during the pre-ESRD phase. The proportions for laboratory monitoring and the results from metabolic disease monitoring tended to be higher in the MDC group than the non-nephrology referral group. Anemia, proteinuria, electrolyte imbalance, and disease controls substantially contribute to mortality and dialysis risk. It is thus reasonable to infer that if adequate laboratory monitoring is provided, prescriptions can be modified as required and complications can be promptly dealt with. This, in turn, could potentially result in a lowered risk of mortality and slower renal progression.^[28] In addition, we observed a considerably lower risk of requiring dialysis for patients who had a nephrology referral and patients who had received MDC. This result is strongly corroborated by most findings of previous randomized clinical trials, $^{[29-31]}$ but it differs from those of some observa-tional studies. $^{[10,11,32]}$ This difference $^{[9-11,32]}$ might be due to





Cumulative incidence of dialysis



Figure 2. Risk of end-stage renal disease. The cumulative incidence of end-stage renal disease was estimated with consideration for the competing risk of mortality. Differences between the MDC, non-MDC, and non-nephrology referral groups were analyzed using modified Kaplan–Meier and Grey methods. MDC = multidisciplinary care.

these studies' methods of patient selection for their non-MDC groups. For example, Chen et al^[11] selected a non-MDC group using diagnostic codes and observed that MDC reduced the requirement for renal replacement therapy. However, an inverse relationship was observed by another study using propensity score matching.^[9] By contrast, this present study included all patients with CKD for comparison, making our results more representative of real clinical practice. Nevertheless, future large randomized trials must be conducted to clarify the effects of MDC on the incidence of dialysis.

Our study revealed similar levels of medical utilization and costs between the non-MDC and MDC groups, which differed from the findings of related studies.^[10,11,32] This difference might be due to our different method of measuring the levels of health care costs and utilization. Chen et al^[11] observed that without adjustments for covariates, an MDC program resulted in total savings of US\$ 1931 per patient annually. Rather than summing the costs over the period of observation, we estimated annual levels of medical utilization and costs and then analyzed the differences between groups while holding other covariates constant. Compared with other methods, our approach was able to more precisely determine the differences in measurements between groups during long-term observations. Differences in our methods of patient selection for the comparison group might also have contributed to these

Table 2	
Risk of end-stage renal disease in relation to having received multidisciplinary care.	

				Model 1 [†]		Model 2 [‡]		Model 3 [§]	
Group	Case	PY	ľ	aSDHR (95% CI)	Р	aSDHR (95% CI)	Р	aSDHR (95% CI)	Р
Non-nephrology referral	40	715	55.9	1.00 (Reference)	_	1.00 (Reference)	-	1.00 (Reference)	_
Non-MDC	45	971	46.3	0.79 (0.51-1.24)	.30	0.46 (0.29-0.72)	<.001	0.44 (0.28-0.69)	<.001
MDC	74	1094	67.6	0.94 (0.61-1.45)	.78	0.53 (0.36-0.76)	<.001	0.44 (0.30-0.65)	<.001

aSDHR = adjusted subdistribution hazard ratio, CI = confidence interval, I = incidence, MDC = multidisciplinary care, PY = patient year.

* Incidence (per 1000 person-years).

⁺ Model adjusted by age and sex.

* Model adjusted for age, sex, and baseline estimated glomerular filtration rate.

[§] Model adjusted for age, sex, baseline estimated glomerular filtration rate, major coexisting disease (diabetes, hypertension, hyperlipidemia, cerebrovascular disease, chronic obstructive pulmonary disease), confounding drugs (antihypertensive, diabetic, antilipid, nonsteroidal anti-inflammatory, and analgesic drugs other than nonsteroidal anti-inflammatory drugs), and Charlson score.

Table 2

Medical utilization	n in relation to previous m	ultidisciplinary care in pat	tients with chronic kidnev dis	ease.

Measures Group	Year 1	Year 2	Year 3	Year 4	Year 5	Adjusted difference in increase (95% CI)	Р
Outpatient visit, time							
Non-nephrology referral	13.4±8.3	10.1 ± 10.1	8.2±9.6	5.2 ± 6.2	4.7±6.9	0 (Reference)	
Non-MDC	19.1 ± 12.9	15.9 ± 13.4	14.4±14.8	9.9±11.4	6.7 <u>+</u> 9.9	3.33 (2.03; 4.63)	<.001
MDC	17.4±9.9	15.7±11.0	13.9 ± 10.9	9.0 ± 9.2	5.4±7.7	3.29 (1.98; 4.60)	<.001
Outpatient expenses, USD							
Non-nephrology referral	1508 ± 2236	838 ± 1301	662 ± 535	401 ± 380	374 <u>+</u> 358	0 (Reference)	
Non-MDC	1892±3395	1502 ± 3065	1470 ± 3219	1213 ± 3045	647 <u>+</u> 890	272 (63; 480)	.01
MDC	1258±1009	1089±744	1082±770	878±1153	514 <u>+</u> 740	46 (-166; 259)	.67
Hospital admission, time							
Non-nephrology referral	0.5 ± 0.9	0.2 ± 0.5	0.3 ± 0.8	0.3 ± 0.9	0.3 ± 0.7	0 (Reference)	
Non-MDC	0.6 ± 1.0	0.4±1.0	0.5±1.0	0.4 ± 1.1	0.4±1.1	0.09 (-0.01; 0.19)	.07
MDC	0.4 ± 0.9	0.3 ± 0.8	0.3 ± 0.9	0.3 ± 0.8	0.3 ± 0.8	-0.06 (-0.16; 0.04)	.26
Length of stay, day							
Non-nephrology referral	3.8±8.8	1.2±3.4	2.2 ± 9.0	3.4±14.1	2.8±10.4	0 (Reference)	
Non-MDC	4.6±11.0	3.3±12.4	3.5 ± 9.0	3.9±11.0	3.4±10.5	-0.4 (-0.7; 1.4)	.49
MDC	3.2±8.8	2.1±5.8	3.1 ± 9.0	2.9±10.4	2.7 <u>+</u> 8.7	-1.3 (-2.3; -0.3)	.01
Inpatient expenses, USD							
Non-nephrology referral	2749 <u>+</u> 2731	1423±1222	2986 <u>+</u> 2694	3042±3803	3756 ± 6397	0 (Reference)	
Non-MDC	2381 ± 2725	2538 ± 3585	2772 ± 3228	4162±5495	2951 <u>+</u> 4836	-243 (-927; 441)	.49
MDC	1961 ± 2149	1615±1481	2703 ± 3228	3478±5312	2744 <u>+</u> 4832	-906 (-1622; -190)	.01
Overall expenses, USD							
Non-nephrology referral	2346±3193	1218 ± 1615	1311 <u>+</u> 1880	1316 ± 2586	1510±3846	0 (Reference)	
Non-MDC	2792±4157	2151 ± 3759	2357 <u>+</u> 3947	2372 ± 4582	1612 ± 3170	253 (-204; 710)	.28
MDC	1847 <u>+</u> 2102	1553±1398	1805 <u>+</u> 2275	1692±3322	1341 <u>+</u> 3038	-830 (-1295; -367)	<.001

Parameters were estimated using generalized linear mixed model after adjustment for age, sex, estimated glomerular filtration rate, major coexisting diseases (diabetes, hypertension, hyperlipidemia, cerebrovascular disease, and chronic obstructive pulmonary disease), confounding drugs (antihypertensive, diabetic, antilipid, nonsteroidal anti-inflammatory, and analgesic drugs other than nonsteroidal anti-inflammatory drugs), and Charlson score.

Cl = confidence interval, MDC = multidisciplinary care.

discrepancies. Thus, we did not intend to account for all these discrepancies in detail, and reemphasized that appropriate care in CKD is required and may reduce costs.

This study had several limitations. First, the mindsets of patients who received other specialist, nephrological, or multidisciplinary care could not have been measured and cannot be determined retrospectively. Different attitudes on health behavior, or compliance to care between groups, may have influenced our estimation. Second, we could not obtain electronic medical data from other clinical institutions. Thus, medical service utilization and costs may have been underestimated. However, this would have only slightly influenced the results because our hospital requires relatively low copayments for most medical services. Third, a few patients may have died at home, resulting in a misclassification of death in this study. Finally, the generalizability of our results may be limited to patients with an eGFR of ≤ 45 mL/min/1.73 m². These are likely to be patients in health care systems that afford them easy access to specialists.

In conclusion, this study demonstrated that MDC can substantially reduce ESRD risk, increase the frequency of complication monitoring, and lower costs for patients with an eGFR of \leq 45 mL/min/1.73 m². We advocate that all patients with an eGFR of \leq 45 mL/min/1.73 m² should receive MDC and should not be cared for by only 1 type of physician or specialist (nephrologist or otherwise). An appropriate MDC referral mechanism for these patients must be developed.

Acknowledgments

We thank the Department of Medical Informatics, Kaohsiung Municipal Hsiao-Kang Hospital for providing access to their databases.

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