Investigation of the Progression and Management of Chronic Kidney Disease in Adult Patients with Diabetes and/or Hypertension

นิพนธ์ต้นฉบับ

Original Article

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วารสารไทยเภสัชศาสตร์และวิทยาการสุขภาพ 2560;12(4):157-165.

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บทคัดย่อ

วัตถุประสงค์: เพื่อตรวจสอบอัตราการกลายเป็นโรคไตเรื้อรังเป็นระยะ 4 ในผู้ป่วยโรคไตเรื้อรังระยะ 3a และ 3b และการจัดการดูแลรักษาผู้ป่วยโรคไตเรื้อรังในระยะ 3a และ 3b **วิธีการศึกษา:** การศึกษานี้เป็นการศึกษาย้อนหลัง 3 ปี จากฐานข้อมูลอิเล็กทรอนิกส์ของโรงพยาบาลส่งเสริมสุขภาพตำบล (รพ.สต.) ในจังหวัดนครราชสีมา จำนวน 12 แห่ง โดยคัดเลือกผู้ป่วยโรคเบาหวานและ/หรือความดันโลหิตสูงที่มีอายุตั้งแต่ 18 ปีขึ้นไป และเป็นโรคไตเรื้อรังระยะ 3a และ 3b ก่อนหน้าหรือระหว่างปีงบประมาณ 2556 และติดตามจนสิ้นสุดการศึกษาในปีงบประมาณ 2558 **ผลการศึกษา:** ในปี 2556 มีผู้ป่วยระยะ 3a และ 3b จำนวน 162 และ 142 คนตามลำดับ ที่มีการดำเนินโรคเป็นระยะ 4 จำนวน 6 คน (ร้อยละ 3.70) และ 14 คน (ร้อยละ 9.86) มีระยะเวลาที่โรคไตยังไม่กลายเป็นระยะ 4 เท่ากับ 2.42 ปี ในปี 2558 มีผู้ป่วยระยะ 3 จำนวนรวม 142 คน ซึ่งพัฒนาเป็นระยะ 4 จำนวน 20 คนส่วนอีก 122 คนยังไม่เปลี่ยนแปลง ในด้านการจัดการดูแลผู้ป่วยที่กลายและไม่กลายเป็นระยะ 4 พบว่าสามารถควบคุมระดับน้ำตาลในเลือดหลังอดอาหารให้อยู่ในช่วง 80 ถึง 130 มก% ได้ทุกครั้ง (ร้อยละ 7.69 และ 6.00) ควบคุม HbA1c ให้น้อยกว่าร้อยละ 7 ได้ทุกครั้ง (ร้อยละ 23.08 และ 40.00) และควบคุมความดันโลหิตให้ไม่เกิน 140/90 มม.ปรอทได้ทุกครั้ง (ร้อยละ 35.00 และ 40.16) จำนวนผู้ป่วยความดันโลหิตสูงที่โรคไตแย่ลงได้รับ angiotensin-converting enzyme inhibitors (ACEIs) หรือ angiotensin receptor antagonists (ARBs) น้อยกว่าผู้ป่วยที่ไม่มีการกลายของโรค (ร้อยละ 25.00 และ 51.26) ซึ่งผลนี้เหมือนกับผู้ป่วยโรคเบาหวานที่มี micro-albuminuria และได้รับยา ACEIs หรือ ARBs (ร้อยละ 0 และ 2.00) และผู้ป่วยอายุ 50 ปีขึ้นไปที่ได้รับ statins (ร้อยละ 40.00 และ 58.82) ผู้ป่วยระยะ 3a ได้รับการติดตามการทำงานของไตครบทุกรายอย่างน้อยปีละครั้ง แต่ผู้ป่วยระยะ 3b และ 4 ส่วนใหญ่ได้รับการติดตามแต่ไม่ครบตามแนวทางการรักษา ผู้ป่วยทุกรายไม่ได้รับการติดตามภาวะซีด ภาวะกรดเกินในเลือดหรือความผิดปกติของเกลือแร่และกระดูก **สรุป:** ผู้ป่วยโรคไตเรื้อรังที่ไม่กลายไปเป็นระยะ 4 มีแนวโน้มที่จะได้รับการจัดการดูแลที่ดีกว่าผู้ป่วยที่กลายเป็นระยะ 4 อย่างไรก็ตามผู้ป่วยโรคไตเรื้อรังทุกรายยังได้รับการดูแลไม่ครบตามมาตรฐาน ควรมีการกำหนดนโยบายเกี่ยวกับระบบการจัดการดูแลรักษาผู้ป่วยโรคไตเรื้อรังอย่างมีประสิทธิผลโดยสหสาขาวิชาชีพและปฏิบัติให้บรรลุผลสำเร็จต่อไป

คำสำคัญ: โรคไตเรื้อรัง, การดำเนินของโรค, การจัดการดูแลรักษาโรค, โรคเบาหวาน, โรคความดันโลหิตสูง

Abstract

Objective: To investigate the rate of progression to stage 4 chronic kidney disease (CKD) in patients with CKD stage 3a and 3b, and the management they received. **Method:** In this 3-year retrospective study, the electronic databases of 12 health-promoting hospitals in Nakhon Ratchasima Province were used. Patients with diabetes and/or hypertension who were at the age of 18 years or over and had CKD stage 3a and 3b before or during the fiscal year of 2013 were recruited and followed up until the end of the fiscal year of 2015. **Results:** In 2013, 162 and 142 patients experienced CKD stage 3a and 3b, respectively, but only 6 (3.70%) and 14 (9.86%) of them progressed to stage 4. The progression–free period of CKD stage 4 was 2.42 years. In 2015, 20 of 142 stage 3 CKD patients progressed to stage 4, whereas 122 did not. In terms of disease management for the patients with and without the progression their fasting blood sugar was within the range of 80 – 130 mg% (7.69% vs. 6.00%), HbA1c under 7% (23.08% vs. 40.00%) and blood pressure at 140/90 mmHg or lower (35.00% vs. 40.16%). The number of hypertensive patients with the progression who received angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) was lower than those without the progression (25.00% vs. 51.26%). This result was similar to diabetic patients with micro-albuminuria who took either ACEIs or ARBs (0% vs. 2.00%) and patients aged 50 years or over who received statins (40.00% vs. 58.82%). For laboratory monitoring, all stage 3a patients were tested for the renal function at least once a year, but most patients with stage 3b and 4 were not fully monitored according to the guidelines. None of them were monitored for anemia, acidosis, or mineral and bone disorders. **Conclusion:** CKD patients with no progression to stage 4 were more likely to receive a better management than those with the progression. All patients however did not obtain the complete standard care. A policy on the effective management of CKD patients by a multidisciplinary team should be developed and implemented.

Keywords: chronic kidney disease, disease progression, disease management, diabetes, hypertension

Introduction

In chronic kidney diseases, there are histological and/or physiological damages leading to the kidneys impaired functions. Permanent damage takes a considerably long duration to occur. Based on the clinical guideline of KDIGO, chronic kidney disease (CKD) is defined as the decrease in kidney function or an abnormality in kidney structure for more than 90 days.[1] CKD is a complication of diabetes mellitus and hypertension. Previous studies indicate that most patients with these two chronic diseases were not aware of CKD as the consequence of their illnesses.[2-6] This could be attributable to the fact that CKD is usually asymptomatic at the early stage even with a decrease of

50% of kidney function.[7] A limited availability of the annual physical examination could result in a delayed detection of CKD. In addition, with an increasing trend of the incidents of diabetes and hypertension new cases, unavailability of a clear guideline to manage these CKD patients could result in delayed diagnosis and treatment.

At present, hospitals at all levels of care have been encountering the increasing number of patients with diabetes and hypertension, and hence CKD patients as a result. Clinics and referral systems to take care of patients with diabetes, hypertension and CKD have been developed nationwide. In Thailand, a given community hospital which is a district hospital supervises and forms a network of referral system with a number of health-promoting hospitals within the district. At the chronic disease clinic of Chock Chai Community Hospital, diabetes and/or hypertension accounted for 66.27%, 63.62% and 75.19% of cases referred from the health-promoting hospitals. In the fiscal year of 2014, there were 1,182, 121 and 40 patients with CKD stage 3, 4 and 5, respectively. These numbers were unexpectedly low. In the fiscal year of 2014, CKD clinic was set at Chok Chai Hospital as guided by the service plan policy of the Ministry of Public Health.[9] However, only 100 cases of CKD of all patients referred from health-promoting hospitals were found. Therefore, it was evident that a large portion of CKD patients with or without diagnosis were still treated at the health-promoting hospitals.

Patients with diabetes and/or hypertension should be assessed for kidney complications at the early stage and provided with standard managements for all stages of CKD. These managements include renal function monitoring and management of anemia[10], electrolyte and mineral imbalance[11], hypertension[12], blood glucose control, sodium control, smoking, drug- or substance-induced kidney injury, and the use of angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs) and statins.[1,2,13] Standard treatments could have prevented renal complications and other complications as a result of CKD.

The most common cause of death associated with CKD is cardiovascular diseases (CVDs). In patient with stage 3 CKD or higher in particulr, the risk of CVDs increased by 43%.[13] Therefore, the progression from the early to late stage of CKD is of a great concern. A better understanding could help manage the disease and prevent the complications effectively. This study aimed to determine the rate of progression to stage 4 CKD of patients with stage 3a and 3b. How well the disease management was done was also determined. These management components included risk factor control, drug therapy to slow the progression and prevent cardiovascular complications, and renal function and related complications monitoring. The findings could be used to improve the service for patients with chronic kidney disease.

Methods

In this study, a retrospective cohort design was used. Data from the electronic medical records of 12 health-promoting hospitals under the supervision of Chok Chai Hospital, Nakhon Ratchasima Province, were used. Participants were diabetes and/or hypertension with an age of 18 years or older who were treated during the fiscal years of 2013 to 2015. Participants were selected using convenience sampling method. Since there was a limited number of patients with CKD stages 3 at these health-promoting hospitals, all patients eligible for study criteria were recruited. Participants had to have stage 3a or 3b CKD which were confirmed by the serum creatinine (SCr) level of at least two measures at least 90 days apart, before or within the fiscal year of 2013. Their estimated glomerulus filtration rate (eGFR) was calculated using the formula of CKD-EPI (CKD epidemiology collaboration).[14] Participants' stages of CKD were classified based on the definition of CKD stages provided by KDIGO (2012).[1] No renal histological abnormality was used to classify CKD stages. Based on KDIGO (2012), CKD stage 3a and 3b were those with eGFR of 45.00 - 59.99 and 30.00 - 44.99 mL/min/1.73 m^2, respectively.

In their electronic medical records, these patients were followed until either the development of CKD stage 4 or the end of follow-up period which was the end of the fiscal year of 2015 (September 30, 2015). For exclusion criteria, we excluded patients with acute kidney injury, CKD stage 4 or 5, renal replacement therapy, and incomplete data. Patients who were referred to other hospitals and could not be followed were also excluded. This study was approved by the ethics committee of Mahasarakham University (approval number: 007/2559, approval date: March 28, 2016).

The patient's data obtained were gender, age, body weight, height, illnesses, smoking history, blood pressure,

serum creatinine (SCr), hemoglobin, serum bicarbonate, serum calcium, serum phosphate, parathyroid hormone, HbA1c, FBS, lipid profile, and micro-albuminuria. Their history of medication use and adverse drug events related to ACEIs, ARBs or statins was also obtained.

The management of CKD patients was identified according to the KDIGO's Clinical practice guideline for the evaluation and management of chronic kidney disease[1] and the clinical practice recommendation for the evaluation and management of chronic kidney disease in adults 2015 of the Nephrology Society of Thailand.[3] How well the patients were managed regarding risk factor control, drug therapy to slow the kidney failure progression and prevent cardiovascular complications, and the monitoring of renal function and related complications were identified. For risk factor control, proportions of patients with blood pressure of less than 140/90 mmHg, HbA1c of less than 7%, and fasting blood sugar of less than 130 mg% were identified. For drug therapy to slow the kidney failure progression and prevent cardiovascular complications, proportions of patients receiving ACEIs or ARBs were identified. ACEIs or ARBs should be considered the first-line therapy for hypertensive or diabetic patients with micro-albuminuria (albumin of 20 mg/L or higher). In addition, statins should be given to all patients with 50 years of age or older who had CKD stage 3a or higher, or patients who were 18 to 49 years old with at least one of the following risk factors; diabetes, coronary revascularization, ischemic stroke, and myocardial infarction. Each of these risk factors contributed to at least 10% of Framingham risk score.

In terms of the monitoring of renal function and related complications, type and frequency of laboratory tests were scheduled as shown in Table 1.

Table 1 Monitoring schedule for CKD complications.

Laboratory test	Number of monitoring per year by CKD stage		
	3a	3b	4
Serum creatinine (SCr)	1	2	3
Hb (with anemia)		4	
Hb (without anemia)	1	2	2
Ca^{2+}, PO_4, bicarbonate	1 - 2	2 - 4	2 - 4
Parathyroid hormone	Base line (1)	1 - 2	1 - 2

Statistical analysis

All analyses were carried out using the software program STATA version 14. For time-to-event analysis, Kaplan-Meier survival analysis was conducted to determine progression-free proportions over time of the patients with stage 3a and 3b. Difference between the two curves was compared using Log-rank test. Progression-free proportions over time of all stage 3 CKD patients were also determined. The first day of stage 3a and 3b was the day of the annual check-up in the fiscal year of 2013. Each patient was followed up until the progression to stage 4 CKD, loss to follow-up, or the end of the study (September approaching the end of the study (September 30, 2015), whichever came first.

Descriptive statistics, frequency with percentage and mean with standard deviation, were also used to present demographic and health status information at baseline, and the management of the patient care in the fiscal year of 2015. Frequency with percentage was presented for 1) proportions of patients who had blood pressure under control (at all visits, or not all visits), and fasting blood sugar and HbA1c under control (in all tests, in some tests, none of the tests, or data not available), 2) proportions of patients who were treated with and without ACEIs, ARBs, or statins, 3) proportions of patients with renal function monitoring, and 4) proportions of patients with monitoring of renal function related complications.

Results

Of the 3,552 patients screened, 304 patients were eligible for the study. Of the 304 patients eligible, there were slightly more patients with CKD stage 3a (53.29%) than stage 3b (46.71%). About three-fourths were female (75.00). The majority had the age of 70 years or older (55.59%)) with a mean age of 71.60 years. The majority had hypertension (58.88%) followed by diabetes and hypertension (39.47%). Their eGFR moderately low with a mean of 45.43 mL/min/1.73 m^2.

Risk and rate of progression to CKD stage 4

As expected, the risk of progressing to CKD stage 4 in patients with stage 3a was lower than those with stage 3b. Among 162 patients with CKD stage 3a and 142 with stage 3b, 6 (3.70%) and 14 (9.86%) of them had progressed to CKD stage 4, respectively, with an overall risk of 6.58% (20

of 304 patients). In terms of incidence rate, 142 patients with CKD stage 3b contributed 4,008.19 person-months. With 14 patients progression to stage 4, an incidence rate of 0.35 per 100 person-month in CKD patients with stage 3b was found. Among those with CKD stage 3a, an incidence rate of progressing to stage 4 of 0.13 per 100 person-months was found. The overall rate of progression to stage 4 was 0.23 per 100 person-months (Table 3).

Table 2 Demographic and clinical status of patients with CKD stage 3a and 3b (N = 304).

Characteristics	N (%)
Gender	
male	76 (25.00)
female	228 (75.00)
Age (years), (mean ± SD)	**71.60 ± 10.49**
Age group (years)	
41 – 50	10 (3.29)
51 – 60	36 (11.84)
61 – 70	89 (29.28)
> 70	169 (55.59)
Estimated glomerular filtration rate (eGFR) (mL/min/m^2), mean ± SD	**45.43 ± 7.63**
CKD stage*	
3a	**162 (53.29)**
3b	142 (46.71)
Comorbidity	
Diabetes	**5 (1.65)**
Hypertension	179 (58.88)
Diabetes and hypertension	120 (39.47)

* eGFR by CKD stage: 3a = eGFR 45.00 - 59.99 mL/min/m^2, 3b = 44.99 - 30.00 mL/min/m^2, 4 = 29.99 - 15.00 mL/min/m^2

Table 3 Risk and rate of progression to CKD stage 4 in CKD patients with stage 3a and 3b from 2013 to 2015 (N = 304).

Progression to CKD stage 4	**CKD stage 3a (n = 162)**	CKD stage 3b (n = 142)	Overall (N = 304)
Risk: n (%)	6 (3.70)	14 (9.86)	20 (6.58)
Rate: per 100 patient-months	0.13	0.35	0.23

Once the risk was considered based on the time-to-event basis, the risk of developing CKD stage 4 in patients with CKD stage 3a was significantly lower than those with stage 3b (*P*-value = 0.029, log-rank test) (Figure 1). At 12 and 24 months, patients with CKD stage 3a had pregression-free proportions of 98.77% (95%CI: 95.15-99.69) and 96.91% (95%CI: 92.74-98.70), respectively. With higher chances of becoming CKD stage 4 than those with stage 3a, patients with CKD stage 3b had progression-free proportions of 93.66% (95%CI: 88.17-96.65) and 90.14% (95%CI: 83.92-94.04), at 12 and 24 months, respectively.

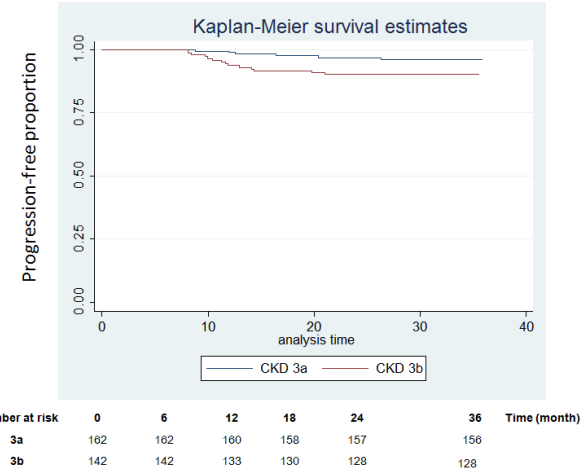

Figure 1 Kaplan-Meier curves depicting the progression-free survival to CKD stage 4 in patients with CKD stage 3a and 3b with statistical significance (P-value = 0.029, Log-rank test) (N = 304).

With all 304 CKD stage 3 patients, the progression to stage 4 was found in 6.58%. With 8,658.11 person-months, the incidence rate of 0.25 per 100 person-months was found. They had a progression-free proportions of 96.38% (95% CI: 93.56-97.98) and 93.75% (95% CI: 90.38-95.97), at 12 and 24 months, respectively. The progression-free period of 29.06 months (2.42 years) was found (Figure 2).

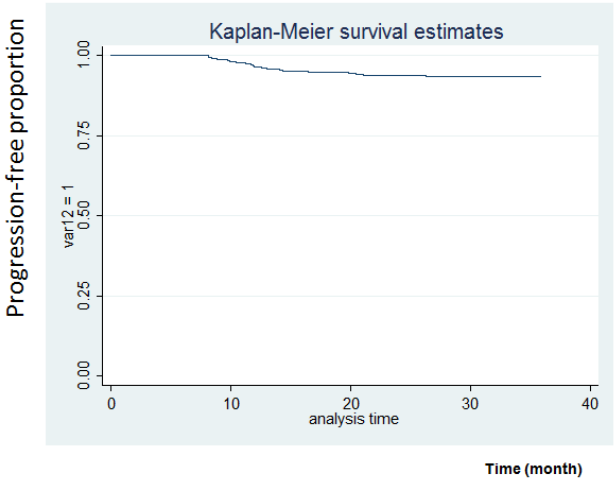

Figure 2 Kaplan-Meier curves depicting the progression-free survival to CKD stage 4 in all patients with CKD stage 3 (N = 304).

The progression to stage 4 CKD among patients with CKD stage 3a and 3b

In the fiscal year of 2013, there were 304 patients with CKD stage 3a and 3b combined. At the end of 2015, 20 of them had their kidney progressed to stage 4, specifically 17 cases in 2014 and 3 cases in 2015. It was found that 122 patients (42.51%) did not experience the progression to stage 4 CKD 4 at the end of 2015. There were 144 patients (50.17%) with no serum creatinine to determine the progression at the end of 2015.

Table 4 The progression to stage 4 of patients with CKD stage 3a and 3b from the fiscal year of 2013 to 2014 and 2015.

	N (%) by fiscal year	
	2014 *(N = 304)*	*2015* (N = 287)*
Progression to stage 4	17 (5.59)	3 (1.05)
Among CKD stage 3a	4	2
Among CKD stage 3b	13	1
No progression to CKD stage 4	158 (51.97)	122 (42.51)
No serum creatinine to determine the progression**	124 (40.79)	144 (50.17)
Loss to follow-up	5 (1.64)	18 (6.27)

* Seventeen patients had developed to stage 4 CKD in the fiscal year of 2014.

** Patients had been treated but with no annual check-up.

The performance of the management to slow the progression to stage 4 CKD in the fiscal year of 2015

Based on the information in the fiscal year of 2015, risk factor control, drug therapy to slow the progression and prevent cardiovascular complications, and renal function and related complications monitoring were evaluated and the results were as follows.

In terms of the adequacy of controlling risk factors of CKD progression, among 20 and 122 patients with and without progression to stage 4 CKD in the fiscal year of 2015, fasting blood sugar (FBS) could be controlled within the target only by 7.69% and 6.00% of the patients, respectively (Table 5). Only 23.08% and 40.00% of the patients had their HbA1c under control, respectively. In addition, blood pressure was well controlled by 35.00% and 40.16% of patients who did and did not experience stage 4 CKD, respectively.

Regarding the effort to slow the kidney function impairment and prevent cardiovascular complications, 25.00% and 51.26% of the patients with and without progression to stage 4 CKD, respectively, received ACEs or ARBs (Table 6). Among patients with micro-albuminuria, 0.00% and 2.00% of them received ACEs or ARBs. However, almost all patients were not tested for micro-albuminuria (100.00% and 96.00% in patients with and without progression, respectively). Regarding the need of statins to prevent cardiovascular diseases, among patients with 50 years of age or older, 40.00% and 58.82% of patients with and without progression to stage 4 CKD were given a statin. In addition, the only one diabetes patients with age of 18 to 49 years old who did not develop stage 4 CKD received a statin (100.00%).

In terms of the adequacy of monitoring the complications among CKD patients, patients with stages 3a, 3b and 4 should be monitored for their renal function at least 1, 2 and 3 times a year, respectively. In the fiscal year of 2015, all patients with stage 3a had their renal function tested for at least one time (100.00%) (Table 7). For 42 patients with stage 3b, one of them (2.38%) had their renal function tested at least two times while the rest 97.62% had the test once. Among 20 patients with stage 4, all of them (100.00%) had their renal function tested at least once or twice. In terms of anemia, parathyroid hormone level and the balance of bone minerals, none had these measures monitored.

Table 5 Risk factor control to slow the progression to stage 4 CKD in the fiscal year of 2015.

Risk factor control	N (%) by progression status (N = 142)	
	Progressing to stage 4 (n = 20)	Not progressing to stage 4 (n = 122)
1. Blood pressure control (SBP/DBP ≤ 140/90 mmHg)#		
- under control in all visits	7 (35.00)	49 (40.16)
- under control in some visits	13 (65.00)	73 (59.84)
2. FBS control (80 - 130 mg%)*	**n = 13**	**n = 50**
- under control in all tests	1 (7.69)	3 (6.00)
- under control in some tests	11 (84.62)	39 (78.00)
- not under control in all tests	1 (7.69)	3 (6.00)
- data of FBS measures not available	-	5 (10.00)
3. HbA1c control (< 7%)*	**n = 13**	**n = 50**
- HbA1c under control in all tests	3 (23.08)	20 (40.00)
- under control in some tests	-	1 (2.00)
- not under control in all tests	5 (38.46)	18 (36.00)
- data of HbA1c measures not available	5 (38.46)	11 (22.00)

Patients with diagnosis of hypertension or anti-hypertensive medications.

* Patients with diagnosis of diabetes or glucose-lowering medications.

Table 6 Drug therapy to slow kidney function impairment and prevent cardiovascular complications in the fiscal year of 2015.

Drug therapy to slow kidney function impairment and prevent cardiovascular complications	N (%) by progression status (N = 142)	
	Progressing to stage 4 (n = 20)	Not progressing to stage 4 (n = 122)
1. Patients receiving ACEIs or ARBs[#]		
1.1 Patients with hypertension	**n = 20**	**n = 119**
- had received the drug	5 (25.00)	61(51.26)
- had never received the drug	15 (75.00)	58(48.74)
1.2 Patients with diabetes and micro-albuminuria	**n = 13**	**n = 50**
- had received the drug	-	1 (2.00)
- had never received the drug	-	1 (2.00)
- data of micro-albuminuria measures not available	13 (100)	48 (96.00)
2. Patients receiving statins[#]		
2.1 Patients with age of 50 years of older	**n = 20**	**n = 119**
- had received the drug	8 (40.00)	70 (58.82)
- had never received the drug	12 (60.00)	49 (41.18)
2.2 Patients with age of 18 – 49 years		
2.2.1 With diabetes	**n = 0**	**n = 1**
- had received the drug	-	1 (100.00)
- had never received the drug	-	-
2.2.2 Without diabetes	**n = 0**	**n = 2**
- no need for the drug because of 10-year coronary risk <10%	-	2 (100.00)

[#] The patient had received drug(s) in the groups of AEIs, ARBs or statins one time or more in the fiscal year of 2015.

Note: ACEIs = angiotensin-converting enzyme inhibitors; ARBs = angiotensin receptor blockers.

Table 7 Monitoring of the renal function, anemia, parathyroid level, acid-base balance and bone mineral balance in the fiscal year of 2015.

Measures to monitor	N (%) by progression status (N = 142)	
	Progressing to stage 4 (n = 20)	Not progressing to stage 4 (n = 122)
1. Renal function monitoring based on serum creatinine		
Stage 3a (≥ 1 time per year)		**n = 80**
Complete	-	80 (100)
Incomplete	-	-
Stage 3b (≥ 2 times per year)		**n = 42**
Complete	-	1 (2.38)
Incomplete	-	41 (97.62)
Stage 4 (≥ 3 times per year)		
Complete	-	-
Incomplete	20 (100)	-
2. Anemia monitoring based on hemoglobin level	**n = 20**	**n = 122**
Complete	-	-
Incomplete	-	-
Not receiving any monitoring	20 (100)	122 (100)
3. Bone mineral balance monitoring based on serum calcium and phosphate		
Not receiving any monitoring	20 (100)	122 (100)
4. Parathyroid hormone level monitoring		
Not receiving any monitoring	20 (100)	122 (100)
5. Acid-base balance monitoring based on serum bicarbonate		
Not receiving any monitoring	20 (100)	122 (100)

Discussions and Conclusion

In this retrospective cohort study, 3.70% and 9.86% of patients with CKD stage 3a and 3b, respectively, had progressed to stage 4. They had a progression-free duration of 2.42 years. At 12 and 24 months, the risks of progression to stage 4 were 3.62% and 6.255%, respectively. This finding was different from the study of Mikkata and colleagues which found the progression-free duration of only 1.9 years but a higher progression risk to stage 4 of 4%. They also found the risk of progression at 12 and 24 months of 4% and 15%, respectively.[15]

In terms of healthcare service provided at the health-promoting hospitals, these patients with stage 3 CKD in our study received the care from a multidisciplinary team consisting of a physician, three nurse practitioners, and a pharmacist. The service has been revised for improvement annually by the multidisciplinary team and healthcare providers at the health-promoting hospitals. Previous report indicated that multidisciplinary care resulted in a 38% lower risk of all-cause mortality (OR 0.62, *P*-value = 0.01) and a 41% lower risk of renal replacement therapy (OR 0.59, *P*-value = 0.02) than the usual care with a statistical significance.[16]

We found that diabetic patients with stage 4 CKD achieved a glycemic control based on HbA1c level in only 23.08% which was lower than those with no progression to stage 4 (40.00%). This could be attributable to the lack of concern about risk factor control, and non-adherence to diet control and medication use. The evaluation of the outcome of HbA1c was somewhat limited and comparisons between different groups of patients could be biased. This was because, with a budget constraint, the measurement of HbA1 level could be done only in some patients.

The study of Chan and co-workers in China found that 26% of the patients could achieve glycemic control based on HbA1c level.[17] Compared with our study, this proportion was higher than our patients with stage 4 CKD but lower than those with no such progression. This discrepancy could be a result of different study design. In Chan's study, their prospective design was used to compare efficacy of a program compared with the usual care to type 2 diabetic patients; while our study used a retrospective data analysis.

In this study, to obtain the complete data of glycemic control was considerably challenging. At health-promoting

hospitals, fasting blood sugar level was usually measured using the finger-tip testing which is somwhat less reliable than the forearm testing. In addition, a follow-up system on the patients who missed the annual check-up was not in place. Blood sugar levels were reported with different channels, especially when they were not transmitted through the electronic system which could lead to the incomplete data of blood sugar levels.

In the fiscal year of 2015, among patients with the progression to stage 4 CKD, 35.00% had their blood pressure under control at all visits while 40.16% of those with no progression did. Our finding was different from the studies of Mikkata and collagues[15] and Chan and co-workers[17] which found only 2.60% and 27.00%, respectively. One of the discrepancy could be attributable to the target blood pressure used in different studies. While out study used a cut-off of 140/90 mmHg; these two studies used a more strict cut-off of 130/80 mmHg.[15,17] With differences in economic systems, socioeconomic status and dietary behavior of the patients in various studies, one could expect blood pressure control to be different.

Patients with hypertension should be given ACEIs or ARBs as the first-line therapy[18] to decellerate the renal function impairment.[12] In our study, unfortunately, only 25.00% of hypertensive patients with progression to stage 4 CKD received these drugs which was lower than those with no progression (51.26%). In the study of Mikkata and colleagues, as high as 55.9% of the patients were given ACEIs.[15] A low proportion of patients receiving ACEIs or ARBs in our study could be due to the fact that not all patients treated at the health-promoting hospitals were treated by the physician. On the other hand, all patients in previous studies were treated by the physician at the hospital. In addition, the JNC 8 guideline (2014) recommended ACEIs or ARBs as the first-line drugs for hypertensive patients with CKD. However, patients with normal kidney function could be treated with a variety anti-hypertensive drugs.[18] Typically, diuretics was recommended as the first-line drug by all previous guidelines. Furthermore, recommendations for patients with CKD were relatively inconclusive. Therefore, the use of ACEIs or ARBs was not fully encouraged and hence the proportion of patients who were given these drugs in our study was low.

In our study, patients with contra-indications to use ACEIs or ARBs were not excluded. The contra-indications included adverse reactions to the drugs, an increase in SCr or a decrease in eGFR of more than 30% from baseline, and a serum potassium level of more than 5.5 millimoles per liter. Since these drugs could cause acute kidney injury, hypertensive patients with CKD should be monitored for SCr and serum potassium at 2 to 4 weeks after the initiation of the drug.[1,3]

The issue of using ACEIs or ARBS to slow micro-albuminuria progression among patients with diabetes was of a great concern. In the fiscal year of 2015, none of diabetic patients with micro-albuminuria with the progression to stage 4 CKD were given ACEIs or ARBS while 2% of those with no progression to stage 4 CKD received the drug. This finding could be somewhat biased since the reports of micro-albuminuria data were limited. This drawback could be due to a lack of the clear protocol to manage these CKD patients, no follow-up system for patients missing their annual check-up, a lack of patient's concern to get their renal function checked, and the incomplete electronic reports. To better determine the progression of the disease and the management performance, a well established protocol or guideline to manage these patients should be in place. The progression of kidney impairment and micro-albuminuria could then be reduced.[1,3]

It was recommended that patients with CKD stages 3 to 5 should be given a statin to prevent cardiovascular complications regardless of lipid level or the need for monitoring such level.[1,3] Our investigation in the fiscal year of 2015 found that 40.00% of patients with progression to stage 4 CKD which was lower than those with no progression (58.82%). However, CKD patients with hyperlipidemia were still managed based on the guideline for hyperlipidemia treatment. As a result, statins were given based on their blood lipid levels. Therefore, a relatively low proportion of CKD patients stages 3 to 5 receiving a statin. It has been found that patients with CKD stages 3 to 5 not receiving a statin experienced a higher risk of cardiovascular complications than patients with less severe CKD. In patients with the last stage of CKD, in particular, the risk of cardiovascular complications was 3.4 times of those with no statin use (HR = 3.4, 95%CI: 3.1 - 3.8) and the risk of death was 5.29 times higher (HR = 5.29, 95% CI: 5.4 - 6.5).[19] Therefore, management protocol of the hospital should be revised to agree with the guideline for management of patients with CKD.

Other complications related to renal failure including renal filtration function, anemia, acid-base balance, and bone mineral balance. The monitoring of these outcomes among individual patients with various CKD stages was different.[1] In our study, in the fiscal year of 2015, all patients with stage 3a CKD had been tested for these renal function and complications at least once which was in agreement with the standard guideline. For patients with CKD stages 3b and 4, most of them were they were tested once which did not meet the criteria of at least 2 and 3 times of testing per year, respectively. Based on these findings, Chok Chai Hospital as the supervisor of the health-promoting hospitals could offer a complete management for stage 3a CKD patients. The hospital could improve the management for patients with higher stages of CKD.

In conclusion, a relatively large proportion of patients with CKD stages 3a, 3b and 4 were still treated at the health-promoting hospitals. Patients with no progression to stage 4 CKD were more likely to be treated according to the guidelines than those with the progression. This shortcoming was because the service to CKD patients in the year 2015 was in its relatively early stage according to the CKD clinic service plan policy of the Ministry of Public Health issued in the year 2014. In addition, no clear management protocol for CKD patients had been established. We recommended that, based on the policy, identifying CKD patients with an early stage should be a focus and a seamless management according to standard guidelines such as those of KDIGO (2012) and/or the Nephrology Society of Thailand should be carried out.[1,3] The management and targets should be tailored made to individual patient's needs and hospital's context. Multidiciplinary team should be encouraged and facilitated. The ultimate outcomes were knowledge and concerns among the patients about how to self-care and adhere to the management plan. On the provider side, an effective referral and follow-up system to offer an early preventive treatment should be fully developed.

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Editorial note
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