The Factors of Chronic Kidney Disease: Diabetes, Hypertension, Smoking, Drinking, Betelnut Chewing

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摘要

包含糖尿病、高血壓以及肥胖等危險因子的慢性腎臟病因廣為被探討。然而研究生活習慣如抽菸、喝酒以及吃檳榔對於慢性腎臟病影響的文獻相對卻較少。本論文針對選定的群眾中去研究這些危險因子對於慢性腎臟病的惡化影響程度。我們發現到如果只針對單一危險因子去研究，如: 糖尿病(odds ratio 1.73)、高血壓(odds ratio 2.25)，其 odds ratio 相對於多重危險因子比較低；數據顯示一個糖尿病人曾有過抽煙或喝酒記錄時，其惡化程度的 odds ratio 會分別提升到 2.65 和 2.67；亦或是一個具有高血壓的病人，如果同時具有抽煙或是喝酒的習慣時，其 odds ratio 會提升到 3.61 和 2.86。因此，我們從這些 odds ratio 數值中觀察到，多重危險因子會比單一危險因子對於慢性腎臟病的惡化會產生更明顯的影響。也就是說，當一個 CKD 病人如果具有糖尿病或是高血壓疾病，同時又有抽煙或喝酒習慣，將會加速慢性腎臟病惡化的程度與速度。

關鍵字：慢性腎臟病、國泰醫院 CKD 資料庫、危險因子、糖尿病、高血壓、抽煙、喝酒、吃檳榔

Abstract

The risk factors of Chronic Kidney Disease (CKD), including diabetes, hypertension, and obesity, are described consistently in the literature. On the contrary, it is seldom studied on the lifestyle factors of CKD, such as smoking, alcohol drinking, betelnut chewing. This paper studies the joint risk factors in a population-based cohort. Compared with single risk factors, diabetes (odds ratio 1.73), hypertension (odds ratio 2.25), the odds ratio of joint risk factors gets higher, the odds ratios of smoking associated with diabetes and hypertension are 2.65 and 3.61, respectively. Furthermore, the odds ratios of drinking with diabetes and hypertension are 2.67 and 2.86, respectively. We observe that the odds ratios of multiple risk factors are higher than single risk factors. That is, the risk of CKD will increase dramatically if a patient of chronic diabetes or hypertension disease has a bad habit of smoking and/or drinking.

Keywords*: CKD, Cathay General Hospital (CKD) database, risk factors, diabetes, hypertension, smoking, drinking, betelnut chewing.*

1. Introduction

The end-stage renal disease (ESRD) is an important public health problem because there was an estimate of over 38,709 patients as of 2004 with an end-stage renal disease in Taiwan. Another study [15] shows an association between lifestyle and the development or progression of kidney disease among people who already had hypertension or diabetes. CKD patients are usually derived from other chronic diseases like hypertension [5-7] and diabetes [6] [8]. On the other hand, smoking, alcohol drinking and betelnut chewing [9-14] are sometimes the risk factors for CKD. Thus motivated, we investigated these risk factors associated with CKD in a population-base study with the emphasis on the role of diabetes, hypertension and lifestyles [4].

2. Population of Study

In this prospective study, we use Cathay General Hospital (CKD) database. The cohort is composed of 790 kidney disease patients whose ages are in the range between 20 and 98 years old. The data in the database are chosen from January 1st, 2000 to July 10th, 2008 as the outcome of interest. Figure 1 summarizes the population of study including 338 females and 454 males with the average age 67 years old.

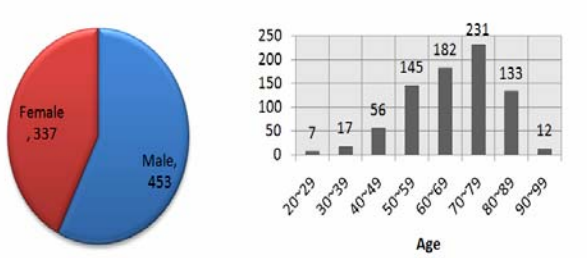

Figure 1 The age distribution of population

Chronic kidney disease is a progressive loss of renal function over a period of months or years. CKD is identified by a blood test for creatinine. Higher levels of creatinine indicate a falling glomerular filtration rate (rate at which the kidneys filter blood), for example, (GFR < 60 ml/minute per $1.73m^2$ by the modification of diet in a renal disease formula), and as a result a decreased capability of the kidneys to excrete waste products. Creatinine levels may be normal in the early stages of CKD. Table 1 lists the definition of chronic kidney disease by stages according to [17].

Table 1 Definition of CKD [17]

Stage		1	2	3	4	5
GFR(mL/min/1.73m²)		≧90	60-89	30-59	15-29	<15(or dialysis)
With Kidney Damage*		1	CRI	CRF	Pre-ESRD	ESRD
Without Kidney Damage*	With HBP*	HBP	HBP and GFR↓	CRF	Pre-ESRD	ESRD
	Without HBP*	Normal	GFR↓			

- Kidney damage is defined as pathologvic abnormallyties or makers of damage, including abnormallyties in blood or uringetests or imaging studies.
- High blood pressure (HBP) is defined ≧140/90 in adults and 90th percentile for height and gender in children.
- CRI：Chronic Renal Insufficiency、CRF：Chronic Renal Failure、ESRD：End-Stage Renal Disease

The National Kidney Foundation further categorizes the CKD into five stages: stage 2 is chronic renal insufficiency (CRI), stage 3 is chronic renal failure (CRF), stage 4 is pre-ESRD and stage 5 is ESRD. We further classify each CKD patient into one of the two categories: early stage (stage 1 and stage 2), late stage (stages 3, 4 and 5) and analyze the stage transfer of the diabetes, hypertension associated with lifestyle. Figure 2 shows, from our database, the number of patients in early stage is less than that of late age because Cathay General Hospital is a hospital which also serves for teaching, the CKD patients in early stage used to go to their family doctors at the beginning. In addition, each personal basic data form contains seven primary etiological factors to CKD, and there are many classes of small disease in those etiological factors, respectively.

Figure 2 Distribution of patients in each stage

Based on this classification, we draw a chart (Figure 3) to show the number of patients from seven main primary etiological factors, the renal parenchyma disease (362, 46%) and the systemic disease (334,43%) both have high percentage in these categories. Moreover, most patients in systemic diseases have the history of hypertension with 92 patients (ICD-9: 401-405) and diabetes with 99 participants (ICD-9: 250) [17].

Figure 3 Distribution of patients with seven primary etiological factors

The basic data of each participant contains the information of age, gender, body height, body weight, hemoglobin, WBC, RBC, Hb, Ht, MCV, MCH, MCHC, platelet count, blood urea nitrogen (BUN), creatinine, uric acid, albumin, cholesterol, triglyceride, sugar (AC). Hypertension is claimed if a participant's blood pressure exceeds 140/90 mmHg or the use of antihypertensive medicine. Diabetes mellitus was defined as a fasting blood glucose level of 140 mg/dL, non-fasting glucose of 200 mg/dL, or a history of treatment for diabetes [14]. The habit of smoking, drinking and betelnut chewing is classified into two categories: used or never. To determine the link between each possible risk factor and CKD, a multivariate logistic regression model for age, sex, BMI, GFR, education level, BUN, uric acid, cholesterol, triglyceride hypertension, diabetes, smoking, drinking and betelnut chewing in each stage was used [14] with the results provided in Table 2.

Table 2 Relation between selected factors and prevalent chronic kidney dise

	Total	Chronic Kidney Disease Stages				
		Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
Participants	790	14	52	242	209	271
Age(years)	67	42.36	59.6	67.8	69.3	67.5
Female	337	7(50.0%)	23(44.2%)	69(28.5%)	96(45.9%)	142(52.4%)
BMI(kg/m^2)	25.0	----	---	25.4	25.3	24.5
Low education level	443	1	23	121	130	168
GFR (mL/min/1.73m^2)*	27.7	106.5	68.2	38.9	22.8	9.5
Creatine (μmol/L)	3.5	0.875	1.1	1.8	2.8	6.9
BUN(mg/dL)	46.0	12.3	17.1	28.3	41.6	66.6
Uric acid(g/dL)	8.1	4.5	6.1	7.5	8.6	9.0
Cholesterol(mg/dL)	187.7	209.3	178.8	183.7	199.3	172.2
Triglyceride(mg/dL)	153.9	173	117.7	154.0	154.8	139.7
Hypertension	316	5	31	169	148	210
Diabetes	563	4	15	92	93	112
Smoking status						
Current smoker	92	1(7.1%)	9(17.3%)	39(16.1%)	17(8.1%)	26(9.6%)
Former smoker	99	1(7.1%)	5(9.6%)	37(15.3%)	30(14.4%)	26(9.6%)
Never	597	12(85.7%)	38(73.1%)	166(68.6%)	162(77.5%)	219(80.8%)
Drinking status						

Current drinking	64	2(14.3%)	6(11.5%)	27(11.2%)	14(6.7%)	15(5.5%)
Former drinking	47	0(0.0%)	1(1.9%)	16(6.6%)	14(6.7%)	16(5.9%)
Never	679	12(85.7%)	45(86.5%)	199(82.2%)	178(85.2%)	240(88.6%)
Betel nut chewing status						
Current betel nut chewing	4	0(0.0%)	0(0.0%)	3(1.2%)	0(0.0%)	1(3.7%)
Former betel nut chewing	6	0(0.0%)	1(1.9%)	3(1.2%)	1(4.8%)	1(3.7%)
Never	780	14(100.0%)	51(98.1%)	236(97.5%)	208(99.5%)	269(99.3%)

- GFR, creatine, BUN, urine acid, cholesterol and triglyceride is average number.
- Low education level: participants with middle-school education or below

In addition, Figure 4 lists the distribution of participants with the history of smoking, drinking or betelnut chewing, which shows there are more participants in the late stage than those in the early stage, which motivates us to further study the links between the diabetes, hypertension and lifestyles with CKD in early stage and late stage.

Figure 4 Distribution of participants with smoking, drinking and betelnut chewing in each stage

On the other hand, we also calculate the distribution of participants with drug habituation, and the medicine taking with prescription as shown in Figure 5. It is believed that most participants are taking the suitable medicine treatment by professional doctors.

Figure 5 Distribution of participants in drug habituation

Besides, the participants with Chinese herbal (210 patients with prescription, and 37 patients without prescription) or other medicines like patent medicine, energy drinks, folk prescription, and health & wellness food also have high percentage. Taking Chinese herbal without prescription is usually with aristolochic acid which is sometimes the key reason to develop a kidney disease, and other medicines without prescription also make the kidney get injured.

3. Results of Statistical Analysis

The mean age of study participants was 67 years old in the study group of age between 20 and 98 inclusively and the mean M-GFR is 27.7 mL/min/1.73m^2. Among 790 CKD participants, 148 (19.0%) participants were reported a history of smoking cigarette, 111 (14.1%) participants have ever had a heavy drinking and there are 10 (1.3%) participants used to frequently chewing betelnuts. Based on the age distribution, we report the relation between age and stage transfer in Table 3. We find that the participants with higher age have higher possibility to transfer to the next stage in less than 8 months which means that the health of an older participant gets declined so that they are easier to step into the next stage.

Table 3 Relation between age and time of entering the next stage

Age	30~39	40~49	50~59	60~69	70~79	80~89
Total	2	4	9	9	13	7
Number of participants who less than 8 months steps into next stage	0(0.0%)	3(75.0%)	6(66.7%)	6(66.7%)	7(53.8%)	5(71.4%)

Table 2 focuses on reporting the statistics of CKD with each stage by adjusting the age, examining data and three kinds of lifestyles from this cohort to that of Cathay General Hospital. It shows that the increasing categories are stage, age, low education level, creatinine, BUN and uric acid. We examine the relation between these lifestyles in more details according to Table 4. Compared with those who are smoking, drinking, betelnut chewing and stage transfer, Table 4 shows that no matter smoking, alcohol drinking or betelnut chewing, the number of participants will get higher along with the stage transfer more seriously.

The betelnut chewing in stage transfer is not an obvious factor due to a small sample size. Tables 5 and 6 focus on the risk factors on early stage and late stage transfer, Table 5 is given to show the effect between a single risk factor and stage transfer, we observe that the odds ratio of hypertension and diabetes are higher than the others.

Table 4 Relation between three life styles and time of get into next stage by adjusting the day range

Steps transfer	Stages			
	1->2	2->3	3->4	4->5
Smoking				
Total	3	4	22	17
Number of participants who less than 180 days steps into next stage	0(0.0%)	2(50.0%)	12(54.5%)	7(41.2%)
Alcohol consumption				
Total	2	4	10	10
Number of participants who less than 150 days steps into next stage	0(0.0%)	1(25.0%)	4(40.0%)	6(60.0%)
Betelnut chewing				
Total	1	0	0	2
Number of participants who less than 90 days steps into next stage	0(0.0%)	0(0.0%)	0(0.0%)	1(50.0%)

Table 5 Odds ratio of risk factors in stage transfer

Risk factors	Odds Ratio	95% CI
Hypertension	2.252	[1.35~3.76]
Diabetes	1.729	[1.05~3.01]
Drinking	1.063	[0.68~1.80]
Smoking	1.002	[0.17~5.93]
Betelnut Chewing	0.821	[1.88~2.28]

Based on the modification of diet in renal disease formula, the 60 ml/minute per 1.73m^2 is the threshold of early stage (stage 2) and late stage (stage 3), and it is the threshold of CKD too. But the odds ratio of lifestyles near 1.0 indicates that the relation between a single risk factor (smoking, drinking, and betelnut chewing) and CKD is too low in our study group. Therefore, we choose the multiple risk factors to check whether it increases the possibility of stage transfer.

Table 6 Relation between lifestyle with systemic disease in stage transfer

Life styles	Only kidney disease	Systemic Disease	
		With diabetes	With hypertension
Smoking	1.002[0.16~95.93]	2.65[-2.31~-0.23]	3.61[-2.37~0.41]
Drinking	1.063[-0.68~1.80]	2.67[-2.05~0.85]	2.86[-2.44~0.68]
Betelnut chewing	0.821[-2.28~1.88]	---	---

So we combine the risk factors, lifestyles with systemic diseases to check whether the participants with multiple risk factors increase the odds ratio of stage transfer. We are interested in checking how the multiple risk factors affect chronic kidney disease. Table 6 reports the relation between the participants with lifestyles first, then check if these participants have systemic disease or not. Based on Table 6, we realize that the lifestyles with systemic diseases really increase the odds ratio in stage transfer especially the lifestyles with hypertension. It says that the participants with either diabetes or hypertension increase the possibility of stage transfer if they were ever smoking, drinking or chewing betelnuts.

4. Discussion

Our discovery of the risk factors such as smoking, betelnut chewing, and alcohol drinking associated with Chronic Kidney Disease (CKD) results into a quick stage transfer for a CKD patient based on the postulates described below is important.

This postulate was supported by some observation: 1) In the late stage, the number of participants with smoking, drinking and betelnut chewing history are much higher and, consequently, if a chronic kidney disease patient has a history of smoking, drinking, or betelnut chewing, the chronic kidney disease gets more critical. 2) The relative risk of CKD in participants with cigarette smoking and alcohol consumption was higher than betelnut chewing. This shows the influence of cigarette using and alcohol consumption may overpower the influence of betelnut chewing. 3) If the participants with multiple risk factors, the possibility of stage transfer gets higher and quickly.

In summary, in this population-based study, individuals who were both systemic diseases and current smokers or drinkers had substantially higher odds of developing kidney disease. It is warned that the participants with kidney disease should quit or decrease smoking, drinking and betelnut chewing, and check the status of CKD on time.

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