

## Chronic Kidney Disease (CKD) — Old diseases with new global challenges

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Nephrology is famous for its 'confusing' terminology, such as acute nephritis, acute glomerulonephritis, post-streptococcal glomerulonephritis, acute nephritic syndrome, nephrotic syndrome, diffuse proliferative glomerulonephropathy, acute renal failure, chronic renal failure and end-stage renal failure (ESRD) etc. A patient may be labelled with two or more such terms at one time. For instance, a patient may suffer from acute nephritic syndrome with *acute renal failure due to diffuse proliferative, post-streptococcal glomerulonephritis*. Some of the terms are clinical and some are pathological. In recent years, there has arisen a new term — **Chronic Kidney Disease (CKD)** which may bring some order out of the 'chaos'.

CKD is not a new disease. It includes all renal diseases lasting more than three months, respective of their pathology. It is divided into 5 stages according to the degree of renal function remaining. It is useful for the following reasons:

1. It is a simple term which is easily understood by doctors all over the world with very little confusion.
2. Apart from treatment of the primary causes (e.g. lupus nephropathy with steroids), the CKD treatment strategy depends very much on the staging of the condition irrespective of the primary pathology. This greatly simplifies the treatment guidelines.
3. Staging greatly facilitates communication between doctors and between doctors and patients. A patient may not grasp the significance of a serum creatinine of 250  $\mu\text{mol/L}$ , but he readily understands if he is told that he suffers from CKD stage 3.

In addition to the development of ESRD, patients with CKD have an increased chance of developing cardiac events such as myocardial infarct and stroke. The cardiovascular complications occur even at the relatively early stage of renal impairment, e.g. when the serum

creatinine is 0.20 mmol/L. CKD is an independent risk factor for the composite outcome of all-cause mortality (myocardial infarction, fatal coronary heart disease, stroke and death)<sup>1</sup>. It is not unusual for CKD patients to die of such complications before they go into ESRD.

### Diagnosis of CKD

The diagnosis of CKD depends on the following:

1. Kidney damage for  $\geq 3$  months as shown by the presence of urine abnormalities like proteinuria or red cells in the urine or abnormalities on X-ray, ultrasound or renal biopsy findings; OR
2. The detection of renal impairment as evidenced by the impairment of the glomerular filtration rate (GFR) at  $< 60 \text{ mL/minute/1.73 m}^2$  for  $\geq 3$  months.

### Staging of CKD

CKD is stratified into 5 stages according to the degree of renal function, with stage 1 being the earliest stage and stage 5 the most severe stage, needing renal dialysis for transplantation. This greatly facilitates communications amongst doctors and between doctors and patients. Patients in Hong Kong are generally very afraid of the term 'renal failure'. If a patient is told that he has 'chronic renal failure', he would take it as meaning 'end-stage renal failure' or something very near that end, though he has creatinine clearance of 50 mL/minute. If he is told that that he has CKD stage 2, he would be more relaxed and would follow the treatment strategy better.

Such staging is also helpful in explaining to the patients about the disease progression.

GFR is the best measure of renal function and the staging of CKD is based on GFR. Since formal determination of GFR by timed collection of urine or by isotope studies is cumbersome, it is done by the MDRD equation based on the age, gender, race and the serum creatinine of the patient.

**MDRD Study Equation:**

$$\text{eGFR (mL/min/1.73 m}^2\text{)} = 186 \times (\text{SCr})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African-American})$$

SCr: serum creatinine in mg/dL; age in years

MDRD stands for Modification of Diet in Renal Diseases. It is a study to evaluate the influence of diet on renal progression and the formula for calculation of the estimated GFR (eGFR) was a result of a 'spin off'. Since the MDRD equation does not require the input of the patient's body weight, laboratories can automatically generate the eGFR based on the age, race, gender and the serum creatinine.

The equation is an exponential one and an average doctor would require a computer program to assist in the calculation. Such programs are available and are usually run on personal computers. The interested reader can contact the author for a free copy (email: cpho@hkma.org). Alternatively there are also programs mounted on Palm and other gadgets and are very convenient to practising nephrologists in the wards (figure 1).



Figure 1. MDRD equation mounted on PDA.

Alternatively, the 'older' Cockcroft-Gault (CG) equation can also be used to calculate the creatinine clearance, an approximation of GFR. The equation is simpler and the calculation can be done by a simple calculator. The author prefers the CG equation because it takes into account the body weight in the calculation. If a patient showed changes in body weight (i.e. in the case of muscle wasting), the creatinine clearance so obtained can reflect the change.

**Cockcroft-Gault Equation:**

$$\text{Creatinine clearance (mL/minute)} = \frac{(140 - \text{Age}) \times \text{weight (kg)}}{72 \times \text{serum creatinine}}$$

Both the MDRD and the CG equations were partially validated in Chinese. They are not suitable for use in children.

The staging of CKD is shown in table 1.

Table 1. The staging of CKD (modified from the K/DOQI)

Stage	Description	GFR mL/min/1.73 m <sup>2</sup> (kidney function)
1	Kidney damage with normal or ↑ GFR	≥ 90
2	Kidney damage with mild ↓ GFR	60–89
3	Moderate ↓ GFR	30–59
4	Severe ↓ GFR	15–29
5	Kidney failure	<15 (or dialysis)

**Causes of CKD**

The main causes of CKD in Hong Kong are diabetes mellitus and hypertension. Other causes include chronic glomerulonephritis, polycystic kidneys disease, analgesic nephropathy and CKD of 'unknown' aetiology.

Good control of hypertension and diabetes mellitus by standard medical means can greatly reduce the progression of renal deterioration.

For patients with diabetes mellitus, the onset of micro-albuminuria is a sign of incipient diabetic nephropathy (figure 2). The use of angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) can prevent the development of diabetic nephropathy. Even for diabetic nephropathy patients with macro-albuminuria (i.e. proteinuria can be detected with usual dipsticks), the use of a combination of ACEI and ARB can slow down the rate of renal progression significantly.

**Treatment for CKD**

The aims of CKD treatment are to delay or arrest the progression of renal deterioration (renal protection) and the prevention of its complications.

Apart from the treatment of the primary causes,



Figure 2. Detection of micro-albuminuria.

treatments of CKD include the following:

### 1. Treatment of hypertension

Hypertension and renal impairment form a vicious cycle. The rate of renal deterioration is directly proportional to the systolic blood pressure. For patients with CKD, the target blood pressure should be around 130/75 mmHg. For patients with diabetic nephropathy and heavy proteinuria, a target blood pressure of 125/75 mmHg is recommended.

ACEI and ARB are shown to have proteinuria lowering effects in addition to the blood pressure lowering effect. The reduction of proteinuria is due to the reduction of glomerular hyperfiltration and has additional renal protective effects. Thus ACEI and ARB are the drugs of choice in CKD patients, either alone or in combination.

Recently, the use of low doses of aldosterone antagonists was shown to have additional renal protective effects in combination with ACEI/ARB. This combination allows a more complete blockade of the renal-angiotensin-aldosterone system (RAAS). The drug should be used with caution as it could cause hyperkalaemia especially in patients with renal impairment and with concurrent administration of ACEI/ARB.

### 2. Control of calcium, phosphate and parathyroid

In patients with renal failure, the calcium level is low due to impairment of vitamin D metabolism. There is also phosphate retention due to reduced renal excretion. The parathyroid glands are stimulated by the hypocalcaemia causing secondary hyperparathyroidism.

Increased phosphate levels cause an increased chance of vascular calcification. Control of the phosphate retention with phosphate binders and the correction of hyper-parathyroidism by vitamin D analogues were shown to be able to reduce the rate of renal deterioration and prevent vascular complications<sup>2</sup>.

### 3. Control of anaemia

Patients with CKD stage 3 and above are usually anaemic. It is now known that some 'uraemic' symptoms such as anorexia, weakness and tiredness are actually anaemic symptoms.

Previously renal anaemia had to be treated with blood transfusions along with its complications such as infection and iron overload. The arrival of erythropoietin revolutionized the treatment of anaemia. The administration of human recombinant erythropoietin will correct the renal anaemia with relief of the symptoms and improvement in the quality of life. It will also prevent the development of left ventricular hypertrophy, which is a risk factor

for cardiovascular events.

4. **Other measures** include the control of elevated blood lipids with statins and achievement of good glycaemia control in diabetic nephropathy. Dietary measures such as moderate protein restriction, giving up smoking and reduction of trunkal obesity would also help.

### 5. Referral to nephrologists

It is recommended that CKD patients be referred to a nephrologist when the GFR is around 30 mL/minute.

## The significance of urine protein

The presence of urine protein by dipsticks is a sign of CKD. The dipsticks are sensitive and specific for albumin. However, urine dipsticks measure only the albumin concentration and is therefore affected by the urine concentration.

A 24-hour urine protein collection gives a reliable and quantitative measurement. However, timed urine collection over 24 hours is cumbersome. One way to get around it is to measure the urine albumin and urine creatinine concentration at the same time and express it as a ratio. This cancels out the urine dilution factor.

If we express the urine creatinine and the albumin concentration as mg/dL, the albumin/creatinine ratio (urine A/C ratio) will be numerical only. This ratio correlates closely with daily protein excretion in g/1.73 m<sup>2</sup> of body surface area. **Thus, a ratio of 6.0 represents daily protein excretion of approximately 6 g/1.73 m<sup>2</sup>.** The accuracy of the total protein-to-creatinine ratio is related to the fortuitous occurrence that daily creatinine excretion is only slightly greater than 1000 mg (8.8 mmol)/day per 1.73 m<sup>2</sup>.

Urine A/C ratio is thus simple to use and it useful for the follow-up assessment of the **same** patient. In a private clinic setting where laboratory costs have been reduced to a minimum, the author has been using the ratio of the albumin and the density (SG) of the urine. This avoids sending the specimen to laboratory and the ratio can be read on a graph in-house.

## Early detection of CKD

In Hong Kong, there are over 1000 new kidney failure patients needing dialysis or kidney transplantation every year. The majority of these patients developed end-stage kidney failure because of CKD. Early CKD usually has no symptoms. **A territory-wide screening and detection program for CKD is therefore of great public health importance.**

Apart from the urine tests, we propose two simple

tests: the serum creatinine and the MDRD eGFR, which has been used in the United States to be able to screen patients with early CKD successfully. The eGFR can be done with a computer program with no additional material cost. The author has been contacting private laboratories to provide such packages for HK\$60 with the computer package supplied to them for free.

### The HKMA Kidney Disease Awareness program

As part of the Kidney Disease Awareness program, the Community Network of the Hong Kong Medical Association organised a 'Caring for your Kidney Day' on Sunday, March 2, 2008 in the Hospital Authority Building (Figure 3). There were health talks and medical check ups including checking the blood pressure, blood sugar, urine protein and abdominal circumference. The latter was shown to be associated with increased chance of CKD.

The meeting was very well received and 370 people attended the function. We detected a large number of people with proteinuria, previously unknown to them. They were counselled by a panel of voluntary nephrologists.

### Conclusion

**CKD is common globally but it is under-diagnosed and under-treated in every part of the world.** CKD is amenable to interventional therapy including medications



Figure 3. Caring for your kidney day.

and lifestyle changes at the early stages. Early treatment will delay the onset of ESRD and it is the mainstay for prevention of ESRD.

To tackle the global problem, the United States developed the K/DOQI guidelines and the UK has the UK CKD guidelines<sup>3</sup>. There have been similar initiatives in the rest of Europe and Australia.

In view of the cost and the morbidity of CKD, mass public screening for early stage CKD is a cost-effective public health measure to tackle this problem.

### References

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2. Lee GH, Brenner D et al. Impact of kidney bone disease and its management on survival of patients on dialysis. *Journal of Renal Nutrition* 2007;17(1):38-44.
3. Aghaie-Jaladerany H, Cowell D, Geddes CC. The early impact of the United Kingdom CKD guidelines on the number of new attendance at renal clinics. *Scottish Medical Journal* 2007;52:28-31.

### Q&A

Answer these on page 14 or make an online submission at:  
[www.hkmacme.org](http://www.hkmacme.org)

Please indicate whether the following questions are true or false

1. CKD includes all renal diseases lasting more than 5 months, irrespective of their pathology.
2. Patients with CKD have an increased chance of developing cardiac events such as myocardial infarct and stroke.
3. CKD is stratified into 5 stages according to the degree of renal function, with stage 1 being the earliest stage and stage 5 being the most severe stage.
4. The MDRD equation is calculated based on the age, gender, race and glomerular filtration rate of the patient.
5. The Cockcroft-Gault equation is calculated based on the age and weight of the patient.
6. The main causes of CKD in Hong Kong are diabetes mellitus, hypertension and cardiovascular disease.
7. Treatment of CKD includes: treatment of hypertension; control of calcium, phosphate and parathyroid; control of anaemia; control of elevated blood lipids with statins, and; achievement of good glycaemic control.
8. The presence of urine protein by dipsticks is a sign of CKD.
9. In Hong Kong there are over 5000 new kidney failure patients needing dialysis or kidney transplantation every year.
10. To tackle the problem of CKD, the United States developed the K/DOQI guidelines.

### ANSWERS TO MARCH 2008

#### Whiplash Associated Disorders — Myths & Controversies – Part 2

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|---------|----------|---------|----------|-----------|
| 1. True | 2. False | 3. True | 4. False | 5. False  |
| 6. True | 7. True  | 8. True | 9. False | 10. False |