"Doctor, I have kidney failure….."

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Medicine is long held as an art because of the extensive interpersonal relationship between the doctor and the patients. It is also considered an inexact science. Our profession developed on the basis of anatomy, physiology and biochemistry and there are formulae and calculations based on biochemistry and physiology such as the partial pressure of oxygen, the Fick's principle and the Henderson-Hasselbalch equation etc. Most of these scientific calculations serve as a reference for the clinicians and the final decision depends on the experience of the physician taking into account of the clinical context.

In nephrology, biochemical science seems to enjoy more respected position and the 'medical informatics' has much to offer. A high blood urea level of a patient indicates that he has renal failure and the blood urea is reduced with dialysis. In a haemodialysis session, the patients' urea level at any point in time can be predicted with reasonable degree of accuracy using urea kinetics calculations, factoring in the urea clearance of the dialyser, the time on dialysis, the body weight of the patient and the fluid removed.

The CKD Management Tool

For the general physicians, it is essential for them to know that Chronic Kidney Disease (CKD) is classified into 5 stages according to the renal function, and the treatment depends largely on the CKD staging. The estimated Glomerular Filtration Rate (eGFR) is widely used as a measurement of renal function, and it can be calculated from the patient's gender, age, race and serum creatinine level using the MDRD equation. The formula is a complicated one as it involved log functions. The author, therefore, developed a program called "CKD management tool", which can calculate the eGFR, stratify the CKD staging and suggest the renal management for general physician's reference. The tool is hosted on the 'kidney classroom' and can be assessed online with any computer (http://www.kidney-classroom.com/#!ckd-tool/coa1).

Figure 1. The online CKD management tool

(Fig.1) The author also developed an app for the same purpose which can be mounted on the ipad or iPhone. The app is free and available in the Apple App Store. Search for 'Diabetic Nephropathy Management Support' in the App Store.

Careful Interpretation of Renal Function is Crucial

We now have user friendly tools which can give a measure of the patient's renal function in terms of glomerular filtration rate (GFR) in ml/minute which patients can readily comprehend. We also have portable tools which can guide the doctors' treatment according to the eGFR. It seems that medical practice might become an exact science, at least in nephrology. Taking it further, the computers may one day replace the doctors. However, this is not the case as illustrated by the 3 cases below.

Patient 1

A 40 year-old patient was referred to a nephrologist with high serum creatinine and high urine microalbumin found on medical check-up. He had no history of renal diseases, and had not taken any medications with potential nephrotoxicity. His blood pressure was 110/70mmHg and his body weight was 205lbs (~93kg). His serum creatinine was 116umol/L (reference value up to 110umol/L for males), the urine analysis was normal. The bedside ultrasonogram showed bilateral normal kidneys.

This 'patient' was clinically normal (normal urine examination, normal blood pressure, normal renal ultrasound) apart from the 'high' serum creatinine and the raised urine microalbumin. He is a physical fitness coach and has a huge muscle mass with a body weight of 205lbs. (Fig.2) The raised serum creatinine can be explained by his huge muscle mass. As creatinine is a metabolic waste from muscle metabolism, the serum creatinine in muscular people is higher because of the increased creatinine load. This, however, is not an indication of renal failure. A more accurate index of the renal function is the creatinine clearance, which requires a 24-hour urine collection. It was being done on this "patient" and was found to be 150ml/minute, which was in fact higher ('better') than normal.

Figure 2. Photo of the 'patient', with special permission granted for this publication.

The urine microalbumin was related to the urine concentration. Since he submitted a concentrated urine sample, the urine microalbumin concentration was higher than the 'normal' range. However, as the urine creatinine was measured at the same time, and is affected by the concentration effect to the same extent, the urine microalbumin/creatinine ratio would give a clearer picture disregarding the urine concentration factor. In this case, the ratio was 0.002, which was normal.

This case reminds us of a basic principle in nephrology: there are limitations for the use of serum creatinine as a measure of renal function because it can be affected by the muscle mass. A man of 205lbs with serum creatinine of 116umol/L can have a good

renal function, while the same serum creatinine level in a thin built lady might indicates renal impairment. **For a person with extremes of body weight, the endogenous creatinine clearance would be a much more reliable index of renal function**.

Patient 2

A 40 year-old Chinese lady attended a private laboratory for a 'body check'. She had no history of kidney diseases. The ultrasound scan of the kidneys was normal and the urine routine was normal. Her serum creatinine was 63umol/L and the eGFR, based on the MDRD equation, was 64ml/minute. She was referred for nephrological opinion for CKD stage 2 (eGFR: 60 - 89ml/minute).

The criteria for CKD are any renal conditons lasting more than three months, together with evidence of renal damage as shown by urine, radiological or pathological abnormalities, or GFR < 60ml/minute/1.73m^2.

This patient did not have any evidence of renal damage although the eGFR was less than the predicted normal range of 75 -125ml/minute. However, the eGFR is an ESTIMATED value based on the patient's age, gender, race and serum creatinine. The MDRD equation is purely a mathematical correlation between the eGFR and the set of variables mentioned above. It is important to note that the correlation was not high for eGFR > 60ml/minute. Hence the eGFR, as calculated by the MRDR formula, is more accurate when it is < 60ml/minute.

In this patient, she had an eGFR > 60ml/minute with no evidence of kidney damage. She, therefore, did not have CKD.

Patient 3

A 74 year-old patient had left nephrectomy done 6 years ago. Since he has only one functioning kidney, he was advised to have his renal function monitored by serum creatinine and creatinine clearance. His degree of glomerular hyperfiltration was also being monitored with the urine microalbumin. He was a meticulous person and had kept a chart of all his test results. (Fig.3)

Date	Hb	Urea <6.7 mmol/ L)	Creat (<126 mmol/ L)	Chol	TG	24hr U.Vol (<1600 ml)	Urine Protein (<149 mg)	Micro-Alb (<15m g/L)	Creat Cleara
15.04.08	* 11.6	6.5	74.4	4.64	1.62				
26.07.08	* 10.8	* 9.2	141.2	* 5.95	1.33				
08.08.08	* 11.3	6.4	131.4	4.84	1.55	*2640	115.4		*39
22.09.08	* 10.8	*6.8	123	3.56	*1.75	*1850	<60		*56
13.02.09	*10.7	5.9	120.2	4.34	1.70	*2200	*149.4	14.9	*62.8
24.08.09	*10.6	*7.8	116.4	4.74	*2.08	*2140	*232.0	*29.9	*65.9
13.12.09	*11.4	*6.9	122.8	5.03	*1.96	*1670	*245.2	*32.7	*64.8
20.04.10	*10.8	*6.4	118.9	4.69	*2.03	*1780	Trace	*41.5	*57.6
23.07.10	*10.5	*7.1	119.9	4.91	*2.43	*1970	128.6	*18.1	*51.6
27.10.10	*10.5	*6.8	*126.1	*6.05	1.48	*1660	*151.7	*43.4	*55.3
26.01.11	*11.3	6.3	125.6	4.71	*2.12	*1860	*224.1	*62.2	*54.7
10.02.11		*8.0	110.5					*25.4	
05.03.11		*8.8	124.4					*50.5	
22.06.11	*10.8	*7.9	121.3	4.37	*2.00	*1620	*149.4	*17.4	*60.0

K+ : 4.2 Alb/Creat Index : 0.9

Figure 3. Part of the lab flow chart

In September last year, he was advised to have a calculated renal function test instead of the clearance creatinine test, which requires a 24-hour urine collection. He relayed the request to the lab and the result showed 'creatinine clearance (by calculated *sic*): 38ml/minute'. The patient was shocked because his measured creatinine clearance was all the time over 50ml/minute.

Currently there are two commonly used formulae for estimating the renal function: the MDRD formula and the Cockcroft-Gault formula (the CG formula). The former was used to estimate the eGFR (see patient 2

above). The latter calculates the creatinine clearance from the age, gender, serum creatinine and the body weight of the patient. Although that laboratory did not specify the formula used, since it returned the value as creatinine clearance, it was apparent that they used the Cockcroft-Gault formula.

Both formulae are rough estimations only, and it may yield different results on the same patient. We fed the patient data into the CG formula and it produced an **estimated** creatinine clearance of 38ml/minute, while the MDRD formula yielded an eGFR of 50ml/minute. Hence this brings us to another principle in nephrology – the MDRD formula and the CG formula return the renal function in the form of eGFR or estimated creatinine clearance respectively. These values **are estimates only and are useful for serial comparison on the same patient over time**. For an individual result, it is important to validate against a properly performed standard creatinine clearance test.

Conclusion

The serum creatinine, measured creatinine clearance, eGFR and the creatinine clearance by CG equation are useful, inexpensive measurement of renal function, and they are very important in renal disease management. However, it is important to recognise the limitations of each of the test, with care taken in the interpretation of the test results to avoid any unnecessary anxiety for the 'patients'.

Reference

1. Ho Chung Ping and Fung So Shan, Developing a mobile clinical decision support tool for the management of diabetic nephropathy, page 5-7, HKMA CME Bulletin, December 2013

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Q&A Self-assessment Questions

Answer these on page 13 or make an online submission at: www.hkmacme.org

Please indicate whether the following statements are true or false.

1. CKD is classified into 5 stages according to the renal function, which can be calculated by the MDRD equation.
2. An increased serum creatinine level MUST mean renal function impairment, despite of the lack of other clinical features or laboratory results.
3. Muscle mass should not be taken into the clinical consideration when estimating the renal function with serum creatinine, as it cannot be measured accurately.
4. The urine microalbumin/creatinine ratio is not affected by urine concentration, giving a better view on the proteinuria.
5. A 24-hour urine collection helps to estimate the creatinine clearance more accurately.
6. eGFR, as calculated by the MRDR formula, is accurate across all values.
7. Cockcroft-Gault formula can also be used to estimate the eGFR.
8. eGFR or estimated creatinine clearance are useful for serial comparison on the same patient over time, instead of cross comparing the two.
9. For an individual eGFR or estimated creatinine clearance result, it is important to validate against a properly performed standard creatinine clearance test.
10. There are limitations to each test, and care should be given when interpreting any results.