

Chronic kidney disease: definition and staging – an orthodox view

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Chronic kidney disease (CKD) is more common than was supposed. If unrecognised, opportunities for prevention and treatment of its consequences, including end-stage renal failure, may be lost. A precise definition and logical staging system are needed by all three tiers of medical care – primary through to tertiary. Orthodox staging systems are based on diagnostic findings which cluster patients who have disease of similar severity, similar expected outcomes and require similar treatment. They should be sufficiently detailed to be precise but not so detailed as to be cumbersome. Patients at various stages should be homogeneous enough to allow the staging number to communicate the implications easily.

Classical staging systems are ordinal:

- stage 1: disease present but without complications
- stage 2: disease causing local or minor effects
- stage 3: disease causing major or systemic effects
- stage 4: disease is life threatening.

The Kidney Disease Outcomes Quality Initiative (KDOQI)/Kidney Disease: Improving Global Outcomes (KDIGO) system of staging CKD is unorthodox and its use can be misleading in clinical practice.¹

- It has five stages, the first two of which are indistinguishable in clinical practice promoting what should be stage 2 (local or minor effects) to stage 3 (a disease causing major or systemic effects).
- Staging relies largely on a measurement of kidney function, the glomerular filtration rate (GFR), acting as a surrogate for the presence of kidney disease. The normal range of GFR cited is incorrect and not congruent with population measurements. The cut-offs for the stages are fixed and do not relate consistently to clinical consequences.²
- The measurement used, estimated (e)GFR, is imprecise so subjects are frequently staged incorrectly.
- Patients in stages 1 to 3 are not homogeneous.
- It uses the word 'disease' loosely.

This has been recognised by a number of authors and authorities, including the National Institute for Health and Clinical Excellence (NICE), some of whom have suggested modifications.^{3–6} A return to orthodox staging is being proposed.⁷

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Evidence of CKD would require that there be specific permanent pathology affecting the kidney with existing or potential threats to the health of the individual as a result. It should recognise that evidence of disease will usually be both structural (including imaging and/or pathology) and based on laboratory testing for signs of kidney damage (such as macro-proteinuria and haematuria or both) and in the later stages, functional (eg GFR related). The degree of reduction in function should be used for staging severity of established CKD not diagnosing CKD. Any eGFR value used for staging should be referenced to age, gender and ethnicity percentiles and the requirement for persistence of the eGFR abnormality/kidney damage for three months or more should be retained.⁸ The term 'chronic renal failure/insufficiency' (CRF/I) should also be retained to mean the state in which there is a reduction in overall kidney function, such that there are defects in kidney-dependent homeostasis causing clinical and metabolic consequences in proportion to the severity of the reduction.

Stage 1 CKD would be applied to the early form of structural disease identified by histology, imaging or inferred from laboratory evidence of kidney damage including, for example, persistent macro-albuminuria, but without any associated reduction in renal function. The eGFR should be >5th percentile. Stage 2 CKD would also require evidence of overt kidney damage but in addition a reduction in kidney function (eGFR <5th percentile). For consistency with the KDOQI/KDIGO system the threshold separating stage 2 CKD from the new stage 3 CKD could arbitrarily be an eGFR of <30 ml/min/1.73m². Evidence of a clinically relevant complication or consequence of reduced kidney function (eg anaemia) would promote the patient to stage 3 CKD. This stage would include patients in whom the eGFR lay between 15 and 30 ml/min/1.73m². Evidence of kidney injury would almost certainly be present as would metabolic, endocrine, hematologic and cardiovascular complications of renal insufficiency. This higher stage takes account of the higher risk of such patients progressing to the new stage 4 CKD and even to the necessity for eventual renal replacement therapy.

Stage 4 CKD would only require that the eGFR be less than 15 ml/min/1.73m², a level of GFR below which it is generally accepted there is a significant risk to the life and health of the patient requiring immediate attention. (Commonsense allows one to infer the presence of structural disease and complications). Stage 5 CKD would be applied to patients receiving regular renal replacement therapy in the form of dialysis. (Patients with functioning renal transplants probably require a separate system or nomenclature, possibly using a modifying term for stages 1 to 4 CKD.)

Subjects with an eGFR <5th percentile for age, gender and ancestry but >30ml/min/1.73m² and without any evidence of

Table 1. Suggestions for a new chronic kidney disease (CKD) staging system.

Stage*	Description	Kidney function	Diagnostic evidence	Implications
1	Structural disease with kidney function	eGFR >5th per centile for healthy matched subjects	Macro-albuminuria and/or glomerular haematuria Abnormal histology Abnormal imaging	Assessment for precise diagnosis and management
2**	Structural disease with reduced kidney function and reserve but without clinically evident functional insufficiency	eGFR <5th per centile for healthy matched subjects but >30 ml/min/1.73m ²	Macro-albuminuria and/or glomerular haematuria Abnormal histology Abnormal imaging No complications of reduced kidney function	As above, but require monitoring of rate of change of kidney function, testing for consequences of kidney insufficiency Awareness of lack of reserve
3**	Structural disease with insufficient kidney function for health (chronic renal failure/insufficiency)	15–30 ml/min/1.73m ² **	Structural disease present or inferred Complications of reduced kidney function	Active management of complications of insufficiency Planning for RRT or not
4	Severe structural disease with life-threatening deficiency of kidney function	<15 ml/min/1.73m ²	Structural disease present or inferred	Close monitoring for triggers to start RRT or enrolment in a conservative care program
5	Advanced/complete destruction	Dialysis dependent	Not applicable	Specialist supervision

* The suffix 'P' could denote 'progression'; ** The distinction between stages 2 and 3 should be clinical rather than based on absolute eGFR. Patients would be tested for evidence of functional consequences of renal insufficiency (metabolic and endocrine). If present they would be placed in stage 3 irrespective of eGFR which may be >30 ml/min/1.73m². eGFR = estimated glomerular filtration rate; RRT = renal replacement treatment.

structural renal damage (ie normal imaging, no urinary abnormalities) and no evidence of renal function-related complications should not be described as having CKD but as having 'reduced kidney function of uncertain significance'. This description will accommodate a significant minority of the elderly, subjects who have undergone unilateral nephrectomy and those who have a non-renal cause of a reduced GFR, such as congestive heart failure.

There is resistance to refining the existing CKD staging systems on the grounds that they are now widely used and any change will cause confusion. This would be a small price to pay for perpetuating a flawed system and irreversibly embedding it into clinical practice for future generations of doctors. It is also argued that the CKD/eGFR construct is important in assessing CVD risk. Stage 3 CKD (as presently defined) does not seem to universally carry such a risk.⁹ Moreover, risk factors are not the same as diseases.¹⁰ In the same way that the geocentric view of the universe gave way to the heliocentric, this nephrocentric construct needs to be changed to a 'vasculocentric' one. Attention to, and research into, CKD should not be diminished by such a change but it would spare nephrology the risk of accusations of overplaying its hand and misdiagnosing large numbers of relatively healthy individuals as having advanced stages of a chronic disease (Table 1).

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References

- 1 National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002;39(suppl2):s1–246
- 2 Erikson BO, Ingebretsen OC. The progression of chronic kidney disease: a 10 year population-based study of the effects of gender and age. *Kidney Int* 2006;69:375–82
- 3 Couser WG. Chronic kidney disease: the promise and the perils. *J Am Soc Nephrol* 2007;18:2803–9.
- 4 Williams B, Rodger RSC. Consensus conference on early chronic kidney disease. Eds. *Nephrol Dial Transplant* 2007;22(Suppl9):ix1–63.
- 5 Bauer C, Melamed ML, Hostetter TH. Staging of chronic kidney disease: time for a course correction. *J Am Soc Nephrol* 2008;19:844–6.
- 6 National Institute for Health and Clinical Excellence. *Chronic kidney disease: early identification and management of chronic kidney disease in adults in primary and secondary care*. London: NICE, 2008.
- 7 Winearls CG, Glasscock RJ. Dissecting and refining the staging of chronic kidney disease. *Kidney Int* 2009;75:1009–14.
- 8 Wetzels JFM, Kiemency LALM, Swinkels DW, Willems HL, den Heijer M. Age- and gender specific reference values of estimated GFR in Caucasians: The Nijmegen Biochemical Study. *Kidney Int* 2007;72:632–7.
- 9 Brantsma AH, Bakker SJL, Hillege HL *et al*. Cardiovascular and renal outcome in subjects with K/DOQI stage 1–3 chronic kidney disease: the importance of urinary albumin excretion. *Nephrol Dial Transplant* 2008;23:3851–8.
- 10 Clase CM, Garg AX, Kiberd BA. Classifying kidney problems; can we avoid framing risks as diseases? *BMJ* 2004;329:912–5.

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