

Early detection of patients with kidney disease

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GUIDELINES

- a. Early detection of patients with renal disease can slow progression of patients to end-stage kidney disease (ESKD), by allowing access to interventions for which there is evidence of efficacy. (Level I evidence)

SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on Level III and IV sources)

An early diagnosis is the cornerstone for prevention of kidney failure, offering the potential for both disease-specific and non-specific interventions to slow disease progression. Even if progression cannot be slowed, patients who have been diagnosed early have better survival when commencing renal replacement therapy.¹ The problem of lead-time bias makes evidence for these observations difficult to accurately assess. Nonetheless, by allowing access to interventions for which there is evidence of efficacy (see other CARI guidelines), the benefits of early diagnosis may be regarded as implicit. The evidence for the value of early referral of patients with renal impairment to specialty services is stronger (see guideline 2) and is clearly dependent on an early diagnosis (although the converse is not true).

The presence of proteinuria and renal impairment should be routinely evaluated in patients at increased risk of chronic kidney disease (CKD) (Level III evidence) including:

- Patients with vascular disease or hypertension
- Immediate relatives of patients with kidney disease
- Aboriginal Australians and Torres Strait islanders
- Patients complaining of prostatic symptoms

The presence of microalbuminuria and renal impairment should be routinely evaluated in patients at increased risk of diabetic kidney disease (Level III evidence) including:

- Patients with diabetes
- Aboriginal Australians and Torres Strait islanders (as part of screening for type 2 diabetes)
- Patients with vascular disease, obesity or hypertension (as part of screening for type 2 diabetes)

- Relatives of patients with type 2 diabetes, vascular disease or hypertension (as part of screening for diabetes and hypertension)

Who should screen for kidney disease?

There is currently no evidence to support the mass screening of the general population for kidney disease by urine dipstick, blood sampling or other means.^{2–4} Moreover, early detection of urine protein to slow progression of CKD and decrease mortality may not be cost-effective when applied to the general population unless selectively directed towards high-risk groups (older persons and persons with hypertension) or conducted at an infrequent interval of 10 years.⁵ However, the increasing prevalence of diabetes in the general population may ultimately change this balance of benefit and cost.

By far, the majority of such at-risk patients (or their relatives) are already in primary care and could be readily identified through screening in general practice routine screening for CKD in the general practice setting, with both urinalysis and estimation of glomerular filtration rate (GFR), should be considered an integral part of the management of high-risk patients in primary care (see below).

Who to screen for kidney disease?

Targeted community screening in a high-risk population is effective in identifying persons with previously unidentified or poorly controlled kidney disease risk factors, as well as persons with renal impairment.⁶ Identification of patients with early kidney disease relies on blood and urine testing as patients with CKD may remain minimally symptomatic until renal function is severely and irreversibly impaired. Selective screening of these high-risk populations may be of value. This would include adult patients with vascular disease, diabetes, hypertension and immediate relatives of patients with diabetes, hypertension and renal disease. Patients with diabetes, vascular disease and hypertension have increased rates of renal

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disease in population studies.⁷ Smoking also increases the risk of nephropathy in patients with diabetes. Regularly checking the renal function in men with prostatic symptoms may prevent late uraemia.⁸ A family history of kidney disease has been associated with an increased risk of ESKD in excess of that predicted by clustering of diabetes and hypertension within families.⁹ Indigenous Australians also have increased rates of kidney disease. There are limited data to support the screening of aboriginal patients during periodic health examinations, particularly where there is a family history of renal or cardiovascular disease.¹⁰ In the paediatric population, early evaluation should include siblings of children with vesico-ureteric reflux and other hereditary kidney diseases. However, it should be noted that, apart from patients with insulin dependent diabetes^{11,12} or men with prostatism,⁸ there are no trials showing that screening specifically improves renal outcomes.

In indirect models looking at the benefits of screening for CKD in the Australian population, it was concluded that screening for proteinuria in middle-aged and older Australian adults would prevent ESKD and save health expenditure.¹³ For every 20 000 people screened, 1000 would test positive and 100 would need to be treated with angiotensin converting enzyme (ACE) inhibitors for about 2–3 years to prevent one case of ESKD, at best saving approximately \$70 000. Nonetheless, further studies are required to evaluate the balance of benefits and risks arising from screening for kidney disease in adult Australians.

What to screen for?

Screening for CKD should include both urinalysis and blood test estimations of kidney function. The newly adopted 'eGFR' automatically reported by clinical laboratories, is able to identify most individuals with a moderate to severe impairment in kidney function. Renal impairment as manifested by a rising serum creatinine concentration may be a late sign of kidney disease, implying significant nephron loss. Testing of creatinine alone may therefore miss early renal injury. Serum creatinine concentration in its own is also an inadequate marker of GFR. For example, in one recent study, 15% of patients with so-called normal serum creatinine concentration had abnormal renal function when GFR was calculated.⁶ Recommendations for the estimation of kidney function are detailed elsewhere in the CARI guidelines.

There is a strong correlation between urinary protein excretion and progression of CKD. Interventions that slow the progression of kidney disease appear to be most beneficial in patients with proteinuria. Therefore, identifying proteinuric patients with high risk of non-diabetic kidney disease progression should be a priority in management. Recommendations regarding the best method for detecting and quantifying proteinuria can also be found detailed in other CARI guidelines.

The detection of occult nephropathy (microalbuminuria) is also a key component for the prevention of ESKD in patients with diabetes. Recommendations for microal-

buminuria screening are found elsewhere in the CARI guidelines. While albuminuria may be a suitable test for general population screening for kidney and cardiovascular risk, it should not replace testing for proteinuria in those with known or suspected CKD.¹⁴

There is no good evidence that routine urine microscopy or screening for microscopic haematuria in individuals not known to have CKD, those without proteinuria, or those without impaired kidney function, facilitates prevention of ESKD. However, as urinalysis is cheap and may be conducted at the same time as estimation of urinary albumin/protein excretion, and incidental renal or urothelial malignancies may occasionally be discovered, it should not be discouraged.

BACKGROUND

Early diagnosis is the cornerstone for prevention of kidney failure, providing an opportunity offering the potential for both disease-specific and non-specific interventions to prevent or delay its progression and decrease morbidity and mortality. Many of the interventions to slow progressive kidney disease detailed in these guidelines are more efficacious the earlier they are initiated. Screening individuals at high risk for chronic kidney failure currently represents a key component step that health-care providers and public health practitioners can perform to reduce the incidence of ESKD. The objective of this specific guideline was to evaluate the available clinical evidence pertaining to the impact of screening for renal disease in preventing progressive renal impairment and ESKD. This guideline does not cover the broader utility to enhance awareness of the disease, and improve health-seeking behaviour.

SEARCH STRATEGY

Databases searched: MeSH terms and text words for CKD were combined with MeSH terms and text words for prostatectomy, lithotripsy, nephrolithectomy and urinary catheterization. The search was carried out in Medline (1966 to November Week 2, 2004).

Date of search: 11 November 2004.

WHAT IS THE EVIDENCE?

There have been no randomized controlled trials or meta-analyses.

SUMMARY OF THE EVIDENCE

There have been no randomized controlled trials or meta-analyses.

WHAT DO THE OTHER GUIDELINES SAY?

Kidney Disease Outcomes Quality Initiative: No recommendation.

UK Renal Association: Serum creatinine concentration should be measured, allowing calculation of estimated GFR, at initial assessment and then at least annually in all adult patients with:

- A. Previously diagnosed CKD, including
- Polycystic kidney disease
 - Reflux nephropathy
 - Biopsy-proven chronic glomerulonephritis
 - Persistent proteinuria
 - Urologically unexplained persistent haematuria
- B. Conditions associated with a high risk of obstructive nephropathy, including
- Known or suspected bladder outflow obstruction
 - Neurogenic bladder caused by spina bifida or spinal cord injury (NB: calculated GFR may overestimate true GFR in these patients because of decreased muscle mass)
 - Urinary diversion surgery
 - Urinary stone disease as a result of primary hyperoxaluria, cystinuria, Dent's disease, infections (with struvite stones), anatomical abnormalities, or a stone episode rate of greater than one per year
- C. Conditions known to be associated with a high risk of silent development of CKD, including
- Hypertension
 - Diabetes mellitus
 - Heart failure
 - Atherosclerotic coronary, cerebral or peripheral vascular disease
- D. Conditions requiring long-term treatment with potentially nephrotoxic drugs, including
- ACE inhibitor and angiotensin receptor blockers
 - Non-steroidal anti-inflammatory drug (NSAID)
 - Lithium carbonate
 - Mesalazine and other 5-aminosalicylic acid drugs
 - Calcineurin inhibitors (cyclosporin, tacrolimus)

Dipstick urinalysis for protein is indicated:

- A. As part of the initial assessment of patients with
- Newly discovered GFR < 60 mL/min per 1.73 m²
 - Newly discovered haematuria
 - Newly diagnosed hypertension
 - Unexplained oedema
 - Suspected heart failure
 - Suspected multisystem disease, e.g. systemic lupus erythematosus, systemic vasculitis
 - Diabetes mellitus
- B. As part of the annual monitoring of patients with
- Biopsy-proven glomerulonephritis
 - Reflux nephropathy
 - Asymptomatic microscopic haematuria
 - Asymptomatic proteinuria
 - Diabetes mellitus (patients with diabetes mellitus should also have annual testing for albumin: creatinine ratio if the dipstick urinalysis for protein is negative).

Monitoring for proteinuria is also required for patients receiving treatment with gold and penicillamine. Recommendations for frequency of monitoring are given in the British National Formulary: for penicillamine, before starting treatment and then every 1–2 weeks for the first 2 months, monthly thereafter, and in the week after any

dose increase; for intramuscular gold, before each intramuscular injection; for oral gold, monthly.

We do not recommend screening of any other groups using dipstick urinalysis.

All other patients with diabetes mellitus should undergo, as a minimum, annual testing for microalbuminuria.

Canadian Society of Nephrology: No recommendation.

European Best Practice Guidelines: No recommendation.

INTERNATIONAL GUIDELINES

US Preventive Services Task Force:⁴

No evidence to support the mass screening of the general population for renal disease by urine dipstick, blood sampling or other means.

Canadian Guide to Clinical Preventive Health Care:²

There is fair evidence to exclude urine dipstick screening for proteinuria from the periodic health examination of asymptomatic adults. There is good evidence to screen include urine dipstick screening for proteinuria in the periodic health examination of adults with diabetes mellitus.

NKF Kidney Early Evaluation Programme for High-Risk Patients:⁶

Early evaluation should be considered for patients with diabetes, hypertension, and immediate relatives of patients with diabetes, hypertension and renal disease (over 70% of patients screened had renal abnormalities).

British Hypertension Society Guidelines:¹⁵

All hypertensive patients should have routine investigations including

- Urine strip test for blood and protein
- Blood electrolytes and creatinine

Australia and New Zealand Society of Nephrology Consensus Statement:¹⁶

'A periodic health exam that includes urinalysis for proteinuria ± haematuria' should be available for Aboriginal and Torres Strait Islander patients.

IMPLEMENTATION AND AUDIT

Primary physicians should be encouraged to identify and screen patients at increased risk of kidney disease in conjunction with secondary or tertiary centres, which need to make referral services available.

SUGGESTIONS FOR FUTURE RESEARCH

Support should be given to studies of the efficacy of renal screening in high-risk groups.

CONFLICT OF INTEREST

Merlin Thomas has a Level II b conflict of interest according to the conflict of interest statement set down by CARI.

REFERENCES

1. Sesso R, Belasco AG. Late diagnosis of chronic renal failure and mortality on maintenance dialysis. *Nephrol. Dial. Transplant.* 1996; **11**: 2417–20.
2. Canadian Guide to Clinical Preventive Health Care. *Dipstick Proteinuria Screening of Asymptomatic Adults to Prevent Progressive Renal Disease*, Chapter 38. Ottawa, Canada: Health Canada, 1994.
3. Frame PS, Carlson SJ. A critical review of periodic health screening using scientific screening criteria. 3. Selected diseases of the genitourinary system. *J. Fam. Pract.* 1975; **2**: 189–94.
4. US Preventive Services Task Force. *A Guide to Preventive Health Services: An Assessment of the Effectiveness of 169 Interventions*. Baltimore, MD: Williams and Williams, 1989; 155–61.
5. Boulware LE, Jaar BG, Tarver-Carr ME *et al.* Screening for proteinuria in US adults: A cost-effectiveness analysis. *JAMA* 2003; **290**: 3101–14.
6. Brown WW, Collins A, Chen SC *et al.* Identification of persons at high risk for kidney disease via targeted screening: The NKF Kidney Early Evaluation Program. *Kidney Int. Suppl.* 2003; **83**: S50–55.
7. US Renal Data System (USRDS). 1999 annual data report National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. Bethesda, MD, April 1999.
8. Sacks SH, Aparicio SA, Bevan A *et al.* Late renal failure due to prostatic outflow obstruction: A preventable disease. *Br. Med. J.* 1989; **298**: 156–9.
9. Kissmeyer L, Kong C, Cohen J *et al.* Community nephrology: Audit of screening for renal insufficiency in a high risk population. *Nephrol. Dial. Transplant.* 1999; **14**: 2150–55.
10. Hoy W. Screening for renal disease and other chronic diseases in Aboriginal adults, and preliminary experience of a medical intervention program. *Nephrology* 1998; **4**: S90–95.
11. Kiberd BA, Jindal KK. Screening to prevent renal failure in insulin dependent diabetic patients: An economic evaluation. *BMJ* 1995; **311**: 1595–9.
12. Borch-Johnsen K, Wenzel H, Viberti GC *et al.* Is screening and intervention for microalbuminuria worthwhile in patients with insulin dependent diabetes? *BMJ* 1993; **306**: 1722–5.
13. Craig JC, Barratt A, Cumming R *et al.* Feasibility study of the early detection and treatment of renal disease by mass screening. *Intern. Med. J.* 2002; **32**: 6–14.
14. Atkins RC, Briganti EM, Zimmet PZ *et al.* Association between albuminuria and proteinuria in the general population: The AusDiab Study. *Nephrol. Dial. Transplant.* 2003; **18**: 2170–74.
15. Ramsay L, Williams B, Johnston G *et al.* Guidelines for management of hypertension: Report of the third working party of the British Hypertension Society. *J. Hum. Hypertens.* 1999; **13**: 569–92.
16. Thomas M. *Australia and New Zealand Society of Nephrology Consensus Statement Delivery of Nephrology Services to Remote Areas of Australia*. Sydney: Australian and New Zealand Society of Nephrology, 1999.

Out of date