

Proteinuria: detection and quantitation in adults using ACR – information for GPs

Proteinuria is an important indicator of underlying kidney disease and its presence is both a strong prognostic indicator of the likelihood of kidney disease progressing and an indicator of increased risk of subsequent cardiovascular event. Together with estimation or measurement of the glomerular filtration rate (GFR), urine protein measurement is required to diagnose, stage and monitor chronic kidney disease (CKD). The National Institute for Health and Clinical Excellence (NICE) has recommended that to detect proteinuria the urinary albumin:creatinine ratio (ACR) should be used in preference to other tests of proteinuria, including the protein:creatinine ratio (PCR), 24 hour urine collections for proteinuria and reagent strip ('dipstick') analyses. This information sheet details the main reasons underlying this decision and gives advice regarding its practical implementation.

Why has ACR been recommended in preference to PCR, 24 hour urine collections and reagent strip analysis?

- Studies have clearly demonstrated that measurement of either ACR or PCR in a spot urine sample accurately reflects 24 hour urinary albumin and protein, rendering 24 hour urine collections unnecessary for detection and quantification of protein in the urine.
- Albumin is the predominant protein in the vast majority of proteinuric kidney diseases, including diabetes, hypertension and glomerular diseases.
- Albumin measurement offers greater sensitivity, and improved precision, for the detection of lower, but clinically significant, levels of proteinuria compared to total protein.
- Albumin measurement can be standardised.
- Albumin measurement is already used to detect and quantify proteinuria in people with diabetes.
- International recommendations favour ACR in preference to PCR.
- In patients with established disease, there may occasionally be clinical reasons for a specialist subsequently to use PCR instead of ACR to quantify and monitor significant levels of proteinuria.
- Commonly used reagent strip devices are insufficiently sensitive for the reliable detection of proteinuria, do not adjust for urinary

concentration and are only semi-quantitative. Furthermore, there is no standardisation between manufacturers.

Who should be tested for proteinuria?

Testing for proteinuria should be offered to people if they have any of the following risk factors:

- a GFR less than 60 mL/min/1.73 m²
- diabetes
- hypertension
- cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease and cerebral vascular disease)
- structural renal tract disease, multiple renal calculi or prostatic hypertrophy
- multisystem diseases with potential kidney involvement – for example, systemic lupus erythematosus
- family history of stage 5 CKD or hereditary kidney disease
- opportunistic detection of haematuria.

What urine sample should be used for measurement of ACR or PCR?

- Albumin can be measured in random ('spot') urine samples: a timed urine collection is not necessary for this purpose.
- An early morning ('first pass') urine sample is ideal as the urine is most concentrated and thus the concentration of protein will be highest and more likely to be detected.
- Where this causes practical difficulties for service organisation a urine sample collected at other times during the day is an acceptable alternative.
- Urine samples should be sent to the laboratory for analysis on the day of collection.

What is a clinically significant ACR and what is the equivalent level of proteinuria?

- There is no constant numerical relationship between albumin and total protein concentrations in urine. At normal levels of protein loss, albumin is a minor component (approximately 10–20%) of total urinary protein. On average, when the total protein concentration is 1 g/L, approximately 70% of this will be accounted for by albumin.

- In people without diabetes consider clinically significant proteinuria to be present when the ACR is 30 mg/mmol or more (this is approximately equivalent to PCR 50 mg/mmol or more, or a urinary protein excretion 0.5 g/24 h or more).
- Heavy proteinuria should be considered present when the ACR is 70 mg/mmol or more (this is approximately equivalent to PCR 100 mg/mmol or more, or a urinary protein excretion 1 g/24 h or more).
- For the initial detection of proteinuria, if the ACR is 30 mg/mmol or more but less than 70 mg/mmol this should be confirmed by a subsequent early morning sample. If the initial ACR is 70 mg/mmol or more, or the PCR 100 mg/mmol or more, a repeat sample need not be tested.
- People with confirmed proteinuria (ACR 30 mg/mmol or more) should have the suffix (p) appended to their CKD staging.
- In people with diabetes consider microalbuminuria (ACR more than 2.5 mg/mmol in men and ACR more than 3.5 mg/mmol in women) to be clinically significant.
- False positives may occur for a variety of reasons, including benign orthostatic proteinuria, symptomatic urinary tract infections and menstrual contamination.

When should people with clinically significant levels of ACR be referred for specialist opinion?

- People with heavy proteinuria (ACR ≥ 70 mg/mmol, approximately equivalent to PCR ≥ 100 mg/mmol, or urinary protein excretion ≥ 1 g/24 h), unless this is known to be due to diabetes and already appropriately treated, should be referred for specialist opinion.
- People with proteinuria (ACR ≥ 30 mg/mmol, approximately equivalent to PCR ≥ 50 mg/mmol, or urinary protein excretion ≥ 0.5 g/24 h) together with haematuria should also be referred for specialist opinion.
- People with isolated proteinuria (ACR $\geq 30 < 70$ mg/mmol, approximately equivalent to PCR $\geq 50 < 100$ mg/mmol, or urinary protein excretion $\geq 0.5 < 1$ g/24 h) may not require referral provided their GFR is stable and their blood pressure is controlled (120–139/ < 90 mmHg).

When should ACR measurement be implemented as the first line test for proteinuria detection?

- NICE has recommended that to detect and identify proteinuria, ACR should be the preferred method but that for quantification and monitoring of proteinuria, PCR can be used as an alternative.
- Some laboratories already offer ACR as their primary test for proteinuria detection.
- Most NHS laboratories already use ACR as their primary test for the detection of diabetic nephropathy.
- It is recognised that full implementation of NICE recommendations may take place over a number of years. A costing template to enable an estimate of likely implementation costs to be made is available from the NICE website (www.nice.org.uk/usingguidance/implementationtools/costingtools/costing_tools_doc.jsp?o=42208).

Further information

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. September 2008, Clinical Guideline 73. Available from: www.nice.org.uk/Guidance/CG66

National Institute for Health and Clinical Excellence. Type 2 diabetes: The management of type 2 diabetes (update). May 2008, Clinical Guideline 66. Available from: www.nice.org.uk/Guidance/CG73



© Crown copyright 2009

293981 1p 40k Mar 09 (CWP)

Produced by COI for the Department of Health

If you require further copies of this title visit www.orderline.dh.gov.uk and quote:

293981/Proteinuria: detection and quantitation in adults using ACR – information for GPs or write to:

DH Publications Orderline

PO Box 777

London SE1 6XH

E-mail: dh@prolog.uk.com

Tel: 0300 123 1002

Fax: 01623 724 524

Minicom: 0300 123 1003 (8am to 6pm Monday to Friday)

www.dh.gov.uk/publications

Gateway reference number 11404