

## 4. Monitoring proteinuria in patients with suspected or known renal disease

*Date written:* February 2003

*Final submission:* June 2004

### Guidelines

No recommendations possible based on Level I or II evidence

### Suggestions for clinical care

(Suggestions are based on level III and IV sources)

- Timed urine collections are recommended when knowledge of absolute level of proteinuria is required.

### Background

There are some issues of concern when protein:creatinine ratio/albumin:creatinine ratio (PCR/ACR) is used to predict accurately the level of proteinuria, firstly with the statistical validity of these studies. Bland and Altman (1986) have demonstrated that correlation measures the strength of the linear association between tests and not the agreement between tests. This becomes increasingly relevant when the actual values are important such as commencing or monitoring response to therapy.

There are two studies that have assessed the agreement between tests rather than correlation. Mitchell et al (1993) found excellent correlation between adjusted PCR and 24 hr urine total protein (UTP,  $r = 0.98$ ,  $p < 0.0001$ ) but poor agreement. The 95% limits of agreement were between +69% and -43%. In spite of the discrepancy between the absolute value of PCR and the 24 hr UTP, adjusted PCR (adjusted for age, weight, gender) remained a fair discriminator of the relative degree of proteinuria and allowed correct broad classification between 81% at UTP < 150 mg/day and 90% at 1.0-3.5 g/day and 100% at > 3.5 g/day. Cundy et al (1992) assessed the agreement between ACR and 24 hr urine albumin excretion (UAE). Again, there was strong correlation between the methods ( $r = 0.94$ ) but the limits of agreement were wide and the coefficient of variation was 158%.

PCR/ACR are semi-quantitative tests that are useful for the broad categorisation of urine protein excretion.

The usefulness of random samples to monitor protein excretion over time is unclear. Rodby et al (1995) studied 33 patients who had paired 24 hr and random collections at least 3 months apart, and demonstrated significant discordance between samples in the direction of change. In 6 patients, the PCR increased while the 24 hr UTP

decreased while in 8 other patients, the reverse was true. Further studies to assess this are required.

## **Search strategy**

Databases searched: MeSH terms and text words for each index test type were combined with text words for the reference standard (ie timed urine collection for proteinuria and albuminuria). The search was carried out in Medline (1966 – January Week 1 2003).\* (Refer to Appendix 1).

Date of search/es: 21 January 2003.

## **What is the evidence?**

No randomised controlled trials were found on this topic.

## **Summary of the evidence**

Not possible.

## **What do the other guidelines say?**

### **Kidney Disease Outcomes Quality Initiative:**

Monitoring proteinuria in adults with chronic kidney disease, the protein-to-creatinine ratio in spot urine samples should be measured using:

- albumin-to-creatinine ratio
- total protein-to-creatinine ratio is acceptable if albumin-to-creatinine ratio is high (> 500 to 1000 mg/g).

## **Implementation and audit**

No recommendation.

## **Suggestions for future research**

No recommendation.

## **References**

Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 1(8476): 307-10.

Cundy TF, Nixon D, Berkahn L et al. Measuring the albumin excretion rate: agreement between methods and biological variability. *Diabet Med* 1992; 9(2):138-43.

Jaeschke R, Guyatt G, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid? Evidence-Based Medicine Working Group. *JAMA* 1994; 271(5): 389-91.

Mitchell SC, Sheldon TA, Shaw AB. Quantification of proteinuria: a re-evaluation of the protein/creatinine ratio for elderly subjects. *Age Ageing* 1993; 22(6): 443-49.

Rodby RA, Rohde RD, Sharon Z et al. The urine protein to creatinine ratio as a predictor of 24-hour urine protein excretion in type 1 diabetic patients with nephropathy. The Collaborative Study Group. *Am J Kidney Dis* 1995; 26(6): 904-09.

## Appendix – Search Strategy

Table 1 - PICOM Table

Question Type	Population / Clinical Problem	Intervention	Comparison	Outcome(s)	(M) Best feasible study design
Diagnosis	Patients with <ul style="list-style-type: none"> <li>vascular disease</li> <li>diabetes</li> <li>hypertension</li> <li>immediate relatives of patients with diabetes, hypertension or renal disease</li> <li>Aboriginal and Torres Strait Islanders (if inadequate data – general population)</li> </ul>	What is the test performance of <ul style="list-style-type: none"> <li>urine dipstick</li> <li>random urine</li> <li>timed collections eg. overnight</li> </ul> Sensitivity/specificity, negative and positive predictive values	Compared with 24 hr urine protein/albumin excretion	Measure of agreement between tests, correlation between tests	Systematic review, cross-sectional study

### Explanatory notes:

The draft CARI guideline ‘Prevention of progression of renal disease – Early detection of patients with renal disease’ suggests that “*the presence of proteinuria and renal impairment should be routinely assessed in patients at increased risk of renal failure including:*

- *patients with vascular disease, diabetes or hypertension*
- *immediate relatives of patients with diabetes, hypertension, or renal disease*
- *Aboriginal and Torres Strait Islanders*
- *patients complaining of prostatic symptoms (renal function most applicable)”*

It was considered appropriate that the search be confined to the same populations and be applied in two situations:

1. population screening/ diagnosis (sensitivity and specificity, positive and negative predictive values)
2. guide to disease management (eg. response to therapy) and progression.

## **Methods**

The search strategy outlined was used in Medline from 1966 to January 2003. Abstracts were screened by MG, S McT and NI and relevant papers obtained.

1. Reagent strips	(1909)
2. dipstick\$.tw	(894)
3. Nitrites/	(7753)
4. Esterases/	(9519)
5. nitrites.tw.	(982)
6. leucocyte esterase\$.tw	(53)
7. random urine\$.tw.	(295)
8. (urine and timed collection\$.tw.	(23)
9. timed urine collection\$.tw.	(103)
10. or/1-9	(20469)
11. ("24" or time\$ or hour\$.tw	(1377513)
12. 10 and 11	(2688)
13. Proteinuria/	(12666)
14. (proteinuria or urinary protein).tw.	(15281)
15. Albuminuria/	(5532)
16. (albuminuria or urinary albumin).tw.	(3794)
17. 13 and 14	(6613)
18. 15 and 16	(2520)
19. 12 and 17	(73)
20. 12 and 18	(53)
21. from 19 keep 1-73	(73)
22. from 20 keep 1-58	(58)

The reference lists of relevant articles and reviews were hand searched and relevant additional papers located.

The quality of the studies was assessed according to the methodology of \*Jaeschke et al (1994).

However, the quality of the data was generally poor and studies were included if they met the following criteria: (1) the studies investigated the use of dipstick, morning or random urine for investigation of proteinuria or albuminuria, (2) the comparator was a 24 hour urine protein or overnight timed collection, and (3) test performance could be determined from the study. Studies were included from both hospital and ambulatory settings. Only English language (or abstract) papers were included. We did not seek unpublished data.