Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

1. Inform discussions on new topics received by HTW.
2. Determine the quantity and type of evidence available on a topic.
3. Assess the topic against HTW selection criteria.

Topic:	Albumin:creatinine ratio (ACR)) testing compared to protein:creatinine ratio (PCR) testing for the detection of proteinuria in patients with hypertension and/or chronic kidney disease
Topic exploration report number	TER005
Referrer:	Dr Soha Zouwail, Consultant Chemical Pathologist, Cardiff and Vale University Health Board
Topic exploration undertaken by:	Health Technology Wales

Aim of Search

Health Technology Wales researchers searched for evidence on the clinical and cost effectiveness of ACR testing compared to PCR testing in the assessment and/or identification of proteinuria in people with chronic kidney disease or primary hypertension.

Initially, a high-level search for any evidence regarding ACR testing in the assessment of chronic kidney disease and/or hypertension was carried out, focussing on relevant secondary evidence (systematic reviews, technology assessments, evidence-based guidelines). Following discussion with the topic proposer and HTW's Assessment Group, we searched the Medline, Embase and Cochrane databases for any evidence published in the last ten years that directly compared outcomes in people tested with ACR or PCR, or the use of ACR or PCR as predictors of patient outcomes.

Summary of Findings

The high-level search identified guidelines from NICE (CG182 and CG127), SIGN (116) and KDIGO that make recommendations about how proteinuria should be assessed in people with hypertension or CKD.

In the absence of clinical evidence directly comparing PCR with ACR, a recommendation was made in NICE CG182 based on the consensus of the guideline committee. The recommendation states that urine ACR is preferred over protein:creatinine ratio (PCR) to detect and identify proteinuria, although PCR can be used as an alternative to ACR for quantification and monitoring of levels of proteinuria of ACR 70 mg/mmol or more. ACR is recommended for people with diabetes (recommendation 1.1.18). SIGN 116 states that ACR should be used to screen for diabetic kidney disease (section 9.3.2 p86), while NICE CG127 states that ACR should be offered to screen for protein in the urine for patients with chronic kidney disease or hypertension (recommendation 1.3.3 p13). The KDIGO Clinical Practice Guideline for

the Management of Blood Pressure in Chronic Kidney Disease does not specifically recommend one test over the other. Other sources of evidence identified by this search are summarised in Table 1.

HTW conducted a further search for any evidence published in the last ten years that directly compared outcomes in people tested with ACR or PCR, or the use of ACR or PCR as predictors of patient outcomes. The criteria used for this search, and the evidence identified by the search, are presented in Table 2.

HTW identified five studies that directly compared ACR and PCR as a test to assess CKD. Two studies assessed the same cohort of patients (included population: people with CKD and proteinuria). The remaining studies considered different populations. One study included people with chronic renal insufficiency (mild to severe CKD), one study assessed people with CKD and kidney transplant patients, and one study included only people with IgA nephropathy. Four studies assessed ACR and PCR by using both tests to predict proteinuria at baseline, and then comparing these findings with long-term clinical outcomes. Outcomes measured varied between studies, but included all-cause mortality and kidney disease progression. Patients were followed up for between 3.5 and 5 years. Three out of four studies found no significant difference in clinical outcomes between cases of proteinuria identified using ACR or PCR. One study tested all patients with ACR and PCR, and assessed outcomes in those with concordant and discordant results between the two tests. In cases where PCR detected proteinuria but ACR did not, patients had high renal risk and high renal mortality, inferring that ACR would have failed to detect some 'at risk' patients whose proteinuria was detected by PCR.

A further study examined the association of ACR and PCR with biochemical measures of CKD complications. The associations of ACR and PCR with each measure of CKD complications were comparable.

We did not identify any relevant published health economic studies that considered the cost effectiveness of ACR compared with PCR in people with CKD and/or hypertension. A recent health economic evaluation from the UK NHS perspective which compared ACR with PCR in a different patient population (pregnant women with hypertension and suspected proteinuria). This study reported the unit costs of each test within East Kent Hospitals University NHS Foundation Trust. Unit costs were reported as £0.70 and £2.71 per test for PCR and ACR, respectively.

Conclusions

Evidence from studies directly comparing ACR and PCR suggests that patients in whom proteinuria is detected by either test have similar clinical outcomes. There is insufficient evidence to suggest that either test leads to superior clinical outcomes when used for the identification and assessment of proteinuria in people with CKD or hypertension.

We did not identify any published evidence on the comparative cost effectiveness of ACR and PCR in people with CKD and/or hypertension.

Areas of Uncertainty

The evidence identified focusses on the effect of ACR and PCR testing on clinical outcomes in the population of interest. We did not search for recent studies on diagnostic accuracy; some studies of this type have been summarised in previous NICE guidelines, but the relationship between the diagnostic accuracy of each test and long term clinical outcomes remains unclear.

No detailed analyses of the cost effectiveness of ACR compared with PCR in people with CKD and/or hypertension has been published. Reported unit costs are higher for ACR than for PCR, but exact costs are likely to vary locally.

Feasibility of Technology Assessment

HTW's Assessment Group concluded not to progress this topic further on the basis of inconclusive evidence and the uncertainties summarised above.

Literature search results

Initially, a high-level search for any evidence regarding ACR testing in the assessment of chronic kidney disease and/or hypertension was carried out, focussing on relevant secondary evidence (systematic reviews, technology assessments, evidence-based guidelines). The findings of this search are summarised in Table 1.

Table 1. Result of a high-level search for any evidence regarding ACR testing in the assessment of chronic kidney disease and/or hypertension

Resource	Results
UK guidelines and guidance	
SIGN	SIGN116 - Management of diabetes https://www.sign.ac.uk/sign-116-and-154-diabetes.html
NICE	CG127 -Hypertension in adults: diagnosis and management https://www.nice.org.uk/guidance/cg127/chapter/1-Guidance CG182 - Chronic kidney disease in adults: assessment and management https://www.nice.org.uk/guidance/cg182
Other guidelines and guidance	
Kidney International	KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease 2012 https://kdigo.org/guidelines/blood-pressure-in-ckd/
Secondary literature and economic evaluations	
Cochrane library	We did not identify any relevant secondary research about the use of ACR or PCR in assessing proteinuria in the population of interest.
Medline	Waugh, J., et al. (2017). "Spot protein-creatinine ratio and spot albumin-creatinine ratio in the assessment of pre-eclampsia: a diagnostic accuracy study with decision-analytic model-based economic evaluation and acceptability analysis." Health Technology Assessment (Winchester, England) **21**(61): 1-90. Wang, H., et al. (2017). "Strategies and cost-effectiveness evaluation of persistent albuminuria screening among high-risk population of chronic kidney disease." BMC Nephrology **18**(1): 135.
Ongoing research	
PROSPERO database	We did not identify any relevant ongoing research about the use of ACR or PCR in assessing proteinuria in the population of interest.
Clinicaltrials.gov	We did not identify any relevant ongoing research about the use of ACR or PCR in assessing proteinuria in the population of interest.

Date of search:	**September 2018**
Concepts used:	hypertension; albumin creatinine ratio, protein creatinine ratio (and related synonyms)

Table 2. Search criteria for studies directly comparing ACR and PCR and evidence identified by the search

	Included	Excluded
Population	People with CKD or hypertension at risk of kidney damage who require proteinuria testing	People with diabetes at risk of CKD, pregnancy, children (<18 years), people with secondary hypertension
Intervention	Urine ACR	
Comparison/ comparators	Urine PCR	
Outcomes	CKD progression, measured by: change in eGFR occurrence of end stage kidney disease acute kidney injury initiation of renal replacement therapy All-cause mortality Cardiovascular mortality	Diagnostic accuracy outcomes
Study design	Randomised or non-randomised trials Studies or models of cost and clinical effectiveness	Studies that only report diagnostic accuracy
Search results: studies identified that meet the criteria above		
Fisher, H., Hsu, C. Y., Vittinghoff, E., Lin, F., & Bansal, N. (2013). Comparison of associations of urine protein-creatinine ratio versus albumin-creatinine ratio with complications of CKD: a cross-sectional analysis. American Journal of Kidney Diseases, 62(6), 1102-1108. doi:https://dx.doi.org/10.1053/j.ajkd.2013.07.013 Methven, S., MacGregor, M. S., Traynor, J. P., Hair, M., O'Reilly, D. S., & Deighan, C. J. (2011). Comparison of urinary albumin and urinary total protein as predictors of patient outcomes in CKD. American Journal of Kidney Diseases, 57(1), 21-28. doi:https://dx.doi.org/10.1053/j.ajkd.2010.08.009 Methven, S., Traynor, J. P., Hair, M. D., St, J. O. R. D., Deighan, C. J., & MacGregor, M. S. (2011). Stratifying risk in chronic kidney disease: an observational study of UK guidelines for measuring total proteinuria and albuminuria. Qjm, 104(8), 663-670. doi:https://dx.doi.org/10.1093/qjmed/hcr026 Ying, T., Clayton, P., Naresh, C., & Chadban, S. (2018). Predictive value of spot versus 24-hour measures of proteinuria for death, end-stage kidney disease or chronic kidney disease progression. BMC Nephrology, 19(1), 55. doi:https://dx.doi.org/10.1186/s12882-018-0853-1 Zhao, Y. F., Zhu, L., Liu, L. J., Shi, S. F., Lv, J. C., & Zhang, H. (2016). Measures of Urinary Protein and Albumin in the Prediction of Progression of IgA Nephropathy. Clinical Journal of The American Society of Nephrology: CJASN, 11(6), 947-955. doi:https://dx.doi.org/10.2215/CJN.10150915		

Date of search:	November 2018
Other criteria applied:	We excluded any evidence published before 2008.