The assessment of kidney function by general practitioners in Australian patients with type 2 diabetes (NEFRON-2)

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ABSTRACT

Objective: To examine factors influencing the identification of kidney impairment in patients with type 2 diabetes in Australian primary care.

Design, setting and participants: 348 general practitioner investigators were asked to estimate kidney function and its severity in 10–15 consecutively presenting patients with type 2 diabetes ($n = 3893$). They were then asked, for each patient, whether they routinely estimated kidney function. No instruction was provided on how kidney function should be estimated or categorised. Data were collected between April and September 2005.

Main outcome measures: Kidney function estimated by the Cockcroft–Gault equation using clinical and laboratory data provided by the GP; estimates of kidney function made by the GP.

Results: In 24% of the patients with type 2 diabetes, their GP routinely estimated kidney function. However, few of these patients had impaired kidney function or risk factors for kidney disease. There was a good statistical correlation between the estimates made by GPs and the data-derived estimates ($R^2 = 0.72$). GPs identified patients with data-derived estimates of kidney function < 60 mL/min in over 83% of cases, with a specificity of 90%. Impaired kidney function was reported by GPs in 34.4% of men and 36.4% of women. These figures were discordant with function categorisation using both GP estimates and data-derived values, overlapping in half of the patients. Despite GPs' ability to assess creatinine clearance, "raw" (unstandardised) serum creatinine levels inappropriately influenced the perception of impairment of kidney function.

Conclusion: GPs can accurately assess kidney function, without reporting of estimated glomerular filtration rate (eGFR). However, even in patients at increased risk of chronic kidney disease, routine estimates are seldom made. Our findings underline the value of the recent initiative recommending automatic reporting of eGFR in Australia.

MJA 2006; 185: 259–262

Diabetes is the leading cause of chronic kidney disease (CKD) in Australia.[1] Despite this, CKD frequently remains undetected in individuals with type 2 diabetes. Much depends on the general practitioner's interpretation of routine biochemical tests to determine appropriate risk stratification.[2] Recently, a working group representing the peak bodies of Australian nephrology, pathology and biochemistry, plus Kidney Health Australia (KHA) proposed that an estimated glomerular filtration rate (eGFR) be automatically calculated by the clinical laboratory whenever a serum creatinine measurement is requested.[3]

In this article, we report the frequency of assessment of kidney function before this initiative. In addition, we demonstrate the ability of GPs to estimate their patients' kidney function from laboratory data and to classify kidney function from these estimates, without automatic reporting.

METHODS

Subjects

The National Evaluation of the Frequency of Renal Impairment cO-existing with Non-insulin dependent diabetes mellitus (NEFRON) study was an incident-driven, clinic-based clustered and stratified survey of patients with type 2 diabetes in Australian primary care.[4] Investigator selection and representation of Australian general practice is described elsewhere.[4] In brief, expressions of interest were invited from all registered GPs across Australia, and investigators were then randomly selected ($n = 500$) proportional to the census population.[5] The selected NEFRON investigators were requested to recruit 10–15 consecutively presenting adult patients with type 2 diabetes, irrespective of the reason for the consultation.

Patient assessment

Data collection took place between April and September 2005. A de-identified case report form was completed for each eligible patient. Case report forms captured demographic information, results of physical examination and the most recent laboratory test results, including serum creatinine level and urinary albumin to creatinine ratio.[6,7] At the time of the study, most GPs had access to resources that enabled the estimation of kidney function using the formula proposed by Cockcroft and Gault. This formula incorporates measures of serum creatinine, age, sex and weight to estimate creatinine clearance.[8] Consequently, for the purposes of our study, creatinine clearance for each patient was also estimated using the Cockcroft–Gault formula from data recorded in the case report forms. No attempt was made to standardise results from different laboratories or regions, but rather to reflect the "raw" (unstandardised) results on which practitioners currently base their assessment and management.

Practitioner assessment of kidney function

On the same case report forms for each patient, GPs were asked whether they routinely estimated kidney function or whether their clinical laboratory provided an estimation of kidney function. On the basis of each patient's current status, GPs were asked to state whether kidney function was impaired. Finally, GPs were also requested to provide their best estimate of their patients' kidney function in mL/min. To reflect resources available to GPs, no instruction was provided on how kidney function should be estimated or defined.

Ethical approval

The Royal Australian College of General Practitioners (RACGP) National Research and Evaluation Ethics Committee gave approval for the study. All participating patients provided written informed consent to take part in the study.

Data handling and statistical methods

Subanalyses for nominal variables consisted of either one-way analysis of variance (ANOVA) for single variables or two-way ANOVA for comparison of three groups.

Subanalyses for categorical variables involved Pearson χ^2 analysis of proportions between independent parameters. Because of incomplete data recording, different patient numbers are presented for different endpoints. Missing variables were not imputed. The predictive association between patients' variables and the perception of impaired kidney function by their GP was assessed by the area under the receiver operating characteristic curve (ROC curve) using SAS software, version 9.1 (SAS Institute Inc, Cary, NC, USA).

RESULTS

Data and informed consent were obtained for 3893 adults with type 2 diabetes. The clinical characteristics of these patients have been described previously.[4] Data were submitted by 348 GPs.

Estimation of kidney function by laboratories

At the time of this survey, an estimation of kidney function was provided by the local laboratory for 2.4% of patients ($n = 92/3783$). The mean creatinine clearance in these patients was similar to that in patients whose kidney function was not reported by a laboratory (77 v 78 mL/min). Seventy-two per cent of the results estimated by laboratories were above 60 mL/min, a level at which the accuracy of predictions of kidney function are suboptimal and thus not currently recommended.[3]

Routine estimation of kidney function by general practitioners

At the time of this survey, one in four patients (24.0%, $n = 904/3766$) with type 2 diabetes had their kidney function routinely estimated by their GP. The clinical characteristics of these patients are detailed in Box 1. The likelihood of patients having their kidney function estimated by their GP was not influenced by the patient's age, sex, or duration of diabetes (Box 1), although these are all key risk factors for impaired kidney function.[4] Patients with a urinary albumin to creatinine ratio in the macroalbuminuric range were marginally more likely to have routine estimation of their kidney function ($P < 0.01$) by their GP; however, only 30% of patients with a urinary albumin to creatinine ratio in the macroalbuminuric range had their kidney function routinely estimated by their GP. Patients receiving metformin or sulfonylureas with active metabolites were as likely as patients not receiving these medications to have their kidney function routinely estimated by their GP (24% and 26%, respectively), despite the risk of side effects of these drugs in patients with impaired kidney function.

1 The clinical characteristics of patients with type 2 diabetes in whom kidney function was, or was not, routinely estimated

Patient parameters	Kidney function routinely estimated ($n = 904$)	Kidney function not routinely estimated ($n = 2862$)
GP-estimated kidney function* (mL/min), mean (SEM)	85 (1)	86 (1)
Data-derived kidney function† (mL/min), mean (SEM)	89 (1)	91 (1)
Impaired kidney function* (%)	46%	34%‡
Age (years), mean (SEM)	65 (1)	66 (1)
Sex (percentage male)	51%	52%
European ethnicity* (%)	76%	84%‡
Duration of diabetes (years), mean (SEM)	8.1 (0.2)	8.1 (0.1)
Obesity (%)	23%	23%
Hypertension* (%)	72%	70%
Blood pressure (mmHg)	132/76	134‡/77
Haemoglobin A_{1c} (%), mean (SEM)	7.4% (0.1%)	7.3% (0.1%)
Fasting plasma glucose (mmol/L), mean (SEM)	8.1 (0.1)	7.9 (0.1)
Treatment with metformin (%)	63%	63%
Treatment with glimepiride or glibenclamide (%)	13%	10%
Normoalbuminuria (%)	62%	66%‡
Microalbuminuria (%)	29%	27%
Macroalbuminuria (%)	9%	7%‡
Retinopathy* (%)	11%	9%‡

* As perceived by the general practitioner. † Derived from case report form data using the Cockcroft–Gault formula. ‡ Difference between the two groups significant at $P < 0.05$. ◆

The accuracy of kidney function estimation by general practitioners

An estimation of kidney function was recorded by GPs in 85% of patients ($n = 3347/3893$). There was a good statistical correlation between practitioner-estimated values and those derived from data on case report forms (R^2, 0.72), even in patients in whom kidney function was not routinely estimated (R^2, 0.70). This meant that, when prompted, practitioners were able to identify individuals with a creatinine clearance < 60 mL/min in over 83% of cases, with a specificity of 90%.

Identification of impaired kidney function by general practitioners

Practitioners were also invited to record whether, on the basis of current results, their patients had impaired kidney function (99%, $n = 3868/3893$). Impaired kidney function was reported to be present in 34.4% of men and 36.4% of women ($P = 0.2$). These figures do not accord with kidney function estimations derived from data on the case report forms using the Cockcroft–Gault formula (Box 2A), or with the level of kidney function estimated by the GPs themselves (Box 2B). In about half of all individuals categorised by GPs as having impaired kidney function, kidney function estimates using the Cockcroft–Gault formula (52%) or by the GPs themselves (49%) were < 60 mL/min.

When kidney function was recorded by GPs as < 60 mL/min, impaired kidney function was perceived to be present in 74% of patients. Those patients in whom GPs estimated kidney function at < 60 mL/min, but in whom impaired kidney function was not perceived to be present (Box 2), were less likely to have an elevated urinary albumin to creatinine ratio (30%), compared with those in whom impaired kidney function was considered to be present (63%, $P < 0.01$). A documented history of CKD, macrovascular disease or hypertension was also less common in these individuals (all $P < 0.01$). The presence of impaired kidney function as perceived by the GP made it marginally more

likely that kidney function would be routinely estimated (30% v 23%, $P < 0.01$).

Impaired kidney function and serum creatinine level

In the NEFRON study, men and women with creatinine levels over 120 μmol/L and 110 μmol/L, respectively, were perceived by their GP to have impaired kidney function in 95% of cases (Box 2C). Indeed, in determining the perception of impaired kidney function, the raw (unstandardised) creatinine level was as strong a determinant as creatinine clearance estimated by the GP (area under the ROC curve, 0.82 v 0.81, $P = 0.9$). Serum creatinine levels were also more likely to be above these levels in male and female patients correctly perceived as having impaired kidney function (50%) than in those in whom GP-estimated kidney function — < 60 mL/min — was not seen as commensurate with impaired kidney function (19%, $P < 0.001$). However, the value of the serum creatinine level in distinguishing normal from abnormal function in individual patients is problematic, as individuals with a serum creatinine level in the normal range may have abnormal creatinine clearance. Indeed, in the NEFRON study, 55.6% of all those with a creatinine clearance < 60 mL/min had a serum creatinine level < 120 μmol/L in men or < 110 μmol/L in women (Box 3).

DISCUSSION

Estimation of kidney function is an important component in the multifactorial care of patients with type 2 diabetes. The NEFRON study shows that, when prompted to do so, most GPs are able to accurately estimate kidney function in their patients and to identify impaired function in over 70% of patients. However, at the time of this survey, fewer than one in four patients with type 2 diabetes had their kidney function routinely estimated by their GP. Moreover, few of the patients whose kidney function was estimated were at risk of impaired kidney function or its consequences (Box 1). Nor did the acknowledged presence of impaired kidney function appear to influence the likelihood of creatinine clearance being routinely estimated by their GP. Yet, it is precisely these patients who are most at risk of adverse outcomes[9-13] and in whom estimation of kidney function may be most important.

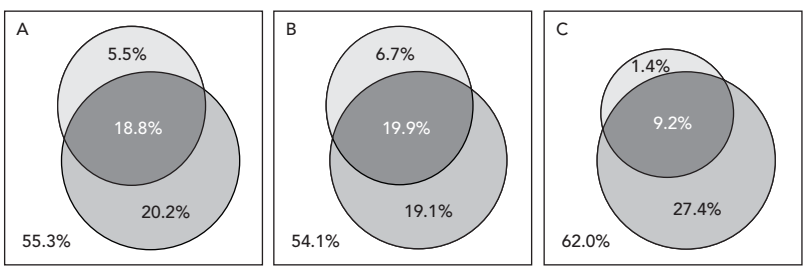
The principal aim of the NEFRON study was to identify management issues during any consultation between an individual with type 2 diabetes and their GP. As a clinic-based incident-driven study, it has a number of limitations. The study sample is biased towards patients who regularly attend their GP, and the findings depend on the non-standardised results on which GPs base their management. While this focus may be relevant to GPs, extrapolation to a wider community of patients with type 2 diabetes is inappropriate. Although every effort was made to ensure a representative distribution of general practices,[4] selection bias in relation to participating investigators and enrolled patients cannot be ruled out.

At the time of this study, most GPs would have had access to resources to estimate creatinine clearance (eg, prescribing software). This is supported by the good correlation observed between creatinine clearance estimated from data on the case report forms and GPs' estimates. Indeed, patients with a creatinine clearance < 60 mL/min were, in most cases, identified with the aid of resources then available to GPs when the GPs were specifically prompted to do so as part of our study. Consequently, the need for the currently proposed initiative for laboratories to routinely report eGFR[3] is not because GPs are not able to estimate kidney function — they can manage perfectly well — but rather because they have not always felt the need to do so.

Kidney function should be measured at least annually in patients with diabetes;[14] yet, at the time of this survey, no Australian guidelines recommended the routine estimation of kidney function in patients with diabetes. In addition, Health Insurance Commission Service Incentive Payments to GPs, based on a minimum cycle of care, did not include the estimation of GFR. Plans to amend the content of the *Diabetes management in general practice* guidelines[15] to include the routine estimation of kidney function in "diabetes patient record forms", would seem an important early step to improve the uptake of screening for CKD in patients with diabetes in Australian general practice.

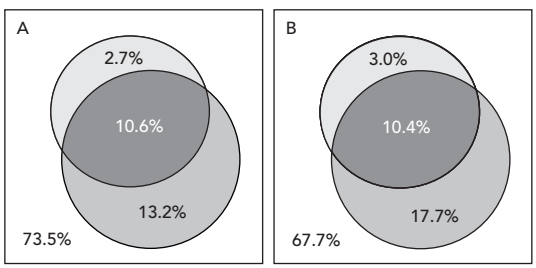
Despite GPs' ability to estimate creatinine clearance in most patients, the raw (unstandardised) creatinine level was an equally strong determinant of GP-perceived impaired kidney function. This means that the important contributions of age, sex and body mass to the assessment of kidney function were seldom considered. Furthermore, over half of the patients in the NEFRON study with a creatinine clearance

2 Venn diagrams showing the proportion of patients perceived as having impaired kidney function by their general practitioner (lower circle) and the proportion with a creatinine clearance of < 60 mL/min estimated by the Cockcroft–Gault formula (upper circle, A) or by the GP (upper circle, B), or by elevated serum creatinine levels (upper circle, C), and the overlap of these groups (central dark area)



The unshaded area denotes all patients without either characteristic.

3 Venn diagrams showing the proportion of patients with elevated serum creatinine levels (upper circle) and the proportion with a creatinine clearance of < 60 mL/min estimated by the Cockcroft–Gault formula (lower circle, A) or by the GP (lower circle, B), and the overlap of these groups (central dark area)



The unshaded area denotes all patients without either characteristic.

< 60 mL/min had a serum creatinine level in the normal range. This over-reliance on creatinine levels significantly contributed to the disparity between patients perceived as having impaired kidney function and those estimated by their GP to have a creatinine clearance < 60 mL/min (Box 3). The proposed automatic reporting of eGFR[3] can be expected to reduce this unreliable focus on serum creatinine levels.

The impact of automatic reporting of eGFR in primary care in Australia[3] remains to be established. Critical to its success will be education to ensure appropriate screening and management of CKD, focusing on the significance of impaired kidney function in the care of patients with type 2 diabetes and the opportunity for early intervention. While the ability of GPs to identify impaired kidney function was not linked to hard outcomes (eg, mortality) in this cross-sectional study, early identification and interventions can help prevent or delay the progression of kidney disease and decrease morbidity and mortality in patients with diabetes.[9,16-18]

ACKNOWLEDGEMENTS

This study was made possible by the generous help of 348 GP investigators from around Australia.

The study was jointly supported by the Baker Heart Research Institute, Kidney Health Australia and Servier Australia.

Merlin Thomas is supported by a National Health and Medical Research Council – Diabetes Australia Research Trust Partnership Career Development Award.

COMPETING INTERESTS

The NEFRON study was conducted as a collaboration between the Baker Heart Research Institute, Kidney Health Australia and the pharmaceutical company, Servier Australia. It was unconditionally funded by Servier Australia. All groups had an equal role in the study design, writing of the article and the subsequent decision to submit for publication. Data and project management services were provided by Quintiles Ltd (Australia) and statistical services by Statistical Revelations, Australia.

Andrew Weekes and Olivia Broadley are employed by Servier Australia as Medical Affairs Manager and Associate Project Manager, respectively.

Data interpretation was primarily the responsibility of Merlin Thomas, who received an honorarium of $15 000 for his role in study design, analysis and interpretation, and writing of this article.

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REFERENCES

1 ANZDATA Registry. 26th report. Adelaide: Australia and New Zealand Dialysis and Transplant Registry, 2003.
2 Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Ann Intern Med* 2003; 139: 137-147.
3 Mathew TH. Chronic kidney disease and automatic reporting of estimated glomerular filtration rate: a position statement. *Med J Aust* 2005; 183: 138-141.
4 Thomas MC, Weekes AJ, Broadley OJ, et al. The burden of chronic kidney disease in Australian patients with type 2 diabetes (the NEFRON study). *Med J Aust* 2006; 185: 140-144.
5 Australian Bureau of Statistics. Census of population and housing: selected characteristics for urban centres and localities, 2001. Canberra: ABS, 2003. (Catalogue No. 2016.)
6 Atkins RC, Polkinghorne KR, Briganti EM, et al. Prevalence of albuminuria in Australia: the AusDiab Kidney Study. *Kidney Int Suppl* 2004; 92: S22-S24.
7 International Diabetes Federation Clinical Guidelines Task Force. Global guideline for type 2 diabetes. Brussels: IDF, 2005.
8 Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; 16: 31-41.
9 Corsonello A, Pedone C, Corica F, et al. Concealed renal failure and adverse drug reactions in older patients with type 2 diabetes mellitus. *J Gerontol A Biol Sci Med Sci* 2005; 60: 1147-1151.
10 Keith DS, Nichols GA, Gullion CM, et al. Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. *Arch Intern Med* 2004; 164: 659-663.
11 Srivastava PM, Thomas MC, Calafiore P, et al. Diastolic dysfunction is associated with anaemia in patients with Type II diabetes. *Clin Sci (Lond)* 2006; 110: 109-116.
12 Perazella MA, Khan S. Increased mortality in chronic kidney disease: a call to action. *Am J Med Sci* 2006; 331: 150-153.
13 Jawa A, Kcomt J, Fonseca VA. Diabetic nephropathy and retinopathy. *Med Clin North Am* 2004; 88: 1001-1036, xi.
14 Summary of revisions for the 2006 Clinical Practice Recommendations. *Diabetes Care* 2006; 29 Suppl 1: S3.
15 Royal Australian College of General Practitioners. Diabetes management in general practice. 11th ed. Diabetes Australia Publication NP 1055. Sydney: Diabetes Australia, 2005. http://www.racgp.org.au/guidelines/diabetes (accessed Aug 2006).
16 Levin A. Identification of patients and risk factors in chronic kidney disease — evaluating risk factors and therapeutic strategies. *Nephrol Dial Transplant* 2001; 16 Suppl 7: 57-60.
17 Snyder S, Pendergraph B. Detection and evaluation of chronic kidney disease. *Am Fam Physician* 2005; 72: 1723-1732.
18 Thomas MC, Cooper ME. Facing the music: managing kidney disease in diabetes. *Australas J Gen Pract* 2005; 5: 1-5.

(Received 27 Feb 2006, accepted 11 Jul 2006) ❑