Centre variation in incidence, indication and diagnosis of adult native renal biopsy in Scotland

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Abstract

Background. UK native renal biopsy incidence is unknown. Biopsy registries in other countries indicate that the incidence of renal biopsy varies widely. Indications for renal biopsy are largely opinion based.

Methods. The Scottish Renal Biopsy Registry aimed to analyse the incidence of native renal biopsy in Scotland and examine indications and diagnoses obtained where practice varied widely.

Results. Consecutive native adult renal biopsies performed in eight of the nine Scottish regions that include 82.4% of the population between 2002 and 2006 were examined. A total of 2480 native renal biopsies were performed equating 126.3 biopsies per million population per year (PMP/year). A total of 56.9% of patients were male, mean age 55.6 years (SD 1.3). The centres varied widely, from a lowest mean annual incidence of 65.8 PMP/year in Fife to the highest of 170.7 PMP/year in Tayside. The prospectively recorded indications and diagnoses were compared between Greater Glasgow, Clyde and Forth Valley (GC&FV) (population 1.56 million, 101.6 biopsies PMP/year) and Tayside (population 0.39 million, 177.4 biopsies PMP/year). Differing incidence of renal biopsy in these regions was mainly explained by patients with proteinuria and preserved renal function in the absence of nephrotic syndrome (19.2 PMP/year in GC&FV versus 60.8 PMP/year in Tayside), probably due to variation in nephrologists’ opinion about the utility of biopsy for this indication. Tayside diagnosed more primary glomerulopathies, diabetic nephropathy and chronic ischaemia than GC&FV.

Conclusions. We have demonstrated wide regional variability in incidence of native renal biopsy within a single country, with analysis suggesting that this is mainly explained by uncertainty about the utility of renal biopsy for patients with proteinuria and preserved renal function.

Further studies are required to determine the value of renal biopsy in this setting.

Keywords: epidemiology; glomerulonephritis; kidney biopsy; proteinuria; registry

Introduction

Native renal biopsy is the definitive diagnostic test in patients with renal parenchymal disease. However, few studies have addressed the utility of renal biopsy, and accepted that indications for renal biopsy are largely opinion based [1]. Changes in the understanding of the epidemiology and treatment of renal parenchymal disease, as well as advances in the safety of the technique [2], are likely to have changed renal biopsy practice. The incidence of native renal biopsy in the UK is unknown. Evidence from biopsy registries indicates that the incidence of renal biopsy in other countries varies widely [3–13].

The Scottish Renal Biopsy Registry was set up in 2004 to improve the understanding of the utility of renal biopsy and as a framework for research into renal parenchymal disease [22]. The aim of the present study was to analyse the incidence of native renal biopsy in each renal unit and to compare the indications and histological diagnoses in the centres with low and high incidence.

Subjects and methods

We obtained data on all consecutive adult (patient ≥16 year) native renal biopsies performed in eight of the nine Scottish regions, each of which is served by one renal unit and its accompanying satellite services. Data were collected via the regional renal pathologist for 5 years between 2002 and 2006 inclusive, and population estimates were taken from the most recent government census [14]. The eight centres were Lanarkshire (population 552 819); Ayrshire...
and Arran (A&A) (368 149); Dumfries and Galloway (D&G) (147 765); Tayside (389 012); Greater Glasgow & Clyde and Forth Valley (GC&FV) (1 564 504); Grampian (525 850); Fife (349 690) and Highland (250 100).

Together these renal units serve a population of 4.15 million people, 82.4% of the Scottish population [14]. From these data, we calculated the incidence of native renal biopsy per million population (PMP). One region (Lothian) was unable to provide data.

**Comparison of indications and diagnoses in Greater GC&FV and Tayside**

The indication for biopsy has been recorded prospectively in the electronic patient record (EPR) at the time of biopsy using pre-defined categories in both the GC&FV and Tayside centres since 2003. Therefore, the biopsy indication for these two centres for a 3-year period between 2003 and 2006 was compared, along with the histological diagnoses retrieved from the EPR. Indications were classified as ‘acute renal failure’, ‘nephrotic syndrome’, ‘mild proteinuria (≤1 g/24 h) with normal renal function ± microscopic haematuria’, ‘moderate-to-severe proteinuria (>1 g/24 h) with normal renal function ± microscopic haematuria; not nephrotic syndrome’, ‘chronically reduced function, not nephrotic syndrome’ and ‘others’.

Diagnoses were classified as ‘glomerulonephritis’ (including Henoch-Schonlein purpura), ‘vasculitis’, ‘systemic lupus erythematosis’, ‘interstitial nephropathy’ (including chronic pyelonephritis), ‘acute tubular necrosis’, ‘chronic ischaemia’ (histological changes of chronic ischaemia including glomerulosclerosis, tubular atrophy, hypertensive changes in arteries or evidence of cholesterol emboli in the absence of other pathology to explain the clinical features [15]), ‘diabetic nephropathy’ and ‘others’ (including myeloma, amyloidosis). All samples were examined using light microscopy, immunofluorescence and electron microscopy wherever possible. Where a biopsy revealed more than one diagnosis, the most relevant one to the indication for renal biopsy was recorded. All pathologists reporting these biopsies participate in a national quality assurance scheme to promote consistent diagnosis.

**Statistics**

For the comparison of incidence of renal biopsy, indication and histological diagnosis expressed PMP, tests of statistical significance are not appropriate since the whole population in each region is reported rather than samples from the population.

Mean urine protein excretion at the time of renal biopsy was compared by the t-test of the mean with $P < 0.05$ being regarded as statistically significant.

**Results**

**Overall incidence of renal biopsy**

Between 2002 and 2006, 2480 native renal biopsies were performed in eight Scottish centres. The mean annual incidence was 496 biopsies per year equating to 126.3 biopsies per million population per year (PMP/year). A total of 56.9% of patients were male with a mean age of 55.6 years (SD 1.3). The overall incidence varied from year to year, but there was no clear upward or downward trend in the 5-year period studied. The annual incidence in 2002 was 130.2 PMP compared with 127.3 PMP in 2006.

The mean annual incidence and demographics for each regional renal unit are shown in Figure 1. There was wide variation from a lowest mean annual incidence of 65.8 PMP/year in Fife to the highest of 170.7 PMP/year in Tayside. There was also variability in annual incidence within centres. For example in A&A (population 368 149) the annual incidence varied from as low as 84.2 PMP in 2002 to 165.7 PMP in 2005. The mean age at the time of biopsy was lowest in Fife (51.4 years) and highest in D&G (59.4 years). The proportion of males was lowest in D&G (43.9%) and highest in Fife (69.2%).

**Indication and histological diagnosis in GC&FV and Tayside**

The biopsy indications and histological diagnoses were identified in these regions during a 3-year period between 2003 and 2006. These regions were chosen because they had widely differing incidences of biopsy, had large absolute numbers and had both been recording previously agreed indication categories prospectively since 2003. During this period, GC&FV (population 1 564 504) performed 477 biopsies (101.6 biopsies PMP/year) and Tayside (population 389 012) performed 207 (177.4 biopsies PMP/year).

Figure 2 demonstrates prospectively recorded indications for native renal biopsy in the two centres. The incidence of biopsy for the indication ‘acute renal failure’ was similar (GC&FV 27.0 PMP/year, Tayside 31.7 PMP/year) as was ‘chronically reduced function, not nephrotic’ (GC&FV 36.0 PMP/year, Tayside 48.0 PMP/year). Biopsy incidence was markedly higher in Tayside for ‘mild proteinuria (≤1 g/24 h), normal renal function ± microscopic haematuria’ (GC&FV 4.7 PMP/year, Tayside 18.0 PMP/year),...
proteinuria (>1 g/24 h), normal renal function ± microscopic haematuria; not nephrotic syndrome’ (GC&FV 14.5 PMP/year, Tayside 27.4 PMP/year). There were no significant differences in mean urine protein excretion between GC&FV and Tayside for the indication ‘mild proteinuria (<1 g/24 h), normal renal function ± microscopic haematuria’ (0.49 versus 0.69 g/24 h, respectively; P = 0.20) or ‘moderate-to-severe proteinuria (>1 g/24 h), normal renal function ± microscopic haematuria; not nephrotic syndrome’ (3.7 versus 3.0 g/24 h, respectively; P = 0.21).

The histological diagnoses are shown in Figure 3. There was a markedly lower incidence of primary glomerulopathies in GC&FV compared with Tayside (44.3 versus 84.0 PMP/year, respectively), with the main difference seen in rates of IgA nephropathy (14.1 versus 27.4 PMP/year), although this was the commonest glomerulopathy in both centres. The main other primary glomerulopathies were membranous nephropathy 10.7 versus 13.7 PMP/year and focal segmental glomerulosclerosis 9.8 versus 12.0 PMP/year. There were similar differences in rates of diagnosis for chronic ischaemia (5.8 versus 12.0 PMP/year, respectively) and diabetic nephropathy (7.5 versus 14.6 PMP/year, respectively).

The diagnoses attained for the three indication categories that differed substantially were analysed separately. In biopsies performed for ‘mild proteinuria (<1 g/24 h) with normal renal function ± microscopic haematuria’, Tayside identified more patients with primary glomerulopathies (9.4 versus 3.2 PMP/year, respectively) and vasculitis (1.7 versus 0.2 PMP/year) than GC&FV. For ‘moderate-to-severe proteinuria (>1 g/24 h) with normal renal function ± microscopic haematuria; not nephrotic syndrome’, Tayside diagnosed more primary glomerulopathies (26.6 versus 8.7 PMP/year). Similarly, Tayside diagnosed more primary glomerulopathies (17.1 versus 13.4 PMP/year) in patients biopsied for nephrotic syndrome and more diabetic nephropathy (4.3 versus 2.3 PMP/year).

Discussion

Here we present complete data regarding the incidence of adult native renal biopsies for the 5-year period 2002–06 inclusive in centres covering over 80% of the Scottish population. The renal biopsy practice in Scotland varies widely between centres with the incidence among centres studied ranging from 65.8 to 170.7 PMP/year. We believe, after comparing practice between two centres at either end of this spectrum, that the difference may be attributable to differing opinions as to the utility of renal biopsy in patients with isolated proteinuria.

Other national and regional biopsy registries highlight a wide range of biopsy incidence rates from 11.3 PMP/year in Romania [6] to 254 PMP/year in a single centre in Finland [13] and 261 PMP/year in a region of Australia.
Centre variations in biopsy incidence in Scotland

The incidence in Scotland (126 PMP/year) lies somewhat in the middle of this wide range. Knowledge of the incidence of renal biopsy is important when comparing the incidence of biopsy proven diseases such as primary glomerulopathies. This is illustrated in Figure 4 where the incidence of primary glomerulopathies and IgA nephropathy are shown for different national and regional biopsy registries including ours. It can be seen that the regions with the highest incidence of biopsy also have the highest incidence of primary glomerulopathy. Previous studies have suggested that this is due to a difference in threshold for renal biopsy in patients with mild proteinuria or isolated haematuria rather than a difference in disease incidence [16]. Our data show that patients undergoing renal biopsy in Scotland are generally older than in other reported series with a mean age of 55.6 years [7]. The male preponderance, which is well documented in other series [9], is thought to reflect a higher incidence of primary glomerulopathy in males.

The incidence of renal biopsy is likely to be influenced not just by incidence of diseases that require a renal biopsy for diagnosis but also by many other variables. These include demographic and geographic factors, variations in the provision and organization of nephrology services and the training background of individual nephrologists as well as their opinion as to the utility of renal biopsy.

Patterns of referral to nephrologists in Scotland are likely to differ, but will have become more uniform following the implementation of the UK CKD guidelines in March 2006 [17]. All units work within the National Health Service with the vast majority of new patients arriving at renal services via general practitioner (GP) or specialty referral. Routine screening, including workplace, is not common in Scotland. Patients referred to renal services via their GP are often identified as part of management of other conditions such as hypertension, diabetes and pregnancy in the community. Scotland has a wide range of urban and rural communities. Geographical accessibility to nephrology services, therefore, varies between the centres studied. However, this did not seem to play a role in the variability in incidence of renal biopsy we observed as centres serving mainly rural communities (Highland, D&G) did not have a lower incidence than that in centres serving large cities (GC&FV). The populations served by the regions described have similar mean population age (38.0–41.8 year) and gender distribution (47–49% male), and 96.5% of the population is white Caucasian [14]. Therefore, it seems unlikely that demographic variability explains the differences in biopsy incidence described.

The centre with the lowest overall incidence of renal biopsy also had the lowest mean age and highest proportion of males in their biopsy population (Fife). The implication is that older patients and females are less likely to have a renal biopsy in this centre, perhaps because of differences in referral patterns or the perception of the value of renal biopsy. However, the same relationship with incidence of renal biopsy, mean age and sex was not seen in the other seven centres.

The number of nephrologists PMP in the units studied does not vary widely (range 0.55–1.2 whole time equivalents per 100 000 population). Interestingly, however, the centre with the highest biopsy rate (Tayside) also has the greatest number of nephrologists per 100 000 population. Nearly all of the nephrologists practicing in Scotland trained in the UK. Most Scottish training programmes are single-centre-based, which could result in trainees adopting the practice in their training unit. Most biopsies are performed by nephrologists with the remainder performed by radiologists. Nephrologists in Scotland are not reimbursed according to the number of renal biopsies performed.

Variation in the incidence of ESRD may be a surrogate for disease burden in a particular area. Scottish registry data show that there is little variability in incidence of overall established renal failure or established renal failure due to primary glomerulopathies [18].

The variability we observed is, therefore, by deduction, likely to be explained by variation in nephrologists’ opinion about the utility of renal biopsy.

Despite being a common investigation in patients with evidence of renal disease, the indications for renal biopsy are not clear and there are no evidence-based guidelines [19]. Studies that examine the utility of renal biopsy in guiding clinical decision making are scarce. It is generally accepted that kidney biopsy is useful in patients with acute renal failure with no obvious evidence of reduced effective plasma volume, sepsis or urinary tract obstruction, and in patients with nephrotic syndrome that is not typical of diabetic nephropathy [20,21]. In these patients, the histological diagnosis provides an important guide to application of a variety of evidence-based therapies. Our analysis of the difference in indication for renal biopsy between the centres with low and high incidence of renal biopsy shows that the incidence of biopsy for these indications was similar. There was, however, considerable variability in the incidence of renal biopsy in patients with proteinuria and preserved renal function, perhaps due to variation in nephrologists’ opinion about the utility of biopsy in these conditions. Patients undergoing biopsy for proteinuria with preserved kidney function tended to have primary glomerular diseases or chronic ischaemia. Analysis of the clinical utility of biopsy for this indication deserves further attention.

Obtaining accurate registry data is difficult. Single-centre reporting has the benefit of data completeness, but in order to allow meaningful epidemiological interpretation and to reduce the effect of outlying centres, efforts need to be made to collect data from a wider field. Often this means a local or national registry, of which few exist with sufficient coverage or with accurate consecutive reporting. Several of the current renal biopsy registries for which published information exists rely on labour-intensive paper reporting of clinical data [6,7,9]. Other registries exist that document solely the glomerulonephritides. The Scottish Renal Biopsy Registry has been set up to collect demographic and clinical data automatically from the electronic patient record in all patients undergoing native renal biopsy in Scotland to study the epidemiology, safety and utility of renal biopsy and as a framework to study the diseases diagnosed [22].

We have demonstrated wide variability in the incidence of native renal biopsy within a single country, and our analysis suggests that this is mainly explained by uncertainty about the utility of renal biopsy for patients with mild-to-moderate proteinuria and preserved renal function. Further...
studies are required to determine the value of renal biopsy in this setting.

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14. Scotland’s Census 2001; General Register Office for Scotland 2002

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Chronic kidney disease and cardiovascular risk in hypertensive type 2 diabetics: a primary care perspective

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Abstract

Background. Chronic kidney disease (CKD) is associated with poor renal and cardiovascular (CV) outcome, and early identification largely depends on the general practitioners’ (GPs) awareness of it. Only a few studies have evaluated the

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