Kidney Biopsy Patterns in a Brazilian Elderly Population

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Abstract: Background: The elderly population is increasing all over the world. Several chronic diseases are observed in such aging group, including kidney diseases, and their histological patterns are not widely documented. **Methods:** We retrospectively reviewed native kidney biopsies (bx) evaluated in the Department of Pathology of the Federal University of Sao Paulo from 2000 to 2005, selecting 222 of patients > 65 years (ys); 128 bx had diagnosis of glomerulonephritis (GN), and 94 of renal tumors. **Results:** Fifty-five per cent of the patients were males, and median age was 70 ± 5 ys (range 65-90). The most frequent bx indication was hematuria (50%), followed by acute kidney injury (AKI) (20%), nephrotic syndrome (NS) (19%) and non nephrotic proteinuria (11%). Among patients with GN, mean age was 69 ± 5 ys, and 74/128, males; main bx indications were AKI (35%) and NS (33%), without statistical differences between genders for all clinical presentations. **Conclusion:** In this study, it was reinforced the important role of renal biopsy in elderly patients, defining main histological patterns of glomerulopathies (membranous nephropathy, amyloidosis) and other renal diseases in this age range in a Brazilian population. Besides being a useful tool for diagnosis, kidney biopsy certainly contributes to the best management of such patients.

Key words: Glomerulonephritis, kidney biopsy, elderly, renal diseases, Brazilian population.

1. Introduction

The elderly population is increasing all over the world [1]. It is expected that the number of elderly will almost triplicate, from 743 million in 2009 to 2 billion in 2050. By then, the number of individuals aged ≥ 65 years will exceed the number of children under the age of 15 years [2]. So, life expectancy is increasing; in developed countries averages 76.5 years and in developing countries is increasing up to 65.4 years [3]. It is a fact that more elderly patients are surviving longer with acute and chronic kidney disease (CKD). Consequently nephrologists will confront a wide range of age-related functional and morphological renal conditions. There are well documented changes in the anatomy and physiology of the kidneys determined by aging. According to cross-sectional and longitudinal

studies, the glomerular filtration rate (GFR) decreases by approximately $1 \text{ ml}/1.73 \text{ m}^2/\text{year}$ after age of 30 years [3–5]. As a result, elderly patients may be mislabelled as having moderate CKD even when their eGFR corrected for age is normal [4, 6].

Kidney biopsies are increasingly being performed in the elderly and very elderly [7–9]. Although highly variable in severity, common findings are age-related kidney fibrosis associated with increased collagen accumulation [7–10] and advanced vascular changes, similar to chronically damaged kidneys [4, 7, 8]. This is a different spectrum of pathologies as compared with the younger population and requires a careful assessment of risks and benefits of any potential therapeutic intervention. Advanced age is no longer considered a contraindication for renal biopsy, renal replacement therapy and consequently the number of diagnostic kidney biopsies performed in the elderly is increasing [1–10].

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On the other hand, there are some epidemiological studies based on native kidney biopsies in the elderly population that show more frequent pathologies in this population [11–26], especially glomerulonephritis (GN), followed by renal tumors.

The aim of this study was to examine the specific causes of renal disease and their respective clinical presentation in an elderly population that underwent native kidney biopsy.

2. Patients and Methods

2.1 Study Population

It was performed a retrospective study of histological reports of native kidneys evaluated in the period of January 2000 to December 2005 in the Pathology Department of the Federal University of Sao Paulo. A total of 7.008 reports of conventional kidney biopsies and surgically obtained renal tissue for different purposes were analyzed including the available clinical, laboratorial and histological parameters from its medical records. The present study was based on the reports from patients aged ≥ 65 years, in a total of 222, excluded those with two or more final diagnoses (e.g., infection, kidney cysts), as well as biopsies of kidney donors.

The present analysis was focused in the group of elderly that had glomerulopathies ($n=128$) as the main histological diagnosis.

Glomerular diseases were considered as primary if at the time of biopsy there was: (1) no report of any known associated systemic disease; (2) negative serology for hepatitis B or C, HIV and anti-nuclear antibodies, and (3) no report of familial hematuria. The secondary glomerular diseases were divided into four groups, as they were associated with: (1) systemic, (2) metabolic, (3) vascular diseases, (4) infectious diseases/post infectious glomerulonephritis (endocarditis, hepatitis B and C).

Clinical indications for kidney biopsies were defined by the assistant physician of each patient and in most cases corresponded to: chronic kidney disease, acute

kidney injury, nephrotic syndrome, non nephrotic proteinuria, and hematuria. It was evident that surgical procedures that resulted in kidney histological evaluation were mainly motivated by the suspicion of malignancies.

2.2 Histological Analyses

Biopsy specimens of all cases were evaluated by light microscopy (at least four stained slides were used for quantification of histological changes in each biopsy: hematoxylin-eosin, Masson's trichrome, periodic acid-Schiff and silver stains). Most cases of glomerulopathies were also evaluated by immunofluorescence techniques and eventually by electron microscopy.

3. Statistical Analyses

The ages of the patients were considered as continuous variables. Chi square and Fisher's exact tests were performed to compare demographic covariates between groups when appropriate. Values were presented as mean and standard deviation. Student t test was used to compare mean values between the groups. A $p < 0.05$ (two tailed) was considered as statistically significant. All the statistical analyses were performed with the stata statistical software 12.0 (Stata Corporation, TX, USA).

4. Results

4.1 Demographic Analyses of the Enrolled Population

From 2000 to 2005, 7008 histological analyses of native kidney were evaluated in our Department of Pathology, among which 222 corresponded to exams performed in elderly individuals (demographical characteristics described in Table 1).

These 222 patients were 123 males (55%) and 99 females (45%) with median age of 70 ± 5 years (range 65–90). Figs. 1 and 2 show the number of patients distributed by age and by gender, respectively. One hundred and twenty-two patients were in the age range

Table 1 Demographic data of the enrolled population.

Characteristics	Whole population (n = 222)
Patients' age (years) (n = 222) mean	70±5 (65–90)**
Sex (male, n; %)	123; 55%
Histological diagnosis	
Glomerulonephritis (n; %)	128; 47.5%
Renal neoplasia (n; %)	94; 42.5%
Clinical presentation	
Hematuria (n; %)	111; 50%
Acute kidney failure (n; %)	45; 20%
Nephrotic syndrome (n; %)	42; 19%
Proteinuria (n; %)	24; 11%.

*Mean and standard deviation; ** range

Fig. 1 Distribution of elderly patients who underwent renal biopsy by age (mean).

GN: glomerulopathy, RN: Renal neoplasia, MGN: Membranous GN, CGN: Chronic GN, FSGS: Focal segmental glomerulosclerosis, MPGN: Membranoproliferative GN, PIGN: Pauci immune GN, IgAN: IgA nephropathy, MCD: Minimal change disease, LN: Lupus nephritis, Post Inf. GN: Post infectious GN, IS: Inadequate sample.

Fig. 2 Distribution of elder patients who underwent renal biopsy by gender.

of 65–69 years, 87 and 13 patients in the ranges of 70–79 years and 80–90 years, respectively.

Kidney biopsy indications are shown in Tables 1–2. The most frequent indication in the whole elderly

population was hematuria (n = 111; 50%), followed by AKI (n = 45; 20%); NS (n = 42; 19%) and non nephrotic proteinuria (n = 24; 11%).

Considering only patients with GN (n = 128, 74 males, mean age of 69±5 years), the main biopsy indications were AKI (n = 45; 35%) and NS (n = 42; 33%) (Table 2). Women were more likely to present with NS than men (36% vs. 30%; p = ns) and AKI was more frequently observed in men than women (37% vs. 32%; p = ns). There were not statistical differences between men and women as concerned to other clinical presentations.

4.2 Kidney Biopsy Findings

The most common kidney biopsy findings in the elderly patients were glomerulonephritis (n = 128; 47.5%) and renal neoplasias (n = 94; 42.5%; renal carcinoma was present in 90 and urothelial carcinoma in 4 biopsies, Table 1).

Among the cases of glomerulonephritis (n = 128), the most frequent histological pattern was membranous GP in 26 biopsies (20.5%) followed by chronic nephropathy (n = 25; 20%), focal segmental glomerulosclerosis (FSGS) (n = 23; 18%), membranoproliferative GN (MPGN, n = 14; 11%), pauci immune GN (n = 11; 9%), IgAN (n = 6; 5%), lupus nephritis (LN) (n = 4; 3%), minimal change disease (n = 3; 2%) and others.

The main biopsy indication was registered as AKI in more than half of the patients with MPGN (64%). This was a particularly frequent indication in cases diagnosed as LN and pauci immune GN (Table 2).

Pauci immune GN had different clinical presentations: AKI was present in 4/11, hematuria in 4/11, nephrotic syndrome in 2/11 and non nephrotic proteinuria in 1/11 (Table 2). Positive anti-neutrophil cytoplasmatic antibody (p- or c-ANCA) was reported in 99% of patients with pauci immune GN. About 72% of patients with pauci immune GN were men (8 males vs. 3 females). Indications for biopsy are shown in Fig. 3.

Table 2 Clinical presentation among different pattern of glomerulonephritis.

	NS (n = 42; 33%)	Hem (n = 17; 13%)	Prot (n = 24; 19%)	AKI (n = 45; 35%)
Minimal change disease (n = 3)	3; 100%;	0; 0%	0; 0%	0; 0%
Inadequate sample (n = 9)	1; 11%	4; 45%	1; 11%	3; 33%
Membranous GN (n = 26)	23; 88%	0; 0%	2; 8%	1; 4%
IgAN (n = 6)	1; 17%	4; 66%	1; 17%	0; 0%
FSGS (n = 23)	9; 39%	1; 4%	5; 22%	8; 35%
Chronic GN (n = 25)	1; 4%	3; 12%	8; 32%	13; 52%
Membranoproliferative GN (n = 14)	1; 7%	0; 0%	4; 29%	9; 64%
Lupus nephritis (n = 4)	0; 0%	1; 25%	1; 25%	2; 50%
Pauci immune GN (n = 11)	2; 19%	4; 36%	1; 9%	4; 36%
Amyloidosis(n = 3)	1; 33%	0; 0%	1; 33%	1; 33%
Post infectious GN (n = 4)	0; 0%	0; 0%	0; 0%	4; 100%

Fig. 3 Main indication of renal biopsy in the glomerulonephritis group (*AKI: Acute kidney failure, NS: nephrotic syndrome, Prot: proteinuria, Hemat: Hematuria).

5. Discussion

As the demographic profile of the world population is changing, particularly due to an overall life expectancy increase, the diagnosis and management of kidney diseases in the elderly has gained increasing attention [8–9]. It is of note that kidney biopsy is a useful tool in the investigation of nephropathies, but its indication has not been consensual in the elderly.

This study collected information on elderly patients that underwent a native kidney biopsy or a surgical procedure with evaluation of kidney tissue along six years. The most frequent diagnosis was glomerulonephritis, and the histological pattern of glomerular diseases was consistent with most studies in

patients ≥ 65 years [4–26], as membranous nephropathy was the most common diagnosis in our series, followed by FSGS and amyloidosis. Another comprehensive Brazilian study involving a different study group presented a similar profile in the elderly subset of patients [27]. It is of note that there are also reports of relatively high frequencies of FSGS in nephrotic patients over 65 years [8, 17, 24–26].

The male gender has predominated in the present study population, which had also a mean age of 70 years. This finding is not in concordance with those reported by Nair et al. [6], D'Agati et al. [20] and Haas et al. [12], that reported an almost equal number of male and female patients over 80 years who underwent renal biopsy because of AKI [12], but the age range of the patients included could have been the main reason for this difference. In other previously reported renal pathology registry of patients ≥ 65 years, male gender has also predominated [24]. However, nowadays, women have higher life expectancy than men, and this may have an impact on gender frequency and morbidity of this female population in histopathological studies [28–30].

AKI was the most common indication for renal biopsy in the glomerulonephritis group, although in our complete series hematuria has predominated (100% of patients with kidney neoplasia presented hematuria). In a previous study of the same age group [6], AKI was

the second most frequent clinical presentation after NS; however, in that study, acute nephritic syndrome and rapidly progressive renal failure were classified separately, while in our present analysis these groups were classified as AKI. Other studies regarding renal biopsies in the elderly included patients over 60 or 65 years; in most of those studies [11–16], nephrotic proteinuria was the most common indication for renal biopsy, followed by AKI. Lopez-Gomez et al. [15], in a Spanish Registry of GN, reported that AKI was the most frequent biopsy indication in the elderly when AKI and acute nephritic syndrome were included in the same clinical presentation group.

Patients with membranous nephropathy, MCD, FSGS and amyloidosis presented predominantly NS as kidney biopsy indication. These data are consistent with most studies in patients over 65 years [5, 15–17], in which membranous nephropathy is the most common diagnosis, followed by amyloidosis and MCD, with a markedly lower frequency. As abovementioned it has been also reported relatively high frequencies of FSGS in nephrotic patients over 65 years [18, 19]. It is possible that a considerable number of these represent unrecognized secondary forms if this disease related to hypertension, obesity, or other processes as commented by Montzouris et al. [20]. In our study, 23 patients (18%) had diagnosis of primary FSGS. We have carefully sought to exclude secondary forms; 25 cases (20%) had a pattern of secondary FSGS, and in 52% of them patients presented AKI. Haas et al. [12] showed that AKI was the presentation of patients submitted to kidney biopsy which diagnosis was pauci immune crescentic GN; we have documented this clinical presentation in 36% of our elderly patients with pauci immune GN.

It is interesting to note the difference of diagnosis pattern according to the age range in the elderly population, as already mentioned. In a study of patients older than 80 years [20] it was observed that the most frequent histological diagnoses were pauci

immune GN, hypertensive nephrosclerosis and FSGS secondary to hypertension and aging.

In fact kidney biopsies are increasingly being performed in the elderly and very elderly [4, 20], and this was also observed along the last years in our service.

Although highly variable in severity, a common finding is age-related kidney fibrosis that was also remarkable in our series of elderly patients. It is of note that performing kidney biopsy in the elderly may contribute to manage patients with AKI, nephrotic syndrome, rapidly progressive GN, among other conditions.

It was not possible in the present study to evaluate post biopsy complication rate, as it was based only on histological reports of kidney biopsy or surgery, without a clinical follow-up of the patients. Nevertheless it has been reported a similar rate of major complications of kidney biopsy in elderly and other age groups [5, 6, 8, 10].

At last, in this study, we have reinforced the important role of kidney biopsy in elderly patients as a useful tool in diagnosis and management of renal disease in this age group.

Acknowledgements

The authors FIM, AGR, GMK were supported by grants from CNPq – Brazil during this study.

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