Renal Biopsy in Patients Aged 65 Years and Older: A Clinicopathological Analysis

Altmış Beş Yaş ve Üzeri Hastalarda Böbrek Biyopsisi: Bir Klinikopatolojik Analiz

ABSTRACT

AIM: Elderly patients with renal disease have recently attracted increased attention. There has also been an increase in renal biopsies in these patients. The aim of this study was to investigate the influence of the renal biopsy on the diagnosis, management and prognosis of renal diseases in the elderly.

MATERIAL and METHODS: We retrospectively reviewed the clinical files of 632 patients who had undergone renal biopsy in the department of Nephrology, Gulhane School of Medicine between 2000 and 2007. Thirty of these patients included in the present study were 65 or more years old.

RESULTS: The most common indication for renal biopsy was acute renal injury and acute on chronic renal disease (53.3%), nephrotic syndrome (40%) and non-nephrotic proteinuria (6.6%) in these patients. In the acute renal injury group, renal biopsy showed acute interstitial nephritis, acute tubular necrosis and crescentic glomerulonephritis while in the acute on chronic renal disease group it showed chronic interstitial nephritis, renal amyloidosis and chronic glomerulonephritis.

In the nephrotic syndrome group, renal biopsy showed minimal change disease, renal amyloidosis, membranous glomerulonephritis and focal segmental glomerulosclerosis while in the non-nephrotic proteinuric group it showed focal segmental glomerulosclerosis.

CONCLUSION: Study data suggest that renal biopsy has influence on the diagnosis, management and prognosis of renal disease the elderly patients. This procedure should be performed without any age limitation when a renal biopsy indication emerges in elderly patients.

KEY WORDS: Acute renal injury, Elderly patients, Glomerulonephritis, Renal biopsy, Renal pathology

ÖZ

AMAÇ: Son zamanlarda yaşlı hastalarda gelişen böbrek hastalığına ilgi artarken, bu hastalarda yapılan böbrek biyopsi sayısı geçmişe oranla belirgin olarak artış göstermektedir. Bu çalışmadaki amacımız, böbrek biyopsisinin yaşlı hastalarda tanı, tedavi ve prognoz üzerine etkisini araştırmaktır.

GEREÇ ve YÖNTEMLER: Bu çalışmada, 2000 - 2007 yılları arasında Gülhane Askeri Tıp Akademisi Nefroloji Kliniği'nde böbrek biyopsisi yapılan 632 hastanın dosyaları geriye dönük olarak incelendi. Çalışmaya alınan 30 hastanın yaşı 65 ve üzeri olarak saptandı.

BULGULAR: En sık böbrek biyopsi endikasyonları sırasıyla akut böbrek hasarı ve kronik böbrek hastalığı zemininde gelişen akut böbrek hasarı (%53,3), nefrotik sendrom (%40) ve nefrotik düzeyde olmayan proteinüri (%6,6) olarak saptandı.

Akut böbrek hasarı olan hastalarda yapılan böbrek biyopsisinde sırasıyla akut interstisyel nefrit, akut tübüler nekroz ve kresentik glomerülonefrit saptandı. Bununla birlikte kronik böbrek hastalığı zemininde gelişen akut böbrek hasarı hastalarının böbrek biyopsilerinde; kronik tübülointerstisyel nefrit, renal amiloidoz ve kronik glomerülonefrit saptandı.

Nefrotik sendromlu hastalarda yapılan böbrek biyopsilerinde minimal değişiklik hastalığı, renal amiloidoz, membranöz glomerülonefrit ve fokal segmental glomerüloskleroz saptanırken nefrotik düzeyde olmayan proteinürisi olan hastalarda fokal segmental glomerüloskleroz saptanmıştır.

SONUÇ: Bu çalışma ile yaşlı bireylerde böbrek hastalığının tanı, tedavi ve prognozunda böbrek biyopsisinin önemli etkisinin olduğu gösterilmiştir. Yaşlı hastalarda böbrek biyopsi endikasyonu varlığında, yaşa sınırlı kalınmadan biyopsi işlemi yapılmalıdır.

ANAHTAR SÖZCÜKLER: Akut böbrek hasarı, Yaşlı hastalar, Glomerülonefrit, Böbrek biyopsisi, Böbrek patolojisi

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INTRODUCTION

An increased frequency of renal diseases have been reported in the geriatric population in parallel to the growing numbers of this age group. Hypertension is widely observed in this age group and it has been shown to be closely related to renal diseases. This is why relatively minor invasive efforts are exhibited in the diagnosis and these patients are generally followed on clinical grounds (1-4). However, clinical studies have shown a discordance between clinical presentation of the patients and renal histopathological findings, making it necessary to perform renal biopsy in selected cases. The aim of this study was to investigate the role of renal biopsy in diagnosis and management of elder patients.

MATERIAL and METHODS

Renal biopsies of the 29 patients (4.6%) who were 65 years old and elder of the 632 patients that underwent renal biopsy in Gülhane Medical School, Department of Nephrology between 2000 and 2007 were considered in this study. Repeated biopsies and biopsies of renal grafts were excluded. Acute renal injury (deterioration of renal function in hours to days or weeks), rapidly progressive glomerulonephritis (RPGN; deterioration of renal function in hours to days or weeks accompanying proteinuria, hematuria and presence of auto antibodies), asymptomatic urinalysis abnormality (24-hour proteinuria of 2 gr/day/1.73 m^2 and accompanying hematuria), and the nephrotic syndrome (proteinuria of 3.5 gr/day/1.73 m^2 or greater; accompanying edema, hypoalbuminemia, hyperlipidemia and lipiduria) were the selected indications for renal biopsy.

Chronic renal disease was defined as permanent renal dysfunction of 3 months or longer whereas acute dysfunction that developed in days to weeks was acute exacerbation on chronic renal disease.

Complete remission, partial remission and persistent proteinuria were described as normal or stable renal functions with a proteinuria ≤ 0,2 g / day and normal serum albumin concentration; 0.2-2.0 g /day and normal serum albumin concentration and >2.1 g /day or no improvement in urinary protein excretion and serum albumin concentration in patients with nephrotic syndrome respectively. Improvement in renal function was defined as a decrease in serum creatinine level (SCr) by at least 25%, and deterioration was defined as an increase in SCr that is more than 25% of pre-treatment levels or initiation of dialysis therapy.

Serum and urine protein electrophoresis, serum levels of complement, perinuclear and cytoplasmic antineutrophil cytoplasmic antibody, anti-nuclear antibody, anti- double-stranded DNA antibodies, anti-glomerular basement membrane antibodies, and rheumatoid factor were studied. Light microscopy and immunofluorescent staining were used for renal biopsies. Written informed consent was obtained from each patient.

Table I: Demographic and clinical characteristics of the patients.

PATIENT NO	AGE	GENDER	COMORBIDITY	CLINICAL DIAGNOSIS
1	65	F	-	**ARI**
2	72	F	-	**ARI**
3	77	F	-	**ARI**
4	66	M	-	**ARI**
5	67	F	-	**ARI**
6	65	F	-	**ARI**
7	69	F	-	**ARI**
8	65	F	-	**ARI**
9	66	M	DM	**Acute on CRD**
10	76	M	-	**Acute on CRD**
11	65	F	-	**Acute on CRD**
12	65	M	-	**Acute on CRD**
13	65	F	-	**Acute on CRD**
14	67	F	-	**Acute on CRD**
15	65	M	-	**Acute on CRD**
16	69	M	-	**NS**
17	66	F	COPD	**NS**
18	65	F	-	**NS**
19	68	M	-	**NS**
20	71	M	-	**NS**
21	65	M	-	**NS**
22	81	F	-	**NS**
23	68	M	-	**NS**
24	80	M	HCV (+)	**NS**
25	67	M	-	**NS**
26	65	M	-	**NS**
27	65	M	-	**NS**
28	69	F	-	**NNRP**
29	70	F	DM	**NNRP**

ARI: Acute Renal Injury; **NNRP**: Non-nephrotic range proteinuria; **DM**: Diabetes Mellitus; **HCV**: Hepatitis C; **CRD**: Chronic renal disease; **COPD**: Chronic obstructive lung disease; **NS**: Nephrotic Syndrome.

RESULTS

There were 14 male (48%) and 15 female (52%) patients. Table I represents their demographic and clinical characteristics. The median age was 68.7 years. The oldest patient was 81 years old. Twenty-two patients were in the age group of 65-70, whereas 2 patients were in the 71-75 age group and 4 were in the 76-80 and 1 patient was older than 80. The indications for renal biopsy were acute renal injury in 15 cases (8 patients with acute renal injury; 7 patients with acute on chronic renal disease), nephrotic syndrome (n=12) and non-nephrotic range proteinuria (n=2). Comorbidities were diabetes mellitus (n=2), hepatitis C seropositivity (n=1) and chronic obstructive pulmonary disease (n=1).

Renal histopathology findings are shown in Table II. Acute tubulointerstitial nephritis, rapidly progressive glomerulonephritis and acute tubular necrosis were the diagnosis in patients with acute renal injury. Patients with acute on chronic renal disease presentation had chronic tubulointerstitial nephritis**,** amyloidosis and chronic glomerulonephritis. Amyloidosis, minimal change disease, membranous glomerulonephritis and focal segmental glomerulosclerosis were the etiology of nephrotic syndrome. Focal segmental glomerulosclerosis was the diagnosis for patients with non-nephrotic range proteinuria.

Table II: Renal biopsy findings.

BIOPSY INDICATION	NO	(%)	RENAL DISEASE	N	(%)
ARI	8		**RPGN**	3	
			ATIN	3	
			ATN	2	
Acute on CRD	7		**CTIN**	3	
			AMYLOIDOSIS	3	
			CGN	1	
NS	12		**AMYLOIDOSIS**	5	
			MCD	4	
			MN	2	
			FSGS	1	
NNRP	2		**FSGS**	2	
TOTAL	**29**	**100**		**29**	**100**

ATIN: Acute Tubulointerstitial Nephritis; **ATN**: Acute Tubular Necrosis; **FSGS**: Focal Segmental Glomerulosclerosis; **CGN**: Chronic Glomerulonephritis; **CTIN**: Chronic Tubulointerstitial Nephritis; **MCD**: Minimal Change Disease; **MN**: Membranous Nephropathy; **RPGN**: Rapidly Progressive Glomerulonephritis.

Therapy initiated after renal biopsy and its results are shown in Table III. Curability was especially high in patients with acute renal injury. Only one patient had residual renal dysfunction after medication. Two of three patients with rapidly progressive glomerulonephritis had complete remission after immunosupressive medication. Patients with acute tubulointerstitial nephritis were successfully treated with prednisolone only (n=1), or prednisolone and azathiopurine (n=2).

Patients with biopsies for acute on chronic renal disease had lower rates of clinical success probably due to chronic histopathological changes. Angiotensin converting enzyme inhibitors and/or angiotensin type 2 receptor blockers with statins were initiated in these patients. Of these patients, one was treated with hemodialysis while the rest were managed as outpatients with the abovementioned treatment.

Amyloidosis was the most common diagnosis in patients with nephrotic syndrome. Colchicine, angiotensin converting enzyme inhibitors and/or angiotensin type 2 receptor blockers were the choice of treatment in these patients but the proteinuria persisted. Cyclosporine A was effective in patients with minimal change disease. Partial remission was observed with a combination of angiotensin converting enzyme inhibitors and statins in patients with membranous nephropathy and focal segmental glomerulosclerosis. Finally, no complication was observed in the patients after renal biopsy

DISCUSSION

Parallel to the increases in the overall life expectancy in the geriatric population, the diagnosis and management of renal diseases in this age group have gained increasing attention (6, 7). Moreover, renal biopsy is more performed in geriatric patients in recognition of the fact that specific and/or non-specific therapy may lead to partially or completely remission in renal disease (1, 7, 9). In a study by Nair et al., elder patients made up 4.2% of overall patients and 100 of 3227 patients that underwent renal biopsy were 80 year old and elder (1). Actually, this number may seem lower when compared to other age groups. The incidence of renal biopsy has increased in the geriatric population despite the arguments regarding the necessity and complications of renal biopsy in the elderly.

Previous studies have revealed differences in indications for renal biopsy in the elderly compared to other adults and children (1,8,9). Nephrotic syndrome was the most common indication in all age groups whereas acute renal injury was the most common in the elderly (1,8,9). Acute renal injury was also the most common indication for renal biopsy in the

Table III: Clinical and pathologic diagnosis, therapy and outcome.

PATIENT NO	CLINICAL DIAGNOSIS	PATHOLOGICAL DIAGNOSIS	THERAPY	OUTCOME
1	ARİ	**CRESCENTIC GN**	STEROID+CYCLOPHOSPHAMIDE+PLASMAPHERESIS	**N**
2	ARİ	**CRESCENTIC GN**	STEROID+AZATHIOPURINE	**N**
3	ARİ	**CRESCENTIC GN**	STEROID ALONE	**IM**
4	ARİ	**ATIN**	STEROID+AZATHIOPURINE	**N**
5	ARİ	**ATIN**	STEROID+AZATHIOPURINE	**N**
6	ARİ	**ATIN**	STEROID+HD	**N**
7	ARİ	**ATN**	ACE-I	**N**
8	ARİ	**ATN**	DIALYSIS	**N**
9	Acute on CRD	**CTIN**	ACE-I	**ST**
10	Acute on CRD	**CTIN**	ACE-I	**DE-HD**
11	Acute on CRD	**CTIN**	ACE-I	**ST**
12	Acute on CRD	**AMYLOIDOSIS**	COLCHICINE+ACE-I	**ST-PEP**
13	Acute on CRD	**AMYLOIDOSIS**	COLCHICINE +ACE-I	**DE-PEP**
14	Acute on CRD	**AMYLOIDOSIS**	COLCHICINE+ACE-I	**DE-PEP**
15	Acute on CRD	**CGN**	ACE-I	**DE**
16	NS	**AMYLOIDOSIS**	COLCHICINE+ACE-I+STATIN	**PEP**
17	NS	**AMYLOIDOSIS**	COLCHICINE+ACE-I+ STATIN	**PEP**
18	NS	**AMYLOIDOSIS**	COLCHICINE+ACE-I+STATIN	**PEP**
19	NS	**AMYLOIDOSIS**	COLCHICINE+ACE-I+ STATIN	**PEP**
20	NS	**AMYLOIDOSIS**	COLCHICINE+ACE-I+ STATIN	**PEP**
21	NS	**MCD**	CYCLOSPORINE	**CR**
22	NS	**MCD**	CYCLOSPORİNE	**CR**
23	NS	**MCD**	CYCLOSPORİNE	**CR**
24	NS	**MCD**	CYCLOSPORİNE	**CR**
25	NS	**MN**	ACE-I+ STATIN	**PAR**
26	NS	**MN**	ACE-I+ STATIN	**PAR**
27	NS	**FSGS**	ACE-I+ STATIN	**PAR**
28	NNRP	**FSGS**	ACE-I+ STATIN	**PAR**
29	NNRP	**FSGS**	ACE-I+ STATIN	**PEP**

ACE-I: Angiotensin Converting Enzyme Inhibitors; **CR**: Complete Remission; **DE**: Deterioration in Serum Creatinine Level; **HD**: Hemodialysis; **IM**: Improved Serum Creatinine Level; **N**: Normal Serum Creatinine Level; **PAR**: Partial Remission; **PEP**: Persistant Proteinuria; **ST**: Stabile Serum Creatinine Level; **GN**: Glomerulonephritis; **ATIN**: Acute Tubulointerstitial Nephritis; **ATN**: Acute Tubular Necrosis; **FSGS**: Focal Segmental Glomerulosclerosis; **CGN**: Chronic Glomerulonephritis; **CTIN**: Chronic Tubulointerstitial Nephritis; **MCD**: Minimal Change Disease; **MN**: Membranous Nephropathy

present study, which reflects the higher risk of acute renal injury in the elderly. Several papers have mentioned increased predisposition to acute renal injury due to higher prevalence of benign nephrosclerosis, hypertension and diabetes mellitus in the elderly (6,9,11). That might be the reason many authors think clinical clues are sufficient to identify the underlying pathology in older patients with acute renal injury. However, clinical studies have revealed discrepancies between clinical-based diagnosis and histopathological diagnosis in these patients (8,9,12). These studies suggest that renal biopsy may be useful to identify renal parenchymal pathology in the elderly after ruling out the pre- and post-renal etiologies for acute renal dysfunction (8,9,12). Haas et al. reported that the histopathological findings were pauci-immune crescentic glomerulonephritis (31.2%), acute tubulointerstitial nephritis (18.6%), acute tubular necrosis (14.2%) and benign nephrosclerosis (3.2%) (9) in 259 (24.3%) patients 60 years old and older among 4264 patients with acute renal injury between years 1991 and 1998. The study revealed glomerular diseases as the etiology of acute renal injury in patients who had undergone renal biopsy (9). Pauci-immune crescentic glomerulonephritis was responsible for approximately one third of the glomerular diseases while the remaining diagnoses were post-infectious glomerulonephritis, anti-glomerular basement disease and Ig A nephropathy (9). Also in that study, tubulointerstitial nephritis was the underlying pathology for acute renal failure in approximately 40% of patients (9). In our study, the underlying diseases for acute renal injury were rapidly progressive glomerulonephritis, acute tubulointerstitial nephritis and acute tubular necrosis, similar to the abovementioned study. We believe that changes in the endothelial cells by aging may trigger the development of vasculitic diseases and play an important role in the increased frequency of pauci-immune (vasculitic) crescentic glomerulonephritis in renal biopsies.

Nephrotic syndrome has been said to be the second most important indication for performing a renal biopsy (1,7,8). Although some geographical differences exist, the most common disease responsible for nephrotic syndrome in adults is membranous nephropathy (1,7,8,13,14). However, minimal change disease, focal segmental glomerulosclerosis and amyloidosis are frequent in patients older than 60 (1,7,8,13,14). Nair et al. have reported that the frequency of minimal change disease was 46%, focal segmental glomerulosclerosis was 38% and membranous nephropathy was 15% in patients older than 80 years with nephrotic syndrome (1). The authors also concluded that benign nephrosclerosis was a frequent finding which is interesting because benign nephrosclerosis is generally associated with non-nephrotic range proteinuria (1). Minimal change disease but not focal segmental glomerulosclerosis was ruled out based on clinical and pathology data in that study (1). There is a possibility that idiopathic focal segmental glomerulosclerosis may exist in patients who are thought to have benign nephrosclerosis (1). In our study, patients with nephrotic syndrome had amyloidosis (n=5), minimal change disease (n=4), membranous nephropathy (n=2) and focal segmental glomerulosclerosis (n=1). Our study also differs from the previous ones in that amyloidosis was responsible for the majority of cases. Geographical difference and frequency of chronic inflammatory disorders leading to secondary amyloidosis might account for this difference. Consistent with other studies, minimal change disease was the second most common etiology of nephrotic syndrome.

Performing renal biopsy in the elderly may contribute to manage patients with acute renal injury, especially in diseases such as rapidly progressive glomerulonephritis, acute tubulointerstitial nephritis and nephrotic syndrome that require specific treatment (1,3,7,9,15). Nair et al. reported potentially treatable diseases like crescentic glomerulonephritis, membranous nephropathy, minimal change disease and acute tubulointerstitial nephritis in more than 40 of 100 cases (1). In the rest of the patients, renal biopsy aided to provide prognostic information and protect from cytotoxic empirical therapies (1).

Previous studies have reported a similar rate of major complication after renal biopsy in the elderly compared to other age groups. The absence of a major complication in the present study indicates that renal biopsy may be performed safely in the presence of clinical indication (1,8,9,16,18).

In conclusion, the present work confirms the usefulness of renal biopsy in diagnosing and managing underlying renal disease in the elderly. Moreover, the complication risk was not different from the number observed in other age groups. We therefore suggest that renal biopsy should be considered in the presence of an indication in the elderly.

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