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Original Article

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Kidney Biopsy in Older Individuals: Impact on Patient Management, Risks, and Consequences - Single Center Experience

Mehmet Ası Oktan[1], Cihan Heybeli[1], Hayri Üstün Arda[1], Serkan Yıldız[1], Mehtat Ünlü[2], Caner Çavdar[1], Aykut Sifil[1], Ali Çelik[1], Sulen Sarıoğlu[2], Taner Çamsarı[1]

[1]Department of Nephrology, Dokuz Eylül University School of Medicine, İzmir, Turkey
[2]Department of Pathology, Dokuz Eylül University School of Medicine, İzmir, Turkey

Abstract

Objective: The incidence of chronic kidney diseases increases in older individuals, like all other chronic diseases. Renal biopsy provides important guidance in the diagnosis of many kidney diseases. The impact of biopsy on patient management in older individuals is controversial. In this study, we evaluated the patient population of over 65 years of age in our clinic in the last decade, biopsy-related complications, and the effects of biopsy results on clinical evaluation.
Materials and Methods: Medical records of patients who underwent native kidney biopsies between 2007 and 2018 in our clinic were evaluated. One hundred and fifteen patients were enrolled. The demographic, clinical, and laboratory findings of the patients at the time of biopsy were noted. Effects of renal biopsy on patient management and clinical outcomes, renal biopsy-related complications, and adequate material acquisition rates were noted.
Results: Acute kidney injury was the most common renal biopsy indication in older individuals (36.6%). Glomerulonephritis containing crescents was the most common diagnosis (26.8%); 40% (n=12) of this patient group achieved complete remission with immunosuppressive treatment. In approximately two thirds of patients, diagnostic information had the potential to modify treatment (67%). Twenty-four percent of the patients had a diagnosis of malignancy, and the complication rate was 7.1%.
Conclusion: Although the complication risk is mildly increased following renal biopsy, valuable clinical information is obtained in a considerable number of patients. Malignancy should be suspected in certain renal diseases in older individuals.
Keywords: Biopsy, fine needle, elderly, glomerulonephritis

Corresponding Author: Mehmet Ası Oktan ✉ mehmetasioktan@hotmail.com
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INTRODUCTION

There is an increase in the population of older individuals due to increased life expectancy and developments in medicine. Today, the number of people over the age of 65 in the world is approximately 962 million (13%) and by 2050, it is expected to reach 2.1 (22%) billion. In developed countries, the fastest growing age range is in the population of over 65 years of age. In 2017, one in five people in was over 60 years of age in Europe and North America. It is estimated that 1 out of every 3 people in the 2050s will be over 60 years old. It is thought that the elderly population (>60 years) in 2050 will be more than the population of children and adolescents (10-24 years) worldwide (2.1 versus 2 billion) (1).

The incidence of chronic kidney diseases is increased in the elderly population, like all other chronic diseases. In terms of morbidity-mortality results, it has an important place in the geriatric population (2). The incidence of stage 3-4 chronic renal failure is 0.7% in the 20-40 age range and increases to 40% at 70 years (3). The increase in the incidence of co-morbid diseases, increased likeli-

hood of exposure to potential nephrotoxic medical or surgical procedures, and the negative impact of aging on the glomerular filtration rate are the main causes of increase in the incidence of renal diseases in this age group.

In geriatric patient populations, kidney disease related symptoms, increase in serum creatinine, proteinuria, or hematuria are often attributed to other systemic diseases such as diabetes and hypertension or drug use. Thus, kidney diseases requiring specific treatment such as interstitial nephritis and vasculitis can be excluded. In one study, it is reported that the rate of primary kidney disease neglected in older individuals is approximately 25% (4). Renal biopsy provides important guidance for the diagnosis and management of many kidney diseases. Clinicians may be reluctant to perform a biopsy due to possible biopsy-related complications in older individuals; however, kidney biopsies provides critical diagnostic and prognostic information. In a study that included patients ≥80 years of age, the rate of primary kidney disease requiring specific treatment was reported to be approximately 40% (5).

The aim of this study was to evaluate the contribution and risks of renal biopsy to patient management in older individuals.

MATERIALS AND METHODS

Design and Participants

After obtaining the approval of the Ethics Committee of Dokuz Eylül University (Approval Date: October 11, 2018; Approval No: 2018/25-01), renal biopsies performed in our clinic between August 01, 2007 and July 11, 2018 were retrospectively reviewed. Of 1088 patients who underwent adult native kidney biopsies, 115 patients were older than 65 years (10.5%). Three patients were excluded owing to insufficient clinical knowledge. Finally, 112 patients were enrolled. For patients who had more than one kidney biopsy, the first procedure was evaluated.

Demographic (age, gender), clinical (referral reason, biopsy indication, presence of major complication), and laboratory variables (serum creatinine, eGFR according to CKD-EPI, proteinuria level, presence of hematuria, imaging findings, and histopathological diagnosis) were noted.

Main Points

- Kidney biopsy should not be avoided over 65 years.
- Kidney biopsy provides significant guidance in obtaining a definite diagnosis and planning specific treatment in patients over 65 years.
- Approximately in two thirds of patients, a reversible cause can be detected by biopsy.
- Malignancy should be suspected in certain renal diseases in elderly.

Indications for Kidney Biopsy

The indications for renal biopsy were classified as follows:

- Acute kidney injury (AKI): Referred to by the clinician as acute or rapidly progressive renal damage.
- Chronic renal failure (CRF): Gradual decline in renal function, but the cause could not be determined.
- Nephrotic syndrome: Accompanied by edema or hypoalbuminemia with >3.5 g/day proteinuria without azotemia.
- Nephritic syndrome: Acute renal failure with hematuria and proteinuria.
- Non-nephrotic proteinuria: <3.5 g/day proteinuria and/or hematuria without azotemia.

Kidney Biopsy

Kidney biopsies were performed in the prone position for patients who did not use any antiaggregants or anticoagulants or who discontinued the drugs for a sufficient period of time. The region to be entered was marked with USG; biopsies was performed using a 14-gauge thickness automatic trucut biopsy gun. Patients were observed in the hospital for 1 day following the biopsy procedure for possible complications.

Histopathological Evaluation

Histopathological diagnosis was made by agreement of two independent pathologists (SS and MU) in all patients. Renal biopsy specimens were evaluated with light microscopy after staining with hematoxylin-eosin, Masson's trichrome, periodic acid-Schiff, and methenamine silver. Staining with antibodies against immunoglobulin G (IgG), immunoglobulin A (IgA), immunoglobulin M (IgM), complement 3c, C1q, kappa, and lambda was performed for immunofluorescence. Electron microscopic analysis was not routinely used. Sufficient material was accepted as biopsy specimens containing ≥8 glomeruli and 1 artery. Specimens were stained with Congo-red when a clinical diagnosis of secondary amyloidosis was suspected. Histopathological findings in the kidney were evaluated for chronicity according to the scoring system presented by Sethi et al. (6).

Treatment and Definitions

In the presence of glomerulonephritis containing crescents (anti-GBM, immunocomplex, pauci-immune) (7), clinical characteristics and response to treatments were recorded.

In specimens of glomerulonephritis containing crescents, response criteria were set as:

- Improvement in the glomerular filtration rate or a decrease in glomerular filtration rate of less than 25% and proteinuria <300 mg/day, complete remission.
- Stability of glomerular filtration rate or decrease of 25-50%, no requirement for renal replacement therapy, partial remission.
- Progressive fall in glomerular filtration (>50%) or the need for renal replacement therapy, non-remission (8).

Statistical Analysis

Variables were expressed as mean, standard deviation, and proportions. During the evaluation of study variables, only de-

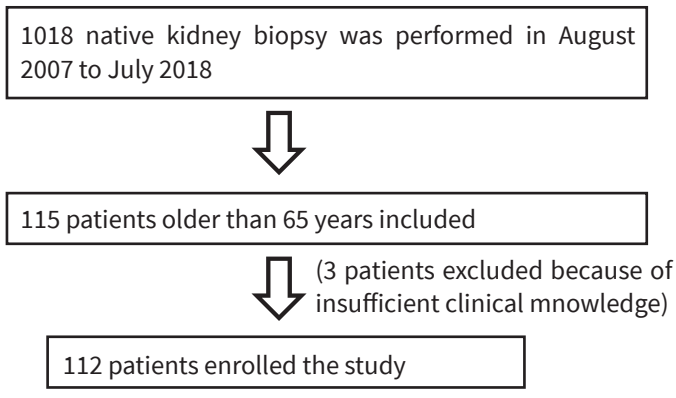

Figure 1. Patients selection.

scriptive statistical methods were used. Data obtained were analyzed using IBM Statistical Package for the Social Sciences software for Windows version 22.0 (IBM SPSS Corp.; Armonk, NY, USA).

RESULTS

Of the 1088 patients in whom kidney biopsies were performed during the 11 years of follow-up, 115 were evaluated. Three patients were excluded due to lack of clinical knowledge. A total of 112 (10.2%) patients were included in the study. Fifty-five patients were women (49%). The mean age of patients was 70.58±4.90 years.

Lower extremity edema was the leading cause of physician admittance (29.5%). The most common biopsy indication was AKI (36.6%). In 42 (37.5%) cases, renal replacement therapy was needed at the time of biopsy (Table 1).

Sufficient samples could be taken in the majority of cases (87.5%). Diagnostic evaluation could also be performed in some of the subjects whose glomeruli were below eight; only three (2.7%) biopsy specimens were reported as not diagnostic.

Glomerulonephritis containing crescents was the most common histopathological diagnosis in older individuals (26.8%) (Table 2) and was most commonly seen in patients with renal biopsy due to AKI (43.9%). Acute interstitial nephritis (n=6, 14.6) and focal segmental glomerulosclerosis (FSGS) (n=4, 9.75%) were among other common diagnoses in patients who underwent renal biopsy because of AKI. Hypertensive nephropathy (n=4, 23.5%) was the leading cause of histopathological diagnosis in patients who underwent biopsy for unidentified CRF. Amyloidosis (n=2, 11.7%) was observed equally as membranoproliferative glomerulonephritis (MPGN) (n=2, 11.7%), diabetic nephropathy (n=2, 11.7%), and non-specific atrophic changes (n=2, 11.7%). As expected, the most common histopathological diagnosis was membranous glomerulonephritis (MGN) (n=8, 27.5%) in patients with nephrotic syndrome. Amyloidosis (n=5, 17.2%) and hypertensive nephropathy (n=4, 13.7%) were followed by a decreasing frequency of MGN. The most common primary cause of renal biopsy due to nephritic syndrome was glomerulonephritis containing crescents (n=9, 69.2%). Hypertensive nephropathy (n=4, 33.3%) was the most common histopathological diagnosis in non-nephrotic proteinuria. Diabetic

Table 1. Baseline demographic, clinical, and laboratory features

Variables	All patients (n=112)	%
Age, years, mean±SD	70.58±4.9	
Female gender, n	55	49.1
Presentation		
Lower extremity edema	33	29.5
Abnormal renal functional tests	27	24.1
Constitutional symptoms	23	20.5
Dysuria, nocturia	11	9.8
Dyspnea	9	8
Hemoptysis	5	4.5
Loin pain	2	1.8
Purpura	2	1.8
Clinical syndrome		
Acute kidney injury	41	36.6
Nephrotic syndrome	29	25.9
Chronic renal failure	17	15.2
Nephritic syndrome	13	11.6
Non-nephrotic proteinuria	12	10.7
Diabetes mellitus	32	28.6
Laboratory values		
Serum creatinine, mg/dL, mean/min-max	2.7/0.61-11.5	
CKD-EPI eGFR (mL/dk/1.73 m^2), mean/min-max	33.17/5-104	
Proteinuria (g/day), mean/min-max	3.91/0.19-27	
Presence of hematuria	31	27.7
Need for renal replacement therapy	42	37.5
Chronicity findings on sonographic evaluation	83	74.1
Increased echogenicity	81	72.3
Atrophy	11	9.8
Parenchymal thinning	6	5.4
Treatment with RAS-blockade	57	50.8

CKD-EPI: chronic kidney disease-epidemiology collaboration; eGFR: estimated glomerular filtration rate; RAS: renin-angiotensin-aldosterone system

nephropathy (n=2, 16.6%), FSGS (n=2, 16.6%) and MGN (n=2, 16.6%) were equally common (Table 3). In addition, 67% patients had a modifiable cause with treatment.

Table 2. Histopathological diagnosis of patients

Diagnosis	n	%
Glomerulonephritis containing crescents	30	26.8
Hypertensive nephropathy	15	13.4
Membranous glomerulopathy	11	9.8
Diabetic nephropathy	10	8.9
Focal segmental glomerulosclerosis	9	8
Acute interstitial nephritis	8	7.1
Amyloidosis	8	7.1
Non-specific atrophic changes	5	4.4
Thrombotic microangiopathy	4	3.6
Pattern of membranoproliferative glomerulonephritis	4	3.6
Non-diagnostic	3	2.7
İgA nephropathy	1	0.9
Lupus nephritis	1	0.9
Crystals nephropathy	1	0.9
Chronic tubulointerstitial nephropathy	1	0.9
Acute tubular necrosis	1	0.9

The majority of patients with glomerulonephritis with crescents had the pauci-immune type (n=20, 66.6%). Of the patients diagnosed with pauci-immune glomerulonephritis, 15 were ANCA-positive (12 patients were MPO-ANCA positive, 3 patients were PR3-ANCA positive) and 5 were ANCA-negative. Nineteen (63%) of the patients who had glomerulonephritis containing crescents had renal replacement therapy at the time of biopsy, and 93% (n=28) of them were provided immunosuppressive treatment. Immunosuppressive therapy was not provided in two patients since spontaneous remission was noted in one and malignancy in the other. Complete remission was achieved in 40% (n=12) of patients with glomerulonephritis containing crescents. During follow-up, four patients died of sepsis secondary to pneumonia, one patient died due to cerebrovascular ischemia, while the cause of death could not be identified in one patient (Table 4).

Malignancy was detected in 24.1% (n=27) of patients. Six patients (5.3%) had a history of malignancy within 5 years prior to renal biopsy. Malignancy was detected in 21 patients (18.7%) after renal biopsy or during follow-up. In patients with malignancy, the most common biopsy indication was nephrotic syndrome (n=13, 48.1%), and the most common histopathological diagnoses were hypertensive nephropathy (n=7, 26%), amyloidosis (n=5, 18.5%), MGN (n=3, 11.1%), glomerulonephritis containing crescents (n=3, 11%), and acute interstitial nephritis (n=3, 11%) in decreasing order. Plasma cell dyscrasia was the most common malignancy (n=8, 29.6%) (Table 5-6).

Complications were reported in eight patients (7.1%). Perirenal hematoma was seen on imaging studies, and all individuals

Table 3. Renal biopsy diagnoses by clinical presentation in older individuals

Acute kidney injury	n (%) 41 (36.6)	Nephrotic syndrome	n (%) 29 (25.9)	Chronic renal failure	n (%) 17 (15.2)	Nephritic syndrome	n (%) 13 (11.6)	Non-nephrotic proteinuria	n (%) 12 (10.7)
Glomerulonephritis containing crescents	18 (43.9)	Membranous glomerulopathy	8 (27.5)	Hypertensive nephropathy	4 (23.5)	Glomerulonephritis containing crescents	9 (69.2)	Hypertensive nephropathy	4 (33.3)
Acute interstitial nephritis	6 (14.6)	Amyloidosis	5 (17.2)	Pattern of MPGN	2 (11.7)	Diabetic nephropathy	3 (23.1)	Diabetic nephropathy	2 (16.6)
FSGS	4 (9.75)	Hypertensive nephropathy	4 (13.7)	Diabetic nephropathy	2 (11.7)	Non-specific atrophic changes	1 (7.6)	FSGS	2 (16.6)
Hypertensive nephropathy	3 (7.3)	FSGS	2 (6.8)	Amyloidosis	2 (11.7)			Membrano us glomerulopathy	2 (16.6)
Thrombotic microangiopathy	2 (4.8)	Diabetic nephropathy	2 (6.8)	Non-specific atrophic changes	2 (11.7)			Lupus nephritis	1 (8.3)
Crystals nephropathy	1 (2.4)	Glomerulonephritis containing crescents	2 (6.8)	Glomerulonephritis containing crescents	1 (5.8)			Thrombotic microangio pathy	1 (8.3)
Other	7 (17)	Other	6 (20.6)	Other	4 (23.5)				

FSGS: focal segmental glomerulosclerosis; GN: glomerulonephritis; MPGN: membranoproliferative glomerulonephritis; TMA: thrombotic microangiopath

Table 4. Clinical characteristics of patients with glomerulonephritis containing crescents

Glomerulonephritis containing crescents	n=30	(%26.7)
Type of disease		
Anti-GBM	1	3.3
Immune-complex	6	20.0
Pauci-immune	20	66.6
Not specified	3	10.0
Age, years, mean±SD	71.6±5.8	
Woman	18	(60)
Diabetes mellitus	3	(10)
Laboratory values, mean/min-max		
Serum creatinine, mg/dL	3.43/1-9	
CKD-EPI eGFR (mL/dk/1.73 m^2)	12.76/5.04-57.4	
Proteinuria (g/day)	2.52/0.19-15.2	
Presence of hematuria	18	(60)
Need for renal replacement therapy	19	(63.3)
Pulmonary infiltrates	9	(30)
Total kidney chronicity score	5.45±1.98	
Treatment with immunosuppression*	28	(93)
Complete remission	12	(40)
Partial remission	5	(16.7)
No remission	11	(36.7)
Unknown	2	(6.7)
Follow-up, day, mean/min-max	980/54-3640	
Mortality	6	(20)

*Initial immunosuppression: cyclophosphamide (500-750 mg/m^2), and methylprednisolone (pulse+0.5-1 mg/kg/day)±plasmapheresis; maintaining immunosuppression: azathioprine (1-2 mg/kg/day), and methylprednisolone

Table 5. Association between renal biopsy and malignancy

Patients with malignancy n, % 27 (24.1)	Clinical diagnosis in patients with malignancy n, %	Histopathological diagnosis of patients with malignancy n, %
Malignancy prior to biopsy, 6, 5.3%	Nephrotic syndrome 13, 48.1%	Hypertensive nephropathy, 7, 26%
Malignancy after biopsy, 21, 18.7%	Acute kidney failure, 6, 22%	Amyloidosis, 5, 18.5%
No malignancy, 71, 63.4%	Chronic renal failure, 4, 14.8%	Membranous GN, 3, 11%
Not investigated for malignancy, 13, 11.6%	Nephritic syndrome, 3, 11%	Glomerulonephritis containing crescents, 3, 11%
	Non-nephrotic proteinuria, 1, 3.7%	Acute interstitial nephritis, 3, 11%
		Pattern of MPGN, 3, 11%
		Non-specific atrophic changes, 1, 3.7%
		FSGS, 1, 3.7%
		TMA, 1, 3.7%

FSGS: focal segmental glomerulosclerosis; GN: glomerulonephritis; MPGN: membranoproliferative glomerulonephritis; TMA: thrombotic microangiopathy

Table 6. Types of malignancies

	n	%
Plasma cell dyscrasia	8	(29.6)
Colorectal cancer	5	(18.5)
Bladder cancer	3	(11.1)
Gastric carcinoma	2	(7.4)
Squamous cell carcinoma (scalp, tongue)	2	(7.4)
Prostate cancer	1	(3.7)
Liver cancer	1	(3.7)
Renal cell carcinoma	1	(3.7)
Lung cancer	1	(3.7)
Peritoneal carcinomatosis	1	(3.7)
Chronic myeloid leukemia	1	(3.7)
Non-Hodgkin's lymphoma	1	(3.7)

needed blood transfusion following the biopsy. Arterial embolization was performed in one patient during follow-up who died of hemorrhagic shock (Table 7).

DISCUSSION

In our study, the rate of diagnosis requiring specific treatment was in parallel with the previous important studies in this age group. In a retrospective study by Moutzouris et al. (9), patients from Mayo Clinic who were 80 years and older were evaluated, and the rate of diagnosis that required specific immunosuppressive treatment was reported as 67%. Another study in which the kidney biopsy results were evaluated by Nair et al. (10) from USA, 40% of the patients were found to have treatable diseases such as crescentic nephritis, membranous nephropathy, minimal change disease, and acute interstitial nephritis. Diagnosis of curable renal disease was more frequent in patients with AKI of undetermined cause, nephrotic, and nephritic syndrome than in other biopsy indications (CKD, non-nephrotic proteinuria, etc.).

Table 7. Complication rate

	Number of complications	%
Erythrocyte transfusion	8	7.1
Angiographic intervention	1	0.89
Death	1	0.89

Renal biopsy was performed in many patients (74.1% of study population) in spite of findings revealing chronicity, which were observed in ultrasonography. The mean kidney chronicity score was 5.85±2.26 according to the classification suggested by Sethi et al (6). In addition, 67% patients had a modifiable cause with treatment. AKI of undetermined cause, nephrotic syndrome, and nephritic syndrome remarkably warrants evaluation by kidney biopsy even in the presence of findings that suggest chronic injury.

The most striking result of our study is that 24% (n=27) of patients who underwent renal biopsy had malignancy, and 10.7% (n=12) of these patients were diagnosed with malignancy in the early period (<3 months) following renal biopsy. The investigation of the etiology of the kidney disease led to the discovery of a solid organ tumor in four patients and plasma cell dyscrasia in eight patients. Findings pointing to renal disease provided identification of malignancy in a considerable number of patients. Evaluation of malignancy that occurred within a 5-year period prior to or just after renal biopsy is the primary feature of our work that differentiates it from previous studies (4, 5).

Regarding concerns on the fragility of elderly patients, clinicians often feel anxious about performing renal biopsy and commencing immunosuppressive treatment even if needed. However, the increase in size of the elderly population and the increase in the incidence of kidney diseases has led them to reevaluate this attitude. Literature data reveal that advanced age alone does not make a significant difference in terms of biopsy-related complications. In a meta-analysis performed by Corapi et al. (11), native kidney biopsies in all age groups were evaluated. It has been reported that an age of 40 years or older, female gender, use of 14-gauge or thicker needles, serum creatinine level ≥2 mg/dL at the time of biopsy, and AKI as the indication of biopsy were associated with increased frequency of bleeding requiring transfusion. In the same study, the rate of bleeding requiring transfusion was reported as 0.9%, angiographic intervention requirement rate was 0.6%, and death rate was 0.02%. In another study that was performed in older individuals, the prevalence of gross hematuria after biopsy was reported as 15.4%. No bleeding requiring blood transfusion or death was reported (12). The high complication rates in our study can be explained by older age, higher serum creatinine level at the time of biopsy, use of 14-gauge biopsy needles, and the high number of patients who had unexplained AKI as the indication for biopsy. Chronicity findings noted in the majority of our cases may also have contributed to the high complication rates. Renal parenchymal thinning and atrophy in sonographic evaluation warrant attention against possible complications.

Obtaining sufficient diagnostic material via renal biopsy is of particular importance in older individuals. Kohli et al. (12) reported that the rate of securing sufficient material for diagnosis in the elderly was 92.3%. In 87.5% of our renal biopsies, sufficient material (≥8 glomeruli and 1 artery) could be obtained, while in 97.3% of all participants, the histopathological diagnosis was clearly made.

Our findings that AKI was the most common indication for renal biopsy, and glomerulonephritis containing crescents was the most common diagnosis that supported the findings of previous studies (9, 10, 13-15). In Turkey, a study from the Gülhane Military Medical Academy (15) addressing the benefits of kidney biopsy in older individuals reported that the most common indication for biopsy over the age of 65 years was acute renal failure. In this patient group, the most common histopathologic diagnosis was acute interstitial nephritis and crescentic glomerulonephritis (15). In a retrospective analysis again from Turkey in two central regions, Antalya and Aydın, FSGS was the most frequent histopathological diagnosis in renal biopsy for patients above 65 years. In this study, renal biopsy was performed only in patients with nephrotic proteinuria, which may explain the most common diagnosis of FSGS (16). A statement made by Turkey in the Ege University is that renal biopsy was performed in 1702 adult patients (mean age 40±15 years). The most common indication for renal biopsy was nephrotic syndrome in all age groups. In this study, the most common histopathological diagnosis was reported as membranous nephropathy. The mean age in the biopsy group was lower than that in our study, which may be the reason for the difference in biopsy indication and diagnosis (17).

In a Japanese study evaluating crescentic glomerulonephritis in older individuals by Uezono et al. (18) 11 patients had improvement in renal function, while no response and deterioration was noted in 2 and 3 patients, respectively. In our study, 40% (n=12) of patients with crescent-containing glomerulonephritis had complete remission and in 16% (n=5) partial remission was achieved. As immunosuppressive treatment was not reported in the Japanese study, it is not possible to comment on the difference in remission rates.

CONCLUSION

Kidney biopsy is valuable in patients over 65 years of age as it provides significant guidance in obtaining a definite diagnosis and planning specific treatment.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Commitee of Dokuz Eylül University (Approval Date: October 11, 2018; Approval No: 2018/25-01).

Informed Consent: Written informed consent was obtained from the patients who were included in this study.

Peer-review: Externally peer-reviewed.

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