

Relationship between renal biopsy and renal survival in elderly patients with chronic kidney disease: A propensity score matching approach

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Abstract

Background The effect of renal biopsy on the prognosis of elderly patients with chronic kidney disease remains unclear. Thus, in this study, we aimed to evaluate the relationship between renal biopsy and renal survival in this population.

Methods In this multi-centre retrospective study, the baseline characteristics among three groups were balanced by propensity matching. All patients were divided into three groups according to age and renal biopsy. The clinicopathological features at biopsy and renal outcomes during the follow-up were collected and analysed. Renal outcomes were defined as estimated glomerular filtration rate < 15 mL/min/1.73 m², dialysis, renal transplantation, or death. The prognostic effects of renal biopsy were evaluated using Cox regression models.

Results A total of 1313 patients were identified. After propensity matching, 390 patients were selected and divided into three groups. After a total follow-up period of 55 months, 20 (13.3%) patients (47.6% group 1 vs 7.41% group 2 vs 39.1% group 3) reached renal outcomes. No significant differences were found in renal outcomes among aged patients whether they underwent renal biopsy or not. Cox regression analysis revealed risk factors in aged patients including low albumin and high levels of proteinuria and serum creatinine ($P < 0.05$). Platelet count was significant only in aged patients who underwent renal biopsy (hazard ratio: 0.642, $P < 0.05$).

Conclusion In conclusion, renal biopsy in the elderly has not shown benefits in terms of renal survival, conservative treatment appears to be a viable therapeutic option in the management of those people.

Introduction

Chronic kidney disease (CKD) is a condition that poses a serious threat to human health and quality of life. According to the latest statistics from the National Kidney Foundation, 26 million people were affected with CKD in the United States as at 2012 and that caused a heavy social and economic burden.^{1–3}

The disease is characterised by varied clinical manifestations, which earned it the name ‘silent killer’. Accurate diagnosis and early prevention of disease progression are crucial to the treatment of CKD. The diagnosis of renal diseases largely depends on renal biopsy, which is considered as the gold standard. Since its first use in humans in 1951, it has been widely applied to diagnosing renal diseases, quantifying disease severity, and assessing disease prognosis.^{4–5}

Percutaneous renal biopsy plays an important role in the diagnosis of kidney diseases. A series of precise treatments, such as hormone therapy, can be carried out only after the pathological classification of renal diseases. Although percutaneous renal biopsy is well known and safe, various complications including needing blood transfusion, developing an arteriovenous fistula and requiring a surgery procedure, which have an incidence rate between 1.2 and 8.0%, occur among the biopsied population.^{6–7} The need for blood transfusion (0.9%–5.3%) is the most common major complication in patients.^{8–10} With the improvement in renal biopsy techniques, the incidence of serious and minor complications has decreased to 0.1%¹¹, and between 10%^{6,12} and 86%¹³, respectively.

The proportion of the elderly population is constantly growing because of improving living standards and medical conditions.¹⁴ However, the basic condition of elderly people is poor; therefore, some minor complications after renal puncture may lead to poor prognosis. Without a kidney biopsy, elderly people cannot receive the same standard treatment as the younger patients. Therefore, the advantages and disadvantages of renal biopsy in elderly people need to be discussed. With the continuous expansion of indications for renal biopsy, renal biopsy in elderly patients has been removed from the relative contraindications. However, the effect of renal biopsy on the prognosis of elderly patients is not clearly elucidated. In our study, a retrospective analysis of a single-centre renal biopsy cases was conducted to study the prognosis of elderly patients who underwent renal biopsy and standard treatment according to pathological classification with the aim of providing a basis for clinical decision-making for elderly patients with renal disease.

Materials And Methods

Study population and grouping

This was a multi-centre retrospective study. Four department of Nephrology in different cities of Zhejiang province participated in this experiment. These cities were Hangzhou, Tiantai, Tongxiang, and Haining. All patients with CKD diagnosis who were recorded in the Hospital Information System database from 1 January 2011 to 31 December 2017 were identified. The inclusion criteria were as follows: clinically diagnosed CKD, age ≥ 18 years, and willingness to sign the informed consent form. Patients who had diseases leading to poor prognosis, including heart failure, cerebral infarction, severe infection, cancer, severe malnutrition, and severe anaemia, were excluded.

The patients were divided into three groups. Group I included patients aged 18–70 years who received renal puncture biopsy and then underwent glucocorticoid or immunosuppressive therapy. Group II was composed of elderly patients aged over 70 years who received renal puncture biopsy and then underwent glucocorticoid or immunosuppressive therapy. Group III was the elderly non-biopsy group aged ≥ 70 years who did not receive

renal biopsy and glucocorticoid or immunosuppressive therapy; they only received symptomatic support treatment. The remaining patients who were under 70 years old and did not undergo renal biopsy were excluded.

Data collection

The data of patient's demographic information, primary disease diagnosis, and other laboratory test results were obtained from each patient's medical history. Clinical parameters included sex, age, blood pressure (BP), hypertension²⁶ (defined as systolic BP \geq 140 mmHg and/or diastolic BP \geq 90 mmHg or requirement for anti-hypertensive therapy), diabetes²⁷ (defined as fasting blood glucose \geq 7.0 mmol/L and/or 2 h postprandial plasma glucose \geq 11.1 mmol/L or requirement for anti-diabetes therapy) haemoglobin, platelet count, total protein, serum albumin, serum creatinine), total cholesterol and triglycerides.

Renal biopsies

In supine position, two renal biopsies were performed with a Tru-cut needle under the guidance of B-ultrasound. After the operation, the patients were bandaged with pressure abdominal belt and had absolute bed rest for 24 hours. Anticoagulants were not used routinely. All renal biopsies were performed by two experienced doctors.

Outcomes of interest

The primary endpoint was renal outcome including eGFR $<$ 15 mL/min/1.73 m², dialysis, renal transplantation, or death. The renal outcomes were derived from the patients' follow-up medical records. Some patients had incomplete data; these data were supplemented by face-to-face interview or telephone follow-up.

Statistical analysis

Statistical analysis was performed using SPSS 20.0 (SPSS, Inc., Evanston, IL) and R x64 3.6.0 (Development Core Team, New Zealand). A 2-sided P-value $<$ 0.05 indicates statistical significance. Continuous data with a normal distribution were expressed as mean \pm SD and compared using Student t-tests. Continuous data with a skewed distribution were expressed as median (inter-quartile range) and were analysed using Wilcoxon rank sum tests. Categorical variables were summarised as frequencies and percentages, and comparisons were calculated using chi-square tests.

Because of the differences in the baseline characteristics among patients in the three groups (Table 1), propensity score matching was used to select a cohort of patients with certainly similar baseline characteristics. The propensity score was estimated with the use of a non-parsimonious multivariable logistic regression model²⁸, with renal biopsy and age as dependent variables and diabetes; hypertension; platelet count; haemoglobin, total protein, albumin, serum creatinine, triglyceride, and cholesterol levels; and proteinuria as covariates (Table 1). We performed 1:1 matching using nearest neighbour matching with a calliper width of 0.2 standard deviation of the propensity scores. Standardised differences were conducted for all the baseline covariates before and after matching to indicate prematch imbalance and postmatch balance. Standardised differences greater than 10% were defined as a meaningful difference.

Table 1
Baseline characteristics of patients before and after propensity score matching

Group	Observed data						Matched data					
	G1	G2	G3	P	Standardised difference, %		G1	G2	G3	P	Standardised difference, %	
					G1 vs G2	G2 vs G3					G1 vs G2	G2 vs G3
Total patients, no.	130	1028	335				130	130	130			
Female, no. (%)	47 (36.15)	678 (43.80)	116 (42.96)				47 (36.15)	62 (47.69)	44 (33.85)			
Age, years	77 (75, 79)	55 (50, 62)	80 (76, 85)				77 (75, 79)	55 (50, 62)	80 (76, 85)			
Diabetes, no. (%)	31 (23.84)	195 (18.97)	52 (22.13)	0	6.4	3.970	31 (23.84)	33 (25.38)	31 (23.84)	0.998	2.7	0
Hypertension, no. (%)	104 (80)	463 (45.04)	157 (66.80)	0	84.53	47.93	104 (80)	101 (77.69)	104 (80)	0.976	9.5	0
Haemoglobin, g/L	119.73 ± 23.74	129.56 ± 24.83	116.59 ± 23.92	0	40.47	13.17	119.73 ± 23.74	121.62 ± 19.49	121.24 ± 24.06	0.952	8.73	6.33
Platelet count, 10 ⁹ /L	191.48 ± 70.24	210.69 ± 76.89	186.35 ± 65.23	0.001	26.09	7.57	191.48 ± 70.23	190.12 ± 64.92	192.40 ± 84.62	0.991	2.01	1.18
Total protein, g/L	57.26 ± 11.36	62.8 ± 12.02	60.85 ± 11.88	0.021	47.34	30.85	57.264 ± 11.36	57.24 ± 13.00	57.12 ± 11.93	0.999	0.20	1.24
Albumin, g/L	24.77 ± 9.38	30.36 ± 9.54	28.23 ± 8.66	0.004	48.54	27.28	24.77 ± 9.38	24.74 ± 8.71	24.61 ± 8.71	0.874	0.27	1.77
Scr, mmol/L	128.8 (92.20, 261.65)	94.55 (75.18, 142.67)	124.6 (92.20, 229.5)	0	39.84	3.86	128.80 (92.20, 261.65)	124.6 (88.60, 219.50)	123.4 (80.85, 243.60)	0.978	3.19	4.50
Triglyceride, mmol/L	2.75 ± 0.66	2.31 ± 1.82	1.54 ± 0.73	0	40.72	30.59	2.75 ± 0.66	2.74 ± 0.70	2.73 ± 0.69	0.992	2.48	3.55
Cholesterol, mmol/L	5.2 (4.04, 6.04)	5.23 (4.30, 6.66)	4.65 (3.85, 5.64)	0.001	14.06	22.30	5.20 (4.04, 6.04)	4.99 (4.26, 6.83)	4.79 (3.74, 6.62)	0.923	3.09	7.99
Proteinuria, g/d	3.12 ± 0.27	1.71 ± 3.27	2.19 ± 0.87	0	146.98	454.88	3.12 ± 0.27	3.11 ± 0.33	3.09 ± 0.24	0.921	3.32	11.74
Corticosteroids, no. (%)	29 (22.31)	391 (38.04)	112 (47.66)				29 (22.31)	36 (27.69)	47 (36.15)			
Immunosuppressive agents, no. (%)	10 (7.69)	305 (29.67)	47 (20)				10 (7.69)	18 (13.85)	29 (22.3)			

In the matched cohort, the renal survival rates were estimated using the Kaplan-Meier method, and the log-rank test was performed for comparisons. The factors associated with renal outcomes were identified using univariable Cox proportional hazards models. The proportional hazards assumption was evaluated in each multivariable Cox model, and if the assumption was violated, time-dependent covariates were used for adjustments. The results are shown as hazard ratio (HR), 95% confidence interval (CI) and P-value.

Results

Study population

A total of 1593 patients who met our inclusion criteria were identified for this study and were divided into three groups. Before propensity-score matching, differences were found among the three groups in several of the baseline variables (Table 1). After the matching, 130 patients who were older than 70 years and did not undergo renal biopsy were matched with 130 patients who were older than 70 years and underwent renal biopsy and 130 patients who were younger than 70 years and underwent renal biopsy. The propensity score was estimated with renal biopsy and age as dependent variables, and diabetes; hypertension; platelet count; haemoglobin, total protein, albumin, serum creatinine, triglyceride, and cholesterol levels; and proteinuria as covariates. After matching, the standardised differences were less than 10.0% for all covariates in the model, indicating

that only small differences occurred among the three groups (Table 1). We did not put the medication situation into the model; we speculated that a causal relationship existed between it and the kidney biopsy.

Renal survival of patients according to age and renal biopsy

After a total follow-up period of 55 months, 92 (13.3%) patients (47.6% group 1 vs 7.41% group 2 vs 39.1% group 3) showed good renal outcomes. A total of 16 (10.7%) patients died, and 4 (2.7%) patients developed end-stage renal disease (ESRD). Kaplan-Meier curves (Fig. 1) showed that the renal survival rates calculated from the combined events at 10, 20, 30, 40 and 50 months were 76.2%, 61.9%, 57.1%, 57.1% and 52.4% in group 1; 96.3%, 92.6%, 92.6%, 92.6% and 92.6% in group 2; and 87.0%, 78.3%, 73.9%, 60.9% and 60.9% in group 3, respectively. No significant difference was observed in the renal survival rate of combined events (death or ESRD) between the different choices of renal biopsy in elderly patients.

Blood parameters

As shown in Table 2, there were no significant differences in renal outcomes among elderly patients who did and did not undergo renal biopsy (HR: 0.75, P = 0.53) according to univariate analysis; among those who underwent renal biopsy, the prognosis was better in younger than in older patients (HR: 0.13, P = 0.01). We then constructed multivariable Cox models of the groups. As we expected, regardless of factors we adjusted, the prognosis of younger patients was always better than that of older patients among those who had renal biopsy. No significant differences were found in renal outcomes among elderly patients whether they underwent renal biopsy or not after adjustment for sex in model 1 (HR: 0.75, P = 0.52), after adding hypertension and diabetes in model 2 (HR: 1.09, P = 0.89), after adding urine parameters (haematuresis and proteinuria) in model 3 (HR: 0.77, P = 0.75) or after adding blood parameters (haemoglobin, platelet count, albumin, serum creatinine) in model 4 (HR: 0.79, P = 0.81). However, according to groups 1 and 3, renal biopsy did not seem to be related to good prognosis in elderly patients.

Table 2
Association of renal biopsy and ages with renal survival by Cox regression analysis after propensity score matching

Model	Hazard ratios (95% CI)	P-value
Univariate		
G2 (vs. G1)	0.13 (0.03, 0.57)	0.01
G3 (vs. G1)	0.75 (0.30, 1.84)	0.53
Model 1: sex		
G2 (vs. G1)	0.13 (0.03, 0.58)	0.01
G3 (vs. G1)	0.75 (0.30, 1.84)	0.52
Model 2: Model 1 + hypertension and diabetes		
G2 (vs. G1)	0.17 (0.04, 0.80)	0.02
G3 (vs. G1)	1.09 (0.30, 3.95)	0.89
Model 3: Model 1 + haematuresis and proteinuria		
G2 (vs. G1)	0.15 (0.03, 0.89)	0.04
G3 (vs. G1)	0.77 (0.15, 4.02)	0.75
Model 4: Model 1 + haemoglobin, platelet, albumin, and creatinine levels		
G2 (vs. G1)	0.18 (0.02, 1.36)	0.04
G3 (vs. G1)	0.79 (0.12, 5.27)	0.81

In addition, to identify the associated risk factors of composite renal outcomes (death or ESRD) in elderly patients with nephrotic syndrome, univariate and multivariate analyses were performed. As shown in Tables 3 and 4, Cox regression analysis revealed mostly similar risk factors in aged patients, including low albumin and high proteinuria and serum creatinine levels (P < 0.05). Notably, platelet count was significant only in elderly patients who underwent renal biopsy (HR: 0.642, P < 0.05).

Table 3
Associated risk factors of renal survival in renal biopsy and aged patients

Variables	Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Sex	1.28 (0.34, 4.78)	0.72	1.08 (0.65, 1.76)	0.76
Diabetes	1.69 (1.24, 2.31)	< 0.001	1.54 (0.66, 3.54)	0.31
Hypertension	2.99 (1.56, 5.74)	< 0.001	1.98 (1.06, 3.67)	0.03
Proteinuria	1.55 (1.19, 2.01)	< 0.001	2.51 (1.45, 4.34)	< 0.001
Haematuresis	1.89 (1.29, 2.76)	< 0.001	1.79 (0.72, 4.47)	0.21
Haemoglobin	0.89 (0.83, 0.95)	< 0.001	0.93 (0.36, 2.38)	0.88
Platelet count	0.79 (0.68, 0.91)	0.04	0.64 (0.49, 0.83)	< 0.001
Albumin	0.76 (0.58, 0.98)	< 0.001	0.62 (0.46, 0.82)	< 0.001
Creatinine	2.15 (1.36, 3.39)	< 0.001	1.88 (1.29, 2.73)	< 0.001

Table 4
Associated risk factors of renal survival in non-renal biopsy and aged patients

Variables	Univariate		Multivariate	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Sex	0.62 (0.13, 3.02)	0.56	1.56 (0.66, 3.68)	0.31
Diabetes	1.36 (1.13, 1.63)	0.24	1.57 (0.69, 3.54)	0.27
Hypertension	3.42 (1.64, 7.11)	< 0.001	2.70 (1.49, 4.87)	< 0.001
Proteinuria	1.28 (1.10, 1.48)	< 0.001	1.29 (1.11, 1.50)	< 0.001
Haematuresis	1.11 (1.04, 1.18)	< 0.001	0.99 (0.21, 4.77)	0.99
Haemoglobin	0.88 (0.81, 1.02)	0.38	0.98 (0.91, 1.06)	0.67
Platelet count	1.01 (0.99, 1.02)	0.32	1.01 (0.99, 1.03)	0.41
Albumin	0.83 (0.74, 0.93)	< 0.001	0.31 (0.19, 0.51)	< 0.001
Creatinine	1.98 (1.32, 2.97)	< 0.001	2.52 (1.16, 5.49)	0.02

Discussion

To the best of our knowledge, this was the first study to include elderly patients in the investigation of renal survival benefit of renal biopsy. We believe that this is also the first clinical study on renal biopsy based on big data and a propensity score matching approach, which can raise the quality of evidence from this study. With the problems associated with an increasingly aging population, our work has important clinical implications and a significant social meaning.

A previous study¹⁵ showed that early guidance of renal biopsy may confer significant benefits in preserving renal function in patients. Compared with other patients, patients with CKD stages 1 and 2 had significantly better outcomes. This is consistent with the results of studies on patients with high cardiovascular risk.^{16, 17} In an observational study, kidney biopsy also showed significant benefits for elderly patients with acute renal failure.¹⁸ In all patients with suspected glomerulonephritis, kidney biopsies also had a benefit for kidney survival in patients of all ages. Current indications for renal biopsy are derived from surveys and expert opinions.^{19, 20} However, previous studies defined specific diseases and the spectrum of kidney disease varies by age. Our study was not limited to a specific disease but considered all types of elderly patients with CKD. When all patients were taken together, we found that kidney biopsy did not definitively improve the prognosis of elderly patients with CKD.

We speculated that this may be related to the following points. Firstly, the spectrum of renal diseases is different in different age groups, mainly primary renal disease in younger people and secondary renal disease in older people.^{21, 22} The Japan Renal Biopsy and Kidney Disease Registry was established in 2007 by researchers from the standardisation committee for the diagnosis of kidney pathology and to form a working group on the kidney biopsy database of the Japanese Kidney Society. Diabetic nephropathy and amyloid nephropathy had the highest proportion of patients

with nephrotic syndrome aged ≥ 65 years, followed by primary glomerular disease. However, the most common causes of CKD in elderly people, such as diabetic nephropathy, are not treated with drugs, which makes effective treatment impossible even if the diagnosis is clear. Secondly, many elderly people with CKD are generally in a poor condition. Even if the pathological diagnosis is clear, it is difficult for them to receive adequate immunosuppressive treatment as younger patients, which results in the mismatch between diagnosis and treatment. We have observed in clinical practice that the use of immunosuppressive agents similar to that in younger patients after renal biopsy can cause severe adverse effects in elderly patients, including bleeding, wasting, and even fatal infections.²³ Thirdly, the existing guidelines are mainly for middle-aged and young patients. The types, dosages, and treatment courses of drugs in the existing guidelines may not be appropriate for elderly patients, leading to difficulty in achieving effective treatment after definite diagnosis of renal biopsy. Finally, this study only focused on the endpoint of composite renal survival (ESRD or death), not on renal function changes. Based on previous studies, after renal biopsy, diagnosis for treatment can better protect renal function than symptomatic treatment, delay kidney function decline and significantly prolong survival time in younger patients, thus improving their quality of life.²⁴ In elderly patients, it does not improve life expectancy because many of them die from other causes.

In this study, we found that baseline proteinuria and serum creatinine levels were independent risk factors for renal prognosis in elderly patients, regardless of whether renal biopsy was performed or not, and higher haemoglobin levels predicted a relatively long renal survival time. Platelets were an independent risk factor for prognosis in elderly patients who underwent renal biopsy, but not in elderly patients who did not undergo renal biopsy. This is consistent with previous studies on complications of renal biopsy. The most common complication of renal biopsy in the general population is post-puncture haemorrhage,²⁵ which is more pronounced in older people with poor coagulation, so lower platelets may predict poor prognosis due to renal puncture. Therefore, we believe that for elderly patients with poor general conditions, in addition to the traditional standard treatment for definite pathological classification by renal puncture, symptomatic treatments for their general condition, such as creatinine, haematuria, proteinuria, and albumin level, can also improve their prognosis, and prevent a series of complications caused by renal biopsy, reduce patient suffering and improve survival.

This study has several limitations. Firstly, this was a single-centre retrospective study with a maximum follow-up of 55 months, which is not long enough considering the onset of the disease; because of the outbreak of 2019 new coronavirus pneumonia in China, our follow-up was suspended. Therefore, we will continue to follow up these patients as soon as possible. Secondly, treatment may play a role in patient outcomes, but treatment options were flexible based on physicians' clinical decisions, particularly since immunosuppression has not been standardised. Thus, this unadjusted factor may compromise the final conclusion. Finally, taking a large CKD population into consideration, baseline imbalance problem might have occurred. We have adjusted the baseline close to the equilibrium through propensity matching, but this led to a reduction in sample size. Therefore, future studies on the determination of strict indications, assessment of patient satisfaction, and medical economics are warranted. However, ethical concerns may prevent such trials.

Conclusion

In conclusion, renal biopsy in elderly people has not shown benefits in terms of renal survival. The indications and risks of renal biopsy should therefore be prudently taken into consideration. Our findings may help prevent unnecessary biopsy, with its accompanying complications, in elderly patients. Compared to a radical treatment strategy based on renal biopsy, conservative treatment appears to be a viable therapeutic option in the management of elderly people.

Declarations

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Authors' contributions QH and YWL designed and directed the project. XL, SZY, WS, YML, JJ, JGG, and LZ carried out data collection. XL and YWL participated in data analysis. XL, YWL and QH wrote the manuscript. All authors discussed the results and approved the manuscript as submitted. All authors approved the final version of the manuscript.

Compliance with ethical standards

Conflict of interest XL and SZY are the students of Zhejiang Chinese Medical University. WS, YML, QH and YWL are doctors of Zhejiang Provincial People's Hospital. JJ, JGG and LZ are professors of Chinese Medical Nephrology Key Laboratory of Zhejiang Province. All authors report no personal conflicts of interest relevant to this study.

Informed consent Written informed consent was obtained from all patients, where required.

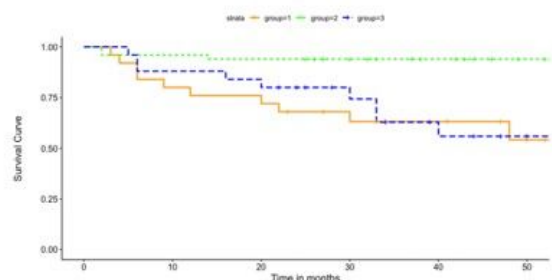
Ethical approval The study protocol was authorized by the Ethics Committee of Zhejiang Provincial People's Hospital. The 4 departments of Nephrology all belong to Zhejiang Provincial People's Hospital Health Alliance, they share the same Ethics Committee and follow the same ethics rules. All procedures performed were in accordance with the ethical standards of the Chinese National Committee on Health Research Ethics and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Figures



Log-rank test: P G1 vs. G2 < 0.001, P G1 vs. G3 = 0.697

Group 1: non-renal biopsy and age > 70 patients, group 2: renal biopsy and age < 70 patients, group 3: renal biopsy and age > 70 patients

No significant difference was observed in the renal survival rate of combined events (death or ESRD) between the different choices of renal biopsy in aged patients.

Figure 1

Renal survival curves of patients after propensity score matching.