

Clinicopathological Features and Outcomes of Diabetic Nephropathy with Crescent Formation



Ayano Saito, Kaori Ito, Fumito Abe, Mizuho Nara, Shin Okuyama, Atsushi Komatsuda, Hideki Wakui, Naoto Takahashi.
Department of Hematology, Nephrology and Rheumatology, Akita University, Japan.



Introduction and objectives

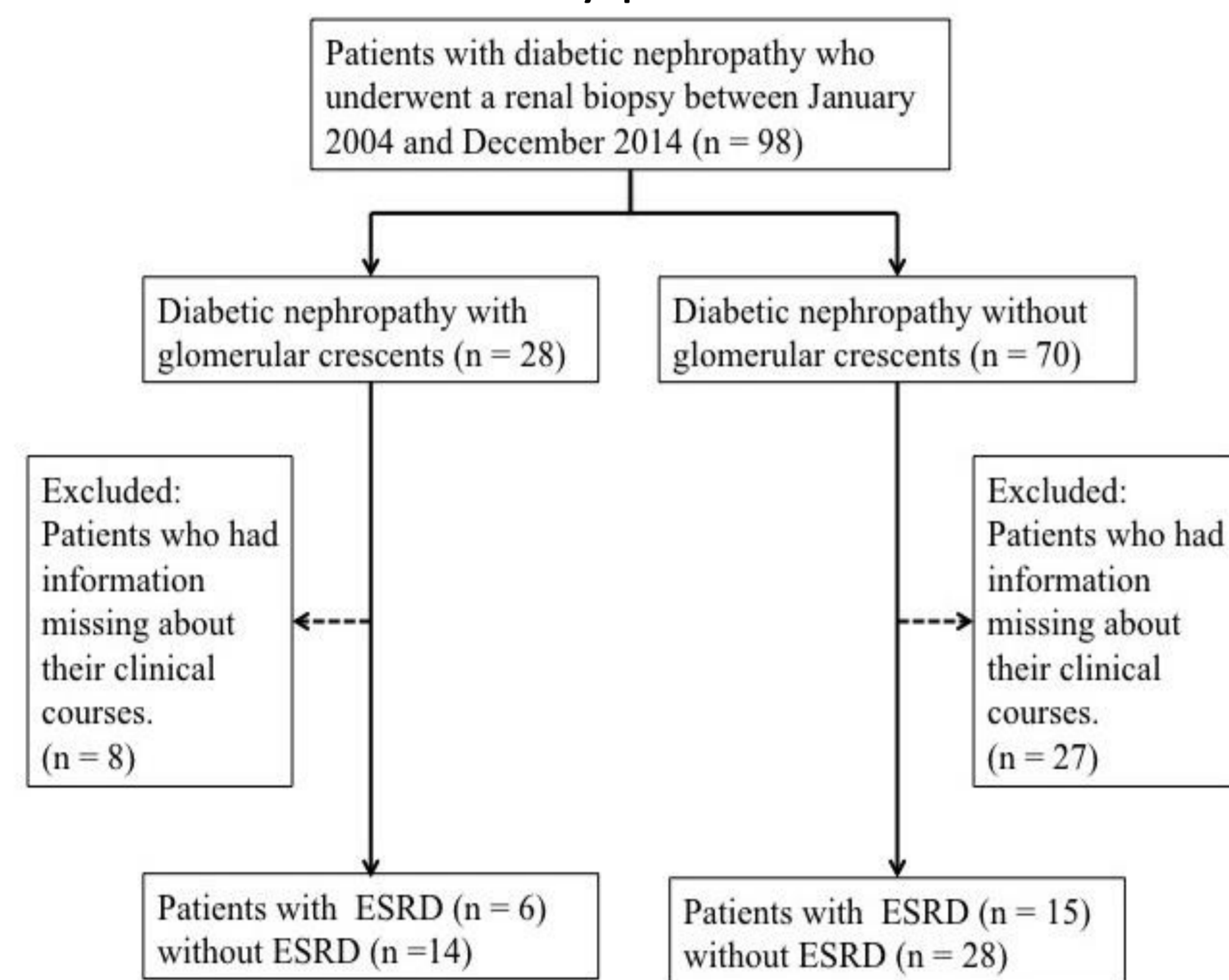
Diabetic nephropathy (DN) is the primary cause of end-stage renal disease (ESRD) in developed countries⁽¹⁾. The renal pathological changes in DN are classified by various degrees of severity of glomerular lesions, interstitial lesions, and vascular lesions by the Renal Pathology Society⁽²⁾. It has been already known that the severity of glomerular and interstitial lesions had a significant impact on renal outcomes⁽³⁾. But the presence of crescent in the glomerular disease of DN has been ignored in the literature^(4,5). Our aim of this study is to investigate the clinicopathological features of DN with crescent formation and to determine whether crescent formation affects renal outcomes.

Methods

We compared clinicopathological features and outcomes in 20 DN patients with crescent formation (crescent group) and 43 DN patients without crescent formation (control group). All patients were Japanese, entering outpatient clinics of Akita University Hospital and its affiliated hospitals between 2004 and 2014. We assessed the renal biopsy specimens by using the classification of Renal Pathology Society⁽²⁾. Clinical and laboratory data were collected at the time of renal biopsy, and renal outcomes were defined by progression to ESRD requiring dialysis. All patients with crescent formation had negative ANCA, anti-GBM antibody, or ANA.

Results

Study profile



Characteristics of patients

| | DMN with crescents (n = 20) | DMN without crescents (n = 43) | P |
|-----------------------------------|-----------------------------|--------------------------------|--------------------|
| Male/female | 16/4 | 31/12 | 0.502 ^a |
| Age (years) | 55.0 (36.0 - 81.0) | 60.0 (18.5 - 40.8) | 0.663 ^b |
| BMI (Kg/m ²) | 24.4 (19.8 - 32.1) | 25.2 (18.5 - 40.8) | 0.317 ^b |
| sBP (mmHg) | 147 (107 - 178) | 150 (108 - 199) | 0.616 ^b |
| dBP (mmHg) | 81 (60 - 108) | 80 (63 - 109) | 0.267 ^b |
| eGFR (ml/min/1.73m ²) | 31.5 (9.6 - 117.7) | 41.5 (2.14 - 133.2) | 0.345 ^b |
| Proteinuria (g/day) | 4.8 (0.3 - 9.9) | 3.4 (0.1 - 9.5) | 0.368 ^b |
| No data | 4 | 13 | |
| Hematuria (≥5/HPF) | 10 | 20 | 0.796 ^a |
| HbA1c (NSGP) | 6.15 (4.5 - 13.1) | 6.35 (5.0 - 13.1) | 0.572 ^b |
| Total cholesterol (mg/dl) | 190 (90 - 361) | 203 (111 - 342) | 0.300 ^b |
| CRP (mg/dl) | 0.36 ± 0.74 | 0.53 ± 1.04 | 0.547 ^c |
| Diabetic retinopathy | 12 | 19 | 0.815 ^a |
| No data | 2 | 13 | |
| antihypertensive drug | 18 | 36 | 0.507 ^a |

^aPearson's chi-square test; ^bMann-Whitney's U test; ^cWelch's t test.

Characteristics of patients

| | DMN with crescents (n = 20) | DMN without crescents (n = 43) | P |
|---|-----------------------------|--------------------------------|-------|
| Crescents (%) | 8 (3-40) | - | - |
| Glomerular classification (n) | | | |
| Class I (Mild or nonspecific LM changes) | 0 | 0 | - |
| Class II a (Mild mesangial expansion) | 2 | 9 | 0.287 |
| Class II b (Severe mesangial expansion) | 1 | 6 | 0.293 |
| Class III (Nodular sclerosis) | 13 | 15 | 0.025 |
| Class IV (Advanced diabetic glomerulosclerosis) | 4 | 13 | 0.394 |
| GBM double contour (n) | 1 | 2 | 0.952 |
| IgG staining (n) | 15 (No data1) | 21 (No data2) | 0.041 |
| IFTA | | | |
| 0 (No IFTA) | 0 | 1 | 0.492 |
| 1 (Mild) | 5 | 9 | 0.718 |
| 2 (Moderate) | 10 | 24 | 0.666 |
| 3 (Severe) | 5 | 9 | 0.718 |
| Interstitial inflammation | | | |
| 0 (Absent) | 0 | 1 | 0.492 |
| 1 (Mild) | 3 | 12 | 0.263 |
| 2 (Moderate) | 14 | 26 | 0.464 |
| 3 (Severe) | 3 | 4 | 0.503 |
| Arteriosclerosis | | | |
| 0 (No intimal thickening) | 1 | 0 | 0.139 |
| 1 (Mild) | 5 | 13 | 0.669 |
| 2 (Moderate to severe) | 14 | 30 | 0.985 |
| Arteriolar hyalinosis | | | |
| 0 (Absent) | 0 | 1 | 0.492 |
| 1 (At least one area) | 0 | 2 | 0.327 |
| 2 (More than one area) | 20 | 40 | 0.226 |

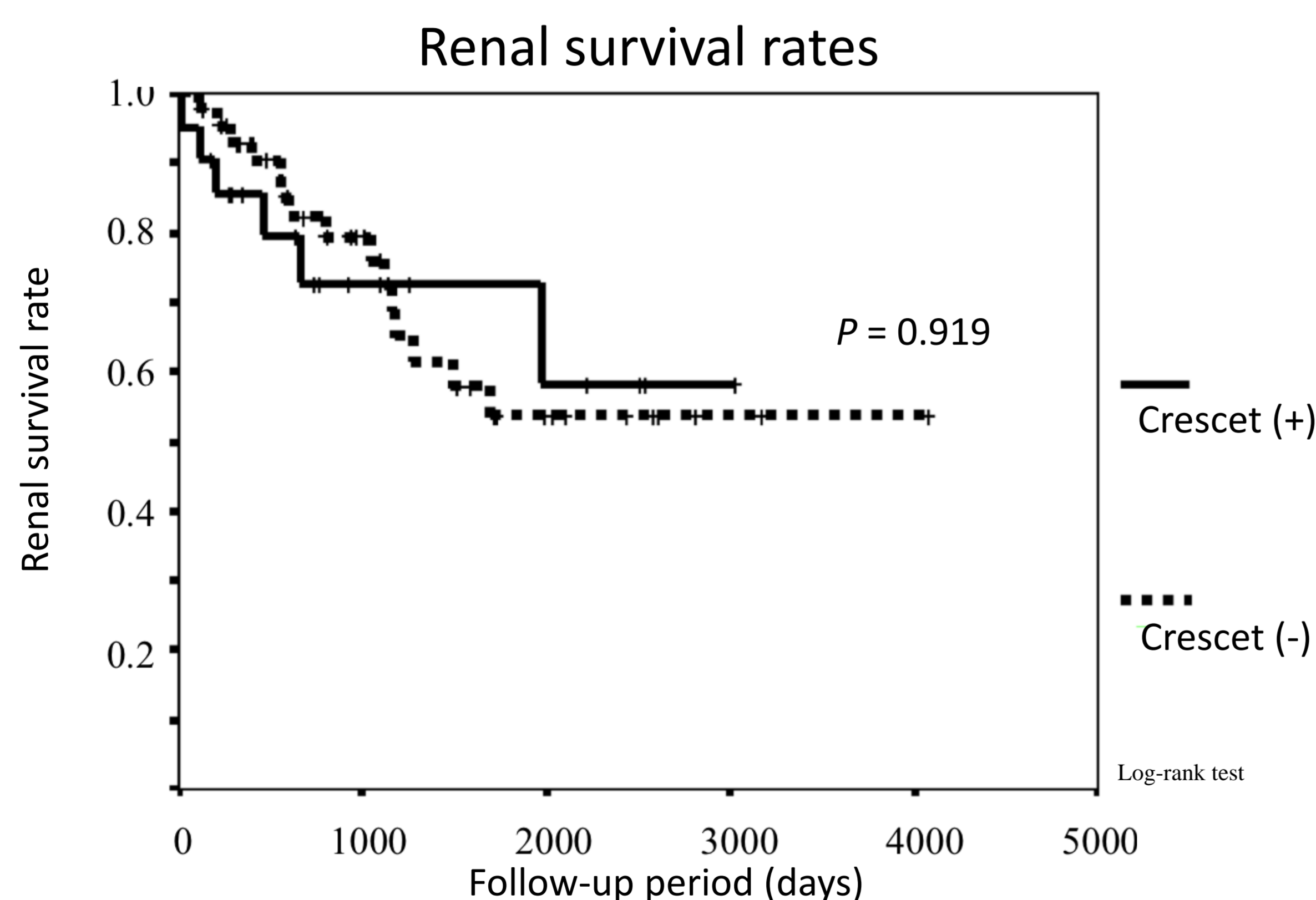
Pearson's chi-square test

Predictors of the risk of ESRD

| Univariate model | RR | 95% CI | P |
|--|--------|--------------------|--------|
| Sex (male) | 1.485 | 0.499 - 4.417 | 0.477 |
| Age (increased by 1 y) | 0.981 | 0.953 - 1.009 | 0.183 |
| Proteinuria (increased by 1 g/day) | 1.131 | 0.945 - 1.354 | 0.178 |
| eGFR (increased by 1 ml/min/1.73m ²) | 0.961 | 0.937 - 0.987 | 0.003 |
| HbA1c (increased by 1 %) | 1.086 | 0.845 - 1.382 | 0.538 |
| Hypertension | 4.081 | 0.547 - 30.437 | 0.170 |
| Crescent formation | 1.073 | 0.416 - 2.772 | 0.884 |
| Class (III, IV vs I, II a, b) | 2.681 | 0.895 - 8.028 | 0.078 |
| GBM double contour | 0.796 | 0.107 - 5.943 | 0.824 |
| IFTA (3 vs 0-2) | 2.323 | 0.934 - 5.777 | 0.070 |
| Interstitial inflammation (3 vs 0-2) | 17.042 | 5.003 - 58.048 | <0.001 |
| Arteriosclerosis (2 vs 0, 1) | 1.178 | 0.474 - 2.929 | 0.725 |
| Arteriolar hyalinosis (2 vs 0, 1) | 21.628 | 0.002 - 219298.238 | 0.514 |

| Multivariate model | RR | 95% CI | P | |
|---|---------------------------|--------|----------------|--------|
| Model 1 (sex, age, proteinuria, eGFR, HbA1c, Hypertension, crescent formation) | eGFR | 0.967 | 0.939 - 0.996 | 0.026 |
| Model 2 (class, GBM double contour, IFTA, Interstitial inflammation, arteriosclerosis, arteriolar hyalinosis, crescent formation) | Interstitial inflammation | 17.042 | 5.003 - 58.048 | <0.001 |

Cox regression analysis



Conclusions

Crescent formation in DN is detected frequently in patients with glomerular lesion of nodular sclerosis and positive IgG staining. Although both nodular sclerosis and positive IgG staining are known as risk factors of renal death⁽⁶⁾, we have identified that there is no difference in renal outcomes between crescent group and control group. It may suggest that it needs to be careful

for following up DN patients with crescent formation. To the best of our knowledge, this is the first study to show the renal outcomes of DN with crescent formation.

References

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