SUPPLEMENTARY DATA

**Supplementary Table 1.** Number (percentage) of patients according to albuminuria (proteinuria) and eGFR categories at the time of renal biopsy

| Category | Normoalbuminuria | Microalbuminuria | Macroalbuminuria |
|---|---|---|---|
| | Normal proteinuria | Mild proteinuria | Severe proteinuria |
| | (n=43, 16.5%) | (n=55, 21.2%) | (n=162, 62.3%) |
| Urinary albumin (mg/day) | < 30 (n=10) | 30-299 (n=31) | ≥ 300 (n=54) |
| Urinary protein (g/day) | < 0.15 (n=12) | 0.15-0.49 (n=24) | ≥ 0.5 (n=105) |
| Dipstick proteinuria | (-, ±) (n=21) | (1+) (n=0) | ≥ (2+) (n=3) |
| eGFR ≥ 60 ml/min/1.73 $m^2$ (n=106, 40.8%) (n (%)) | 28 (26.4%) | 31 (29.2%) | 47 (44.3%) |
| eGFR < 60 ml/min/1.73 $m^2$ (n=154, 59.2%) (n (%)) | 15 (9.7%) | 24 (15.6%) | 115 (74.7%) |

SUPPLEMENTARY DATA

**Supplementary Table 2.** Hazard ratios of renal events, cardiovascular events, and all-cause mortality for patients stratified by albuminuria (proteinuria) and eGFR categories estimated by the Cox proportional hazards model

| Renal events | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Variables | No. of Patients | No. of Events (%) | | | | | HR | (95% CI) | | | | | *P* |
| All | 229 | 118 | ( | 51.5 | % | ) | | | | | | | |
| Normoalbuminuria (normal protinuria) and eGFR ≥ 60 ml/min/1.73 $m^2$ | 24 | 4 | ( | 16.7 | % | ) | 1.00 | ( | Reference | | | ) | |
| Normoalbuminuria (normal protinuria) and eGFR < 60 ml/min/1.73 $m^2$ | 14 | 1 | ( | 7.1 | % | ) | 0.83 | ( | 0.09 | - | 7.55 | ) | 0.87 |
| Microalbuminuria (mild proteinuria) and eGFR ≥ 60 ml/min/1.73 $m^2$ | 27 | 10 | ( | 37.0 | % | ) | 2.47 | ( | 0.77 | - | 7.91 | ) | 0.13 |
| Microalbuminuria (mild proteinuria) and eGFR < 60 ml/min/1.73 $m^2$ | 21 | 7 | ( | 33.3 | % | ) | 2.27 | ( | 0.65 | - | 7.90 | ) | 0.20 |
| Macroalbuminuria (severe proteinuria) and eGFR ≥ 60 ml/min/1.73 $m^2$ | 37 | 25 | ( | 67.6 | % | ) | 8.99 | ( | 3.07 | - | 26.37 | ) | <0.01 |
| Macroalbuminuria (severe proteinuria) and eGFR < 60 ml/min/1.73 $m^2$ | 106 | 71 | ( | 67.0 | % | ) | 20.82 | ( | 7.12 | - | 60.85 | ) | <0.01 |
| Cardiovascular events | | | | | | | | | | | | | |
| Variables | No. of Patients | No. of Events (%) | | | | | HR | (95% CI) | | | | | *P* |
| All | 233 | 62 | ( | 26.6 | % | ) | | | | | | | |
| Normoalbuminuria (normal protinuria) and eGFR ≥ 60 ml/min/1.73 $m^2$ | 25 | 6 | ( | 24.0 | % | ) | 1.00 | ( | Reference | | | ) | |
| Normoalbuminuria (normal protinuria) and eGFR < 60 ml/min/1.73 $m^2$ | 14 | 3 | ( | 21.4 | % | ) | 1.43 | ( | 0.34 | - | 6.03 | ) | 0.63 |
| Microalbuminuria (mild proteinuria) and eGFR ≥ 60 ml/min/1.73 $m^2$ | 27 | 7 | ( | 25.9 | % | ) | 1.03 | ( | 0.34 | - | 3.13 | ) | 0.95 |
| Microalbuminuria (mild proteinuria) and eGFR < 60 ml/min/1.73 $m^2$ | 22 | 8 | ( | 36.4 | % | ) | 1.39 | ( | 0.46 | - | 4.14 | ) | 0.56 |
| Macroalbuminuria (severe proteinuria) and eGFR ≥ 60 ml/min/1.73 $m^2$ | 38 | 8 | ( | 21.1 | % | ) | 1.51 | ( | 0.51 | - | 4.48 | ) | 0.45 |
| Macroalbuminuria (severe proteinuria) and eGFR < 60 ml/min/1.73 $m^2$ | 107 | 30 | ( | 28.0 | % | ) | 3.11 | ( | 1.15 | - | 8.39 | ) | <0.05 |
| All-cause mortality | | | | | | | | | | | | | |

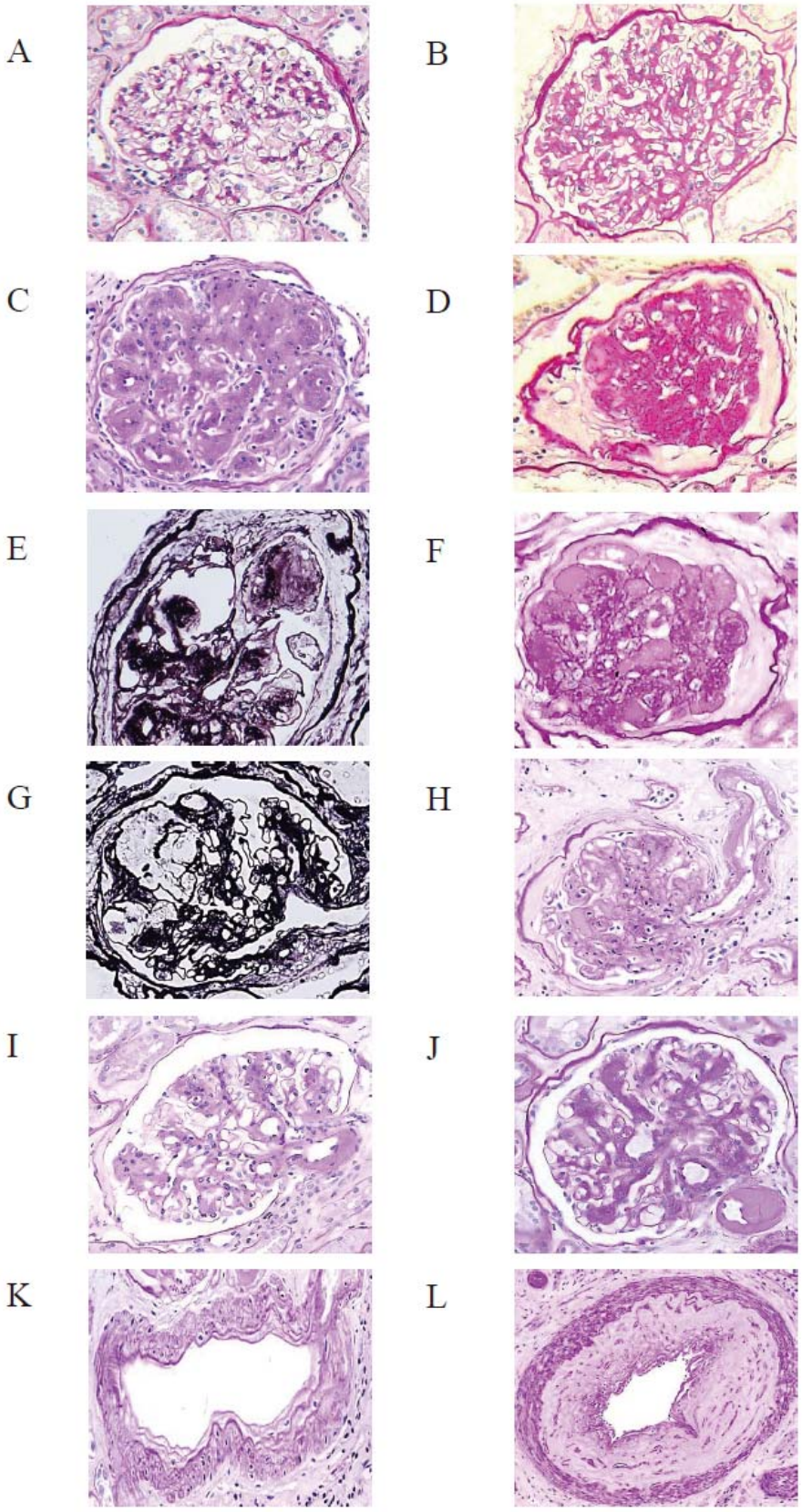
SUPPLEMENTARY DATA

| Variables | No. of Patients | No. of Events (%) | | | | | HR | (95% CI) | | | | | *P* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| All | 233 | 45 | ( | 19.3 | % | ) | | | | | | | |
| Normoalbuminuria (normal protinuria) and eGFR ≥ 60 ml/min/1.73 $m^2$ | 25 | 3 | ( | 12.0 | % | ) | 1.00 | ( | Reference | | | ) | |
| Normoalbuminuria (normal protinuria) and eGFR < 60 ml/min/1.73 $m^2$ | 14 | 1 | ( | 7.1 | % | ) | 0.58 | ( | 0.06 | - | 5.70 | ) | 0.64 |
| Microalbuminuria (mild proteinuria) and eGFR ≥ 60 ml/min/1.73 $m^2$ | 27 | 3 | ( | 11.1 | % | ) | 0.60 | ( | 0.12 | - | 3.05 | ) | 0.54 |
| Microalbuminuria (mild proteinuria) and eGFR < 60 ml/min/1.73 $m^2$ | 22 | 2 | ( | 9.1 | % | ) | 0.37 | ( | 0.06 | - | 2.26 | ) | 0.28 |
| Macroalbuminuria (severe proteinuria) and eGFR ≥ 60 ml/min/1.73 $m^2$ | 38 | 7 | ( | 18.4 | % | ) | 2.37 | ( | 0.61 | - | 9.24 | ) | 0.22 |
| Macroalbuminuria (severe proteinuria) and eGFR < 60 ml/min/1.73 $m^2$ | 107 | 29 | ( | 27.1 | % | ) | 5.87 | ( | 1.62 | - | 21.25 | ) | <0.01 |

Data are hazard ratios (95% CI). Hazard ratios are adjusted for age and gender. The group of patients with normoalbuminuria (normal proteinuria) and eGFR ≥ 60 ml/min/1.73 $m^2$ served as a reference group.

SUPPLEMENTARY DATA

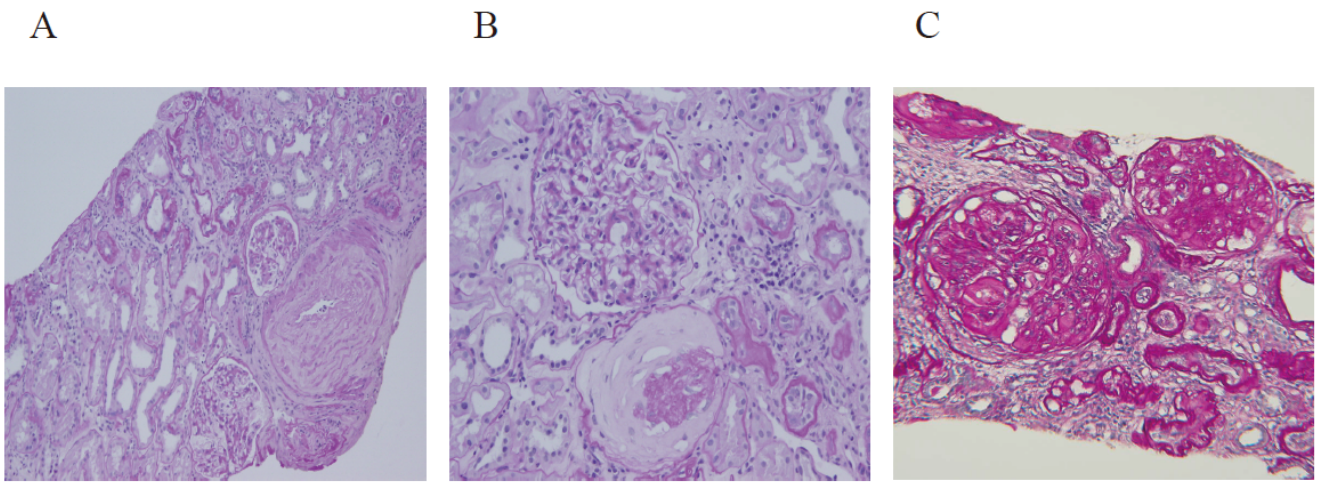
**Supplementary Figure 1.** Representative microscopic findings of glomerular and vascular lesions in diabetic nephropathy



SUPPLEMENTARY DATA

Panels A, B, C, and D show various grades of diffuse lesions. Panel A shows Grade 1 of diffuse diabetic glomerulosclerosis. The lesion is local within each glomerulus and focal within the kidney (PAS stain ×200). Panel B shows Grade 2 of diffuse diabetic glomerulosclerosis. Mesangial thickening is diffuse within the glomerulus and generalized throughout the kidney (PAS stain ×200). Panel C shows Grade 3 of diffuse diabetic glomerulosclerosis. The capillary lumina are narrowed and only locally obliterated (PAS stain ×200). Panel D shows Grade 4 of diffuse diabetic glomerulosclerosis. There is general luminal narrowing. The whole glomerulus has become ischemic and appears to be hyalinized (PAS stain ×200). Panel E shows the glomerulus with nodular lesions (PAM stain ×200). Panel F shows the glomerulus with exudative lesions (PAS stain ×200). Panel G shows the glomerulus with mesangiolysis (PAM stain ×200). Panels H, I, J, K, and L show various grades of vascular lesions. Panel H shows Grade 1 of arteriolar hyalinosis. A light PAS-positive thickening is observed but less than half of the circumference of the arteriole in many arterioles (PAS stain ×200). Panel I shows Grade 2 of arteriolar hyalinosis. Most vessel walls are moderately thickened with PAS-positive deposition without apparent luminal narrowing (PAS stain ×200). Panel J shows Grade 3 of arteriolar hyalinosis. A heavy thickening of the majority of the vessel walls is seen with luminal narrowing or obliteration (PAS stain ×200). Panel K shows Grade 1 of arteriosclerosis. Intimal thickening is less than the media thickness (PAS stain ×200). Panel L shows Grade 2 of arteriosclerosis. Intimal thickening is greater than the media thickness (PAS stain ×200).

**Supplementary Figure 2.** Representative microscopic findings of patients with low eGFR classified based on the absence or presence of albuminuria




Panels A and B show representative microscopic findings of patients with low eGFR and normoalbuminuria. Panel A shows mild diffuse diabetic glomerulosclerosis associated with disproportionately severe arteriosclerosis and moderate to severe tubulointerstitial lesions (PAS stain ×100). Panel B shows mild diffuse diabetic glomerulosclerosis and global glomerular sclerosis (PAS stain ×200). Panel C shows representative microscopic finding of patients with low eGFR and macroalbuminuria. Advanced glomerular lesions (diffuse and exudative lesions) associated with severe tubulointerstitial lesions are shown (PAS stain ×100).