Table 6 The frequency of pathological diagnoses as classified by pathogenesis in J-RBR 2009 and 2010

Classification	2009			2010			Total		
	Total biopsies (n = 3,336)		Native kidneys (n = 3,165)	Total biopsies (n = 4,106)		Native kidneys (n = 3,869)	Total biopsies (n = 7,442)		Native kidneys (n = 7,034)
	n	%	%[a]	n	%	%[a]	n	%	%[a]
IgA nephropathy	1,003	30.1	31.6	1,177	28.7	30.4	2,180	29.3	31.0
Primary glomerular disease (except IgA nephropathy)	862	25.8	27.2	1,090	26.5	28.1	1,952	26.2	27.7
Diabetic nephropathy	184	5.5	5.8	192	4.7	5.0	376	5.1	5.3
Renal graft	161	4.8	–	235	5.7	–	396	5.3	–
Lupus nephritis	137	4.1	4.3	220	5.4	5.7	357	4.8	5.1
MPO-ANCA positive nephritis	129	3.9	4.1	191	4.7	4.9	320	4.3	4.5
Hypertensive nephrosclerosis	123	3.7	3.9	157	3.8	4.1	280	3.8	4.0
Purpura nephritis	64	1.9	2.0	108	2.6	2.8	172	2.3	2.4
Amyloid nephropathy	45	1.3	1.4	58	1.4	1.5	103	1.4	1.5
Infection-related nephropathy	27	0.8	0.9	31	0.8	0.8	58	0.8	0.8
Thin basement membrane disease	26	0.8	0.8	39	1.0	1.0	65	0.9	0.9
PR3-ANCA positive nephritis	13	0.4	0.4	11	0.3	0.3	24	0.3	0.3
Alport syndrome	10	0.3	0.3	16	0.4	0.4	26	0.3	0.4
Thrombotic microangiopathy	9	0.3	0.3	8	0.2	0.2	17	0.2	0.2
Anti-GBM antibody-type nephritis	8	0.2	0.3	16	0.4	0.4	24	0.3	0.3
Others	535	16.0	16.7	557	13.6	13.6	1,092	14.7	15.4
Total	3,336	100.0	100.0	4,106	100.0	100.0	7,442	100.0	100.0

MPO myeloperoxidase, *ANCA* anti-neutrophil cytoplasmic antibody, *PR3* proteinase 3, *GBM* glomerular basement membrane

[a] Patients classified as either "Renal graft" or "Renal transplantation" in other categories were also excluded

The rates of primary glomerular disease (except IgAN) combined with that of IgAN in native renal biopsies were 59.3 %, 56.5 %, 58.8 %, and 58.5 % in 2007, 2008, 2009, and 2010 in the J-RBR. A recent report from a single center in Japan gave the rates as 77.8 % and 75.9 % between 1979 and 2008 and between 2004 and 2008, respectively [5]. In the present report for the J-RBR, the peak distribution of age was in the sixties in the combined data for 2009 and 2010. The difference in the rates of primary glomerular disease including IgAN may have been due to the higher mean ages of native biopsy cases in the J-RBR compared to the single center in this period (mean age, 46.7 vs. 40.8 years; age of the peak number, sixties vs. twenties), because the incidence of secondary glomerular disease increases in elderly patients, as reported previously [5].

IgAN is still the most frequently diagnosed disease in native kidney biopsies in Japan (33.0 %, 30.2 %, 31.6 %, and 30.4 % of cases in 2007, 2008, 2009, and 2010 in the J-RBR) [1, 4–6] similar to other Asian countries [7, 8] and some European countries [9, 10]. The peak distribution of age ranges was the twenties in 2009 and thirties in 2010. In patients with IgAN, the majority (68.1 %) of renal biopsies were performed in CKD stages G1 and G2, with median proteinuria less than 1 g per day (Table 18), suggesting that there was a relatively early diagnosis of this biopsy-proven disease.

In the present clinical data, the degree of proteinuria increased with the progression of the CKD stage, and was more than 1 g per day for the median value in patients with CKD stages G4 and G5 (Tables 18, S1, S2). Previously, the best single predictor for renal deterioration was severe proteinuria on urine dipstick testing (≥100 mg/dL), followed by hypoalbuminemia, mild hematuria, serum total protein levels, diastolic blood pressure, and histological grade, in a cohort study with 10 years follow-up from 1995 in Japan, the cohort of which exhibited a younger median age (27.7 years) and a peak distribution of age ranges in the teens [11, 12]. A recent report suggested that IgAN with nephrotic syndrome had a worse renal outcome compared to IgAN with non-nephrotic syndrome unless partial or complete remission was achieved [13]. Further studies are necessary to elucidate the risk factors or predictors for renal deterioration in IgAN in the present era utilizing the J-RBR, possibly as part of a new secondary clinical study.

MN was the most common histopathology in terms of primary glomerular disease other than IgAN in 2007

Table 7 The frequency of pathological diagnoses as classified by histopathology in J-RBR 2009 and 2010

Classification	2009			2010			Total		
	Total biopsies (n = 3,336)		Native kidneys (n = 3,165)	Total biopsies (n = 4,106)		Native kidneys (n = 3,869)	Total biopsies (n = 7,442)		Native kidneys (n = 7,034)
	n	%	%[a]	n	%	%[a]	n	%	%[a]
Mesangial proliferative glomerulonephritis	1,346	40.3	42.5	1,388	33.8	35.8	2,734	36.7	38.8
Membranous nephropathy	333	10.0	10.5	418	10.2	10.8	751	10.1	10.7
Minor glomerular abnormality	293	8.8	9.2	559	13.6	14.4	852	11.4	12.1
Crescentic and necrotizing glomerulonephritis	180	5.4	5.7	262	6.4	6.8	442	5.9	6.3
Focal segmental glomerulosclerosis	167	5.0	5.2	211	5.1	5.4	378	5.1	5.3
Nephrosclerosis	163	4.9	5.2	208	5.1	5.4	371	5.0	5.3
Renal graft	151	4.5	–	227	5.5	–	378	5.1	–
Membranoproliferative glomerulonephritis (types I and III)	85	2.5	2.7	97	2.4	2.5	182	2.4	2.6
Chronic interstitial nephritis	71	2.1	2.1	61	1.5	1.6	132	1.7	1.8
Sclerosing glomerulonephritis	63	1.9	2.0	44	1.1	1.1	107	1.4	1.5
Endocapillary proliferative glomerulonephritis	61	1.8	1.9	67	1.6	1.7	128	1.7	1.8
Acute interstitial nephritis	45	1.3	1.4	62	1.5	1.6	107	1.4	1.5
Acute tubular necrosis	9	0.3	0.3	10	0.2	0.2	19	0.3	0.2
Dense deposit disease	3	0.1	0.1	5	0.1	0.1	8	0.1	0.1
Others	366	11.0	11.3	487	11.9	12.5	853	11.5	12.0
Total	3,336	100.0	100.0	4,106	100.0	100.0	7,442	100.0	100.0

[a] Patients classified as either "Renal graft" or "Renal transplantation" in other categories were also excluded

Table 8 The frequency of pathological diagnoses as classified by histopathology in primary glomerular disease except IgA nephropathy in native kidneys in J-RBR 2009 and 2010

Classification	2009		2010		Total	
	n	%	n	%	n	%
Membranous nephropathy	259	30.1	330	30.3	589	30.2
Minor glomerular abnormalities	216	25.1	408	37.5	624	32.0
Mesangial proliferative glomerulonephritis	167	19.4	86	7.9	253	13.0
Focal segmental glomerulosclerosis	113	13.1	149	13.7	262	13.4
Membranoproliferative glomerulonephritis (types I and III)	48	5.6	51	4.7	99	5.1
Crescentic and necrotizing glomerulonephritis	19	2.2	18	1.7	37	1.9
Endocapillary proliferative glomerulonephritis	8	0.9	24	2.2	32	1.6
Chronic interstitial nephritis	7	0.8	3	0.3	10	0.5
Sclerosing glomerulonephritis	7	0.8	3	0.3	10	0.5
Nephrosclerosis	5	0.6	7	0.6	12	0.6
Acute interstitial nephritis	1	0.1	0	–	1	0.1
Acute tubular necrosis	0	–	1	0.1	1	0.1
Others	11	1.3	9	0.8	20	1.0
Total	861	100.0	1,089	100.0	1,950	100.0

Table 9 The frequency of pathological diagnoses as classified by pathogenesis in nephrotic syndrome in native kidneys in J-RBR 2009 and 2010

Classification	2009		2010		Total	
	n	%	*n*	%	*n*	%
Primary glomerular disease (except IgA nephropathy)	442	62.3	696	66.7	1,138	64.9
Diabetic nephropathy	85	12.0	78	7.5	163	9.3
IgA nephropathy	30	4.2	36	3.5	66	3.8
Lupus nephritis	30	4.2	58	5.6	88	5.0
Amyloid nephropathy	27	3.8	41	3.9	68	3.9
Infection-related nephropathy	6	0.8	7	0.7	13	0.7
Hypertensive nephrosclerosis	6	0.8	10	0.9	16	0.9
Purpura nephritis	4	0.6	8	0.8	12	0.7
Alport syndrome	3	0.4	0	–	3	0.2
Thrombotic microangiopathy	1	0.1	1	0.1	2	0.1
PR3-ANCA positive nephritis	1	0.1	0	–	1	0.1
MPO-ANCA positive nephritis	1	0.1	2	0.2	3	0.2
Others	74	10.4	106	10.2	180	10.3
Total	710	100.0	1,043	100.0	1,753	100.0

MPO myeloperoxidase, *ANCA* anti-neutrophil cytoplasmic antibody, *PR3* proteinase 3

Table 10 The frequency of pathological diagnoses as classified by histopathology in primary glomerular disease except IgA nephropathy in nephrotic syndrome in native kidneys in J-RBR 2009 and 2010

Classification	2009		2010		Total	
	n	%	*n*	%	*n*	%
Membranous nephropathy	178	40.3	227	32.6	405	35.6
Minor glomerular abnormalities	172	38.9	348	50.0	520	45.7
Focal segmental glomerulosclerosis	47	10.6	82	11.8	129	11.3
Membranoproliferative glomerulonephritis (types I and III)	25	5.7	18	2.6	43	3.8
Mesangial proliferative glomerulonephritis	11	2.5	13	1.9	24	2.1
Crescentic and necrotizing glomerulonephritis	2	0.5	2	0.3	4	0.4
Sclerosing glomerulonephritis	2	0.5	0	–	2	0.2
Endocapillary proliferative glomerulonephritis	1	0.2	5	0.7	6	0.5
Others	4	0.9	1	0.1	5	0.4
Total	442	100.0	696	100.0	1,138	100.0

(31.4 %), 2008 (25.7 %), and 2009 (30.1 %) in the J-RBR and was also the most common type in primary nephrotic syndrome in 2007 (44.0 %) and 2009 (40.3 %) in the J-RBR. MN was also the most common primary cause of nephrotic syndrome in a northern European Caucasian population, with a biopsy rate of 4.5 per million population per year [14]. A total of 68.7 % and 68.8 % of primary MN cases exhibited nephrotic syndrome as the clinical diagnosis at the time of renal biopsy in 2009 and 2010 in the J-RBR. Yokoyama et al. recently reported in their clinical data analysis of 501 cases collected from the combined data of the J-RBR from 2007 to 2010 that nearly half of primary MN (49.1 %) cases showed a daily proteinuria of 3.5 g or higher [15]. The renal survival rate was 60 % at 20 years after diagnosis in patients with primary MN, and the renal survival rate in patients on steroid therapy was significantly higher in patients on supportive therapy alone in Japan [16], while spontaneous remission was reported to be common (32 %) in patients with primary MN with nephrotic syndrome in Spain [17], even in patients exhibiting chronic renal impairment [18]. Whether treatment with renin–angiotensin blockers or immunoglobulins other than steroids has a favorable effect on the renal prognosis of primary MN should be elucidated in future clinical studies.

The minor glomerular abnormalities in primary nephrotic syndrome, which correspond to MCNS, was the most common histopathology reported in 2008 (44.1 %) and 2010 (50.0 %) in the J-RBR. Since MCNS develops in patients at younger ages [5, 15] while primary MN develops in a relatively elderly population [15, 16], the frequency of these diseases may depend on the distribution of

Table 11 The frequency of clinical diagnoses in membranous nephropathy in primary glomerular disease except IgA nephropathy in native kidneys in J-RBR 2009 and 2010

Classification	2009		2010		Total	
	n	%	*n*	%	*n*	%
Nephrotic syndrome	178	68.7	227	68.8	405	68.8
Chronic nephritic syndrome	74	28.6	93	28.2	167	28.4
Recurrent or persistent hematuria	3	1.2	3	0.9	6	1.0
Renal disorder with collagen disease or vasculitis	1	0.4	1	0.3	2	0.3
Hypertensive nephropathy	1	0.4	0	–	1	0.2
Rapidly progressive nephritic syndrome	0	–	1	0.3	1	0.2
Renal disorder with metabolic disease	0	–	1	0.3	1	0.2
Acute nephritic syndrome	0	–	1	0.3	1	0.2
Acute renal failure	0	–	1	0.3	1	0.2
Others	2	0.8	2	0.6	4	0.7
Total	259	100.0	330	100.0	589	100.0

Table 12 The frequency of clinical diagnoses in minor glomerular abnormalities in primary glomerular disease except IgA nephropathy in native kidneys in J-RBR 2009 and 2010

Classification	2009		2010		Total	
	n	%	*n*	%	*n*	%
Nephrotic syndrome	172	79.6	348	85.3	520	83.3
Chronic nephritic syndrome	35	16.2	50	12.3	85	13.6
Recurrent or persistent hematuria	5	2.3	5	1.2	10	1.6
Acute renal failure	1	0.5	0	–	1	0.2
Rapidly progressive nephritic syndrome	1	0.5	1	0.2	2	0.3
Acute nephritic syndrome	1	0.5	1	0.2	2	0.3
Hypertensive nephropathy	0	–	1	0.2	1	0.2
Others	1	0.5	2	0.5	3	0.5
Total	216	100.0	408	100.0	624	100.0

the age ranges of patients registered in each year. Indeed, the rate of native biopsies of subjects younger than 20 years of age slightly increased from 11.4 % in 2009 to 12.7 % in 2010 (Table 3) and the mean age of patients with nephrotic syndrome slightly decreased from 53.5 years in 2009 to 50.1 years in 2010 (Table 5) in the J-RBR.

The average age of rapidly progressive nephritic syndrome was the highest (64.4 years) in the age distribution in the classification of clinical diagnosis in the J-RBR (Table 5). Elderly subjects (65 years and over) comprised nearly 25 % of cases, and very elderly subjects (80 years and over) comprised 2.5 % of the cases in the combined data for 2009 and 2010 in the J-RBR. It has been reported that there were statistically significant differences in the renal disease spectrum between elderly and younger subjects [19, 20]. The frequency of rapidly progressive nephritic syndrome in the clinical diagnosis dramatically increased from 4.0 % in the younger group (20–64 years) to 19.6 % in the very elderly in the combined data from 2007 to November 2011 in the J-RBR [20]. A nationwide survey of rapidly progressive glomerulonephritis (RPGN) was conducted between 1989 and 2007 in Japan, and showed that 64.0 % of patients had pauci-immune-type RPGN, including 42.0 % renal-limited vasculitis, 19.4 % microscopic polyangiitis, and 2.6 % Wegener's granulomatosis (currently granulomatosis with polyangiitis) [21]. Since the frequency of myeloperoxidase–anti-neutrophil cytoplasmic antibody (MPO-ANCA)-positive nephritis has increased recently [22], a further subanalysis of rapidly progressive nephritic syndrome in the J-RBR should be performed to validate the recently published Japanese guidelines for RPGN [23].

Five new secondary research studies of the J-KDR were started in 2009, viz., the J-NSCS, J-IDCS, J-IGACS, J-RPGNCS, and J-DNCS, and the J-PKD was started in 2010. The J-RBR and J-KDR initiated two more clinical

Table 13 The frequency of clinical diagnoses in focal segmental glomerulosclerosis in primary glomerular disease except IgA nephropathy in native kidneys in J-RBR 2009 and 2010

Classification	2009		2010		Total	
	n	%	*n*	%	*n*	%
Chronic nephritic syndrome	62	54.9	55	36.9	117	44.7
Nephrotic syndrome	47	41.6	82	55.0	129	49.2
Rapidly progressive nephritic syndrome	1	0.9	1	0.7	2	0.8
Renal disorder with metabolic disease	1	0.9	3	2.0	4	1.5
Recurrent or persistent hematuria	1	0.9	1	0.7	2	0.8
Hypertensive nephropathy	0	–	2	1.3	2	0.8
Acute nephritic syndrome	0	–	1	0.7	1	0.4
Inherited renal disease	0	–	1	0.7	1	0.4
Others	1	0.9	3	2.0	4	1.5
Total	113	100.0	149	100.0	262	100.0

Table 14 The profile of IgA nephropathy in native kidneys in J-RBR 2009 and 2010

IgA nephropathy	2009	2010	Total
Total native kidney biopsies (*n*)	1,001	1,176	2,177
Average age (years)	38.1 ± 17.2	39.3 ± 17.0	38.7 ± 17.1
Median age (years)	35 (24–52)	38 (26–53)	37 (25–52)
Male, *n* (%)	498 (49.8 %)[a]	585 (49.7 %)	1,083 (49.7 %)
Average age (years)	39.5 ± 18.2[b]	40.5 ± 18.4[b]	40.0 ± 18.3[b]
Median age (years)	38 (24–55)[b]	39 (25–56)	38 (24–56)[b]
Female, *n* (%)	503 (50.2 %)[a]	591 (50.3 %)	1,094 (50.3 %)
Average age	36.6 ± 15.9[b]	38.1 ± 15.4[b]	37.5 ± 15.7[b]
Median age	34 (24–49)[b]	37 (26–49)	36 (25–49)[b]

[a] Ratio indicates percentage of each gender in each biopsy category

[b] $P < 0.05$ compared to other gender

Table 15 Distribution of age ranges and gender in IgA nephropathy in J-RBR in 2009 and 2010

Age (years)	2009			2010			Total		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
0–9	11	5	16	12	9	21	23	14	37
10–19	73	68	141	80	55	135	153	123	276
20–29	91	116	207	91	127	218	182	243	425
30–39	87	115	202	113	153	266	200	268	468
40–49	65	81	146	94	106	200	159	187	346
50–59	87	62	149	84	75	159	171	137	308
60–69	62	45	107	82	48	130	144	93	237
70–79	19	9	28	20	18	38	39	27	66
80+	3	2	5	9	0	9	12	2	14
Total	498	503	1,001	585	591	1,176	1,083	1,094	2,177
Under 20 (%)	16.9	14.5	15.7	15.7	10.8	13.3	16.3	12.5	14.4
65 and over (%)	9.4	5.2	7.3	11.5	5.4	8.4	10.5	5.3	7.9

Table 16 The frequency of classification of clinical diagnoses in IgA nephropathy in native kidneys in J-RBR 2009 and 2010

Clinical diagnosis	2009		2010		Total	
	n	%	*n*	%	*n*	%
Chronic nephritic syndrome	886	88.5	1,064	90.5	1,950	89.6
Recurrent or persistent hematuria	49	4.9	40	3.4	89	4.1
Nephrotic syndrome	30	3.0	36	3.1	66	3.0
Rapidly progressive nephritic syndrome	14	1.4	20	1.7	34	1.6
Acute nephritic syndrome	8	0.8	9	0.8	17	0.8
Renal disorder with collagen disease or vasculitis	4	0.4	1	0.1	5	0.2
Acute renal failure	2	0.2	2	0.2	4	0.2
Drug-induced nephropathy	2	0.2	1	0.1	3	0.1
Renal disorder with metabolic disease	1	0.1	0	–	1	0.0
Hypertensive nephropathy	0	–	1	0.1	1	0.0
Others	5	0.5	2	0.2	7	0.3
Total	1,001	100.0	1,176	100.0	2,177	100.0

Table 17 The frequency of pathological diagnoses as classified by histopathology in IgAN in native kidneys in J-RBR 2009 and 2010

Pathological diagnosis by histopathology	2009		2010		Total	
	n	%	*n*	%	*n*	%
Mesangial proliferative glomerulonephritis	937	93.6	1,111	94.5	2,048	94.1
Endocapillary proliferative glomerulonephritis	12	1.2	2	0.2	14	0.6
Minor glomerular abnormalities	12	1.2	15	1.3	27	1.2
Focal segmental glomerulosclerosis	9	0.9	6	0.5	15	0.7
Crescentic and necrotizing glomerulonephritis	8	0.8	10	0.9	18	0.8
Nephrosclerosis	6	0.6	4	0.3	10	0.5
Membranous nephropathy	4	0.4	2	0.2	6	0.3
Membranoproliferative glomerulonephritis (types I and III)	4	0.4	5	0.4	9	0.4
Sclerosing glomerulonephritis	3	0.3	2	0.2	5	0.2
Chronic interstitial nephritis	1	0.1	2	0.2	3	0.1
Acute interstitial nephritis	0	–	1	0.1	1	0.0
Others	5	0.5	16	1.4	21	1.0
Total	1,001	100.0	1,176	100.0	2,177	100.0

research studies (J-RBR201001 and J-KDR201001) being performed by members of the JSN who had already participated in the registry and who registered cases under the precise regulations presented on the website of the JSN in 2011.

With regard to estimating the number of yearly native renal biopsies in Japan, the Research Group on Progressive Renal Disease from the Ministry of Health, Labor and Welfare of Japan recently reported by a questionnaire method that it was between 18,000 and 21,000 in 2010. The J-RBR may cover nearly one fourth to one fifth of the number of yearly native renal biopsies in Japan in 2010. Since 128,057,352 people resided in Japan in 2010, the estimated rate of renal biopsy was 140.6 to 164.0 per million population. This rate was higher than that in Romania [24], Spain [25], the Czech Republic [10], Denmark [26], and Scotland [27], was similar to that in France [28], and was lower than that in USA, Finland [29], and Australia [30].

There are some limitations in the J-RBR and J-KDR. The J-RBR records three diagnoses for each case, viz., the clinical diagnosis, diagnosis based on the pathogenesis, and the diagnosis based on a histopathological examination, so there may be still some inconsistency in the case records. The terms hypertensive nephropathy, hypertensive nephrosclerosis, nephrosclerosis, and diabetic nephropathy may need to be defined more precisely to improve the accuracy of the report by the J-RBR. The incidence of renal biopsy

Table 18 Distribution of CKD stages and clinical parameters in total in IgA nephropathy in J-RBR: Combined data of 2009 and 2010

	CKD stage					Total	*P* value*
	G1	G2	G3a/b	G4	G5		
Total	663	814	551	111	30	2,169	–
n (%)	30.6	37.5	25.4	5.1	1.4	100.0	–
Age (years), average	23.5 ± 10.9	40.3 ± 13.5	50.9 ± 13.0	55.7 ± 16.2	46.3 ± 20.4	38.7 ± 17.1	<0.0001
Median	22 (17–29)	38 (30–50)	52 (42–61)	59 (44–68)	46 (29–62)	37 (25–52)	<0.0001
Body mass index	21.0 ± 4.0	22.9 ± 3.8	23.6 ± 3.7	23.0 ± 4.5	23.4 ± 5.9	22.5 ± 4.0	<0.0001
Estimated GFR (mL/min/1.73 m^2)	108.2 (96.9–128.0)	75.2 (67.8–82.7)	49.1 (42.0–54.6)	23.6 (20.9–27.6)	8.5 (6.1–12.0)	74.6 (53.8–95.0)	<0.0001
Proteinuria (g/day)	0.30 (0.10–0.81)	0.50 (0.21–1.00)	0.92 (0.40–2.00)	1.60 (0.71–2.84)	2.81 (1.17–4.58)	0.59 (0.22–1.29)	<0.0001
Proteinuria (g/gCr)	0.39 (0.14–0.91)	0.63 (0.28–1.23)	1.03 (0.51–2.01)	1.69 (0.77–4.21)	2.91 (1.30–4.58)	0.70 (0.27–1.47)	<0.0001
Sediment RBC ≥5/hpf (%)	82.4	81.3	74.6	82.0	86.7	80.0	0.0075
Serum creatinine (mg/dL)	0.60 (0.53–0.70)	0.79 (0.70–0.91)	1.16 (1.00–1.36)	2.10 (1.86–2.47)	5.34 (4.06–7.66)	0.81 (0.65–1.07)	<0.0001
Serum albumin (g/dL)	4.15 ± 0.46	4.02 ± 0.49	3.79 ± 0.59	3.45 ± 0.63	3.22 ± 0.59	3.96 ± 0.56	<0.0001
Serum total cholesterol (mg/dL)	184.6 ± 37.4	204.3 ± 46.2	209.9 ± 51.1	211.6 ± 52.3	221.0 ± 58.6	200.2 ± 46.8	<0.0001
Systolic BP (mmHg)	113.9 ± 14.0	123.3 ± 16.2	130.3 ± 17.5	137.6 ± 22.5	147.5 ± 27.9	123.2 ± 18.1	<0.0001
Diastolic BP (mmHg)	67.6 ± 11.4	75.1 ± 12.3	78.9 ± 12.5	81.0 ± 15.6	87.8 ± 18.0	74.2 ± 13.3	<0.0001
Anti-hypertensive agents (%)	13.8	33.3	59.6	75.8	71.4	37.0	<0.0001
Diabetes mellitus (%)	1.5	3.1	7.7	21.1	0.0	4.6	<0.0001

Data are presented as the mean ± SD or the medians (interquartile ranges)

CKD chronic kidney disease, *GFR* glomerular filtration rate, *RBC* red blood cell count, *BP* blood pressure

* ANOVA, Kruskal–Wallis or χ^2-test as appropriate. There are eight (0.4 %) missing values of CKD stage because of inappropriate data for serum creatinine

Table 19 The frequency of classification of clinical diagnoses in other 680 cases than J-RBR in J-KDR 2009 and 2010

Classification	Other cases 2009 (n = 680)		Other cases 2010 (n = 575)		Total (n = 1,255)	
	n	%	n	%	n	%
Chronic nephritic syndrome	165	24.3	72	12.5	237	18.9
Hypertensive nephropathy	142	20.9	43	7.5	185	14.7
Renal disorder with metabolic disease	106	15.6	177	30.8	283	22.5
Nephrotic syndrome	86	12.6	118	20.5	204	16.3
Renal disorder with collagen disease or vasculitis	24	3.5	7	1.2	31	2.5
Rapidly progressive nephritic syndrome	21	3.1	18	3.1	39	3.1
Inherited renal disease	18	2.6	3	0.5	21	1.7
Acute renal failure	9	1.3	10	1.7	19	1.5
Recurrent or persistent hematuria	8	1.2	0	–	8	0.6
Acute nephritic syndrome	5	0.7	4	0.7	9	0.7
Drug-induced nephropathy	5	0.7	0	–	5	0.4
Renal transplantation	2	0.3	9	1.6	11	0.9
Polycystic kidney disease	–	–	82	14.3	82	6.5
Others	89	13.1	32	5.6	121	9.6
Total	680	100.0	575	100.0	1,255	100.0

and the incidence of biopsy-proven renal diseases such as IgAN and primary glomerular disease (except IgAN) could be surveyed in major renal centers in Japan in terms of the epidemiological aspects to work out appropriate countermeasures. In this aspect, the incidence of pediatric IgAN was reported to be 4.5 cases/year per 100,000 children under 15 years of age from 1983 to 1999 in Yonago City, Japan [31], although center variations in the country in terms of the incidence, indications and diagnosis of adult native renal biopsy have been reported [27].

Finally, a committee report of J-KDR including J-RBR in 2009, 2010 and their total was conducted. The J-RBR exhibited the majority of the registry system to elucidate yearly demographic data of renal biopsies in Japan, and J-KDR was utilized to promote advanced clinical research in the field of nephrology in our country.

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Appendix

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References

1. Sugiyama H, Yokoyama H, Sato H, Saito T, Kohda Y, Nishi S, et al. Japan Renal Biopsy Registry: the first nationwide, web-based, and prospective registry system of renal biopsies in Japan. Clin Exp Nephrol. 2011;15:493–503.
2. Churg J, Bernstein J, Glassock RJ, editors. Renal disease, classification and atlas of glomerular disease. 2nd ed. Tokyo: Igaku-Shoin; 1995.
3. Matsuo S, Imai E, Horio M, Yasuda Y, Tomita K, Nitta K, et al. Revised equations for estimated GFR from serum creatinine in Japan. Am J Kidney Dis. 2009;53:982–92.
4. Koyama A, Igarashi M, Kobayashi M. Natural history and risk factors for immunoglobulin A nephropathy in Japan. Research Group on Progressive Renal Diseases. Am J Kidney Dis. 1997;29:526–32.
5. Moriyama T, Suzuki K, Sugiura H, Itabashi M, Tsukada M, Takei T, et al. Frequency of renal disease in Japan: an analysis of 2,404 renal biopsies at a single center. Nephron Clin Pract. 2010;115:c227–36.
6. Nationwide and long-term survey of primary glomerulonephritis in Japan as observed in 1,850 biopsied cases. Research Group on Progressive Chronic Renal Disease. Nephron. 1999;82:205–13.
7. Chang JH, Kim DK, Kim HW, Park SY, Yoo TH, Kim BS, et al. Changing prevalence of glomerular diseases in Korean adults: a review of 20 years of experience. Nephrol Dial Transplant. 2009;24:2406–10.
8. Li LS, Liu ZH. Epidemiologic data of renal diseases from a single unit in China: analysis based on 13,519 renal biopsies. Kidney Int. 2004;66:920–3.
9. Gesualdo L, Di Palma AM, Morrone LF, Strippoli GF, Schena FP. The Italian experience of the national registry of renal biopsies. Kidney Int. 2004;66:890–4.
10. Rychlik I, Jancova E, Tesar V, Kolsky A, Lacha J, Stejskal J, et al. The Czech registry of renal biopsies. Occurrence of renal diseases in the years 1994–2000. Nephrol Dial Transplant. 2004;19:3040–9.
11. Goto M, Kawamura T, Wakai K, Ando M, Endoh M, Tomino Y. Risk stratification for progression of IgA nephropathy using a decision tree induction algorithm. Nephrol Dial Transplant. 2009;24:1242–7.
12. Goto M, Wakai K, Kawamura T, Ando M, Endoh M, Tomino Y. A scoring system to predict renal outcome in IgA nephropathy: a nationwide 10-year prospective cohort study. Nephrol Dial Transplant. 2009;24:3068–74.
13. Kim JK, Kim JH, Lee SC, Kang EW, Chang TI, Moon SJ, et al. Clinical features and outcomes of IgA nephropathy with nephrotic syndrome. Clin J Am Soc Nephrol. 2012;7:427–36.
14. McQuarrie EP, Mackinnon B, Stewart GA, Geddes CC. Membranous nephropathy remains the commonest primary cause of nephrotic syndrome in a northern European Caucasian population. Nephrol Dial Transplant. 2010;25:1009–10 (author reply 1010–1).
15. Yokoyama H, Taguchi T, Sugiyama H, Sato H. Membranous nephropathy in Japan: Analysis of the Japan Renal Biopsy Registry (J-RBR). Clin Exp Nephrol. 2012;16:557–63.
16. Shiiki H, Saito T, Nishitani Y, Mitarai T, Yorioka N, Yoshimura A, et al. Prognosis and risk factors for idiopathic membranous nephropathy with nephrotic syndrome in Japan. Kidney Int. 2004;65:1400–7.
17. Polanco N, Gutierrez E, Covarsi A, Ariza F, Carreno A, Vigil A, et al. Spontaneous remission of nephrotic syndrome in idiopathic membranous nephropathy. J Am Soc Nephrol. 2010;21:697–704.
18. Polanco N, Gutierrez E, Rivera F, Castellanos I, Baltar J, Lorenzo D, et al. Spontaneous remission of nephrotic syndrome in membranous nephropathy with chronic renal impairment. Nephrol Dial Transplant. 2012;27:231–4.
19. Omokawa A, Komatsuda A, Nara M, Fujiwara T, Sato R, Togashi M, et al. Renal biopsy in patients aged 80 years and older: a single-center experience in Japan. Clin Nephrol. 2012;77:461–7.
20. Yokoyama H, Sugiyama H, Sato H, Taguchi T, Nagata M, Matsuo S, et al. Renal disease in the elderly and the very elderly Japanese: analysis of the Japan Renal Biopsy Registry (J-RBR). Clin Exp Nephrol. 2012 (in press).
21. Koyama A, Yamagata K, Makino H, Arimura Y, Wada T, Nitta K, et al. A nationwide survey of rapidly progressive glomerulonephritis in Japan: etiology, prognosis and treatment diversity. Clin Exp Nephrol. 2009;13:633–50.
22. Yamagata K, Usui J, Saito C, Yamaguchi N, Hirayama K, Mase K, et al. ANCA-associated systemic vasculitis in Japan: clinical features and prognostic changes. Clin Exp Nephrol. 2012;16:580–8.
23. Matsuo S, Yamagata K, Makino H, Arimura Y, Muso E, Nitta K, et al. The guideline for rapidly progressive glomerulonephritis. Jpn J Nephrol (in Japanese). 2011;53:509–55.
24. Covic A, Schiller A, Volovat C, Gluhovschi G, Gusbeth-Tatomir P, Petrica L, et al. Epidemiology of renal disease in Romania: a 10 year review of two regional renal biopsy databases. Nephrol Dial Transplant. 2006;21:419–24.
25. Rivera F, Lopez-Gomez JM, Perez-Garcia R. Frequency of renal pathology in Spain 1994–1999. Nephrol Dial Transplant. 2002;17:1594–602.
26. Heaf J, Lokkegaard H, Larsen S. The epidemiology and prognosis of glomerulonephritis in Denmark 1985–1997. Nephrol Dial Transplant. 1999;14:1889–97.
27. McQuarrie EP, Mackinnon B, Young B, Yeoman L, Stewart G, Fleming S, et al. Centre variation in incidence, indication and diagnosis of adult native renal biopsy in Scotland. Nephrol Dial Transplant. 2009;24:1524–8.
28. Simon P, Ramee MP, Boulahrouz R, Stanescu C, Charasse C, Ang KS, et al. Epidemiologic data of primary glomerular diseases in western France. Kidney Int. 2004;66:905–8.
29. Wirta O, Mustonen J, Helin H, Pasternack A. Incidence of biopsy-proven glomerulonephritis. Nephrol Dial Transplant. 2008;23:193–200.
30. Briganti EM, Dowling J, Finlay M, Hill PA, Jones CL, Kincaid-Smith PS, et al. The incidence of biopsy-proven glomerulonephritis in Australia. Nephrol Dial Transplant. 2001;16:1364–7.
31. Utsunomiya Y, Koda T, Kado T, Okada S, Hayashi A, Kanzaki S, et al. Incidence of pediatric IgA nephropathy. Pediatr Nephrol. 2003;18:511–5.

Ⅲ．最近の話題

2．高齢者ネフローゼ症候群

横山　仁

要　旨

わが国の成人ネフローゼ症候群において，その42.4%が65歳以上の高齢者であるとともに高齢者の36.3%，さらに超（後期）高齢者の50.7%がネフローゼ症候群を理由に腎生検が実施されている．高齢者ネフローゼ症候群では，IgA腎症を含む一次性が61.9%（膜性腎症31.5%，微小変化型12.6%，巣状分節性糸球体硬化症5.9%）であり，次いで糖尿病性腎症（9.9%），アミロイド腎（7.6%）と難治性疾患の比率が高い．また，高齢者IgA腎症でも，ネフローゼ状態が9.2%と増加している．

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Key words　nephrotic syndrome，elderly，membranous nephropathy，minimal change nephrotic syndrome，focal segmental glomerulosclerosis

はじめに（動向）

わが国では65歳以上の高齢化率は上昇しつつある．2010年には25.8%を記録し，2025年には30.5%になると予測されており，高齢者腎臓病の増加が推測される．これまで，わが国からの高齢者ネフローゼ症候群に関する報告は，少数の症例ではあるが，腎生検による組織診断とこれに基づく治療の有用性が示されている[1～6]．さらに，75～80歳以上の超（後期）高齢者の腎生検報告は，わが国においては日本腎臓学会と秋田大学のわずか2論文にすぎない[1,6]．

今回，2007年より開始された日本腎臓学会腎生検レジストリー（Japan Renal Biopsy Registry：J-RBR）を用いた，高齢者腎臓病の臨床病理学的背景と重点疾患調査の結果および調査が継続されている日本高齢者ネフローゼ症候群調査研究の中間解析に基づき，わが国における高齢者ネフローゼ症候群の病態と治療について考察する[1,7]．

1．高齢者腎臓病におけるネフローゼ症候群

J-RBRに2007年より2011年までに登録された20歳以上の腎移植を除いた成人10,218例を対象に高齢者（65歳以上）と非高齢成人（65歳未満）を比較検討した成績をみると，高齢者は，2,802例（27.4%）であり，臨床診断において，非高齢

金沢医科大学医学部腎臓内科学

Progressive Renal Diseases:Recent advances in Diagnosis and Treatments. Topics:III. Recent Topics;2. Nephrotic syndrome in the elderly.

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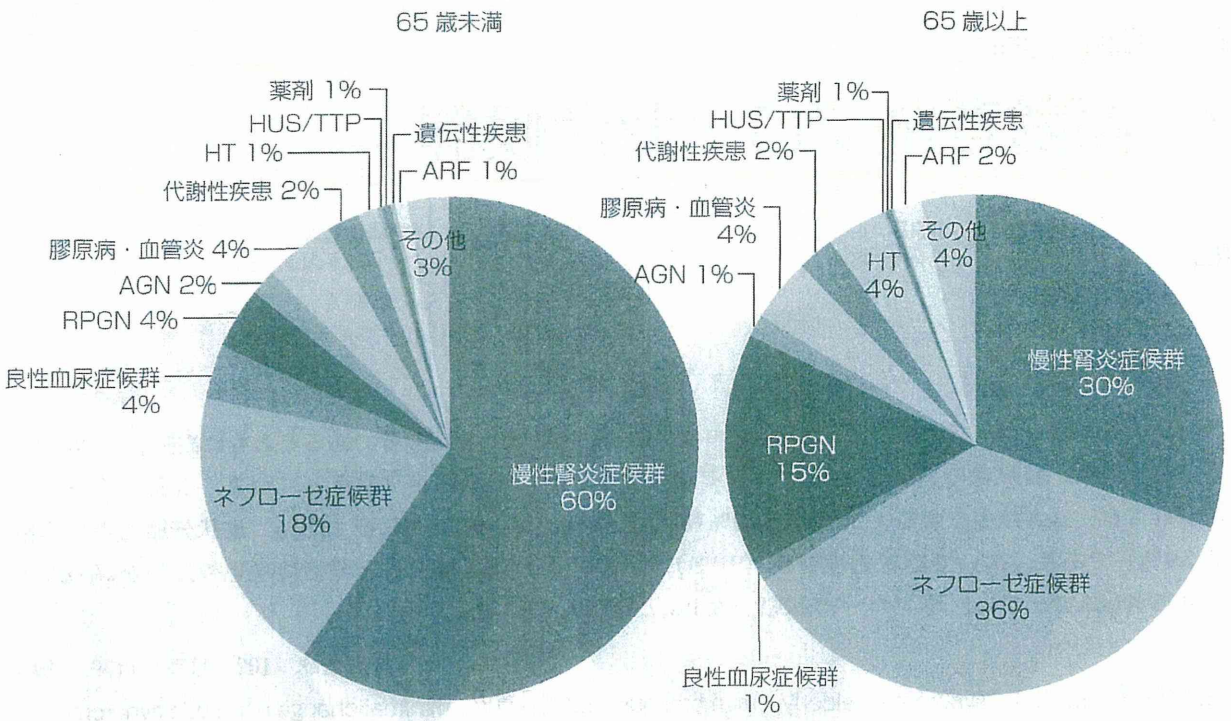

図 1. 高齢者腎生検例の臨床診断

65 歳以上の高齢者は，2,802 例（27.4%）であり，ネフローゼ症候群（36%），急速進行性腎炎症候群（15%）の比率が非高齢成人より高い．一方，慢性腎炎症候群（30%）および良性血尿症候群（1%）の比率は低い．（文献 1 より引用作図）

成人に比してネフローゼ症候群（36.3%），急速進行性腎炎症候群（15.4%）の比率が高い（図 1）．さらに，超（後期）高齢者例の 50.7% がネフローゼ症候群を理由に腎生検が実施されていた．また，高齢者はネフローゼ症候群 2,753 例中 1,160 例（42.4%），急速進行性腎炎症候群（以下，RPGN）732 例中 432 例（59.0%），IgA 腎症 3,109 例中 293 例（9.4%）を占めており，高齢者は人口比率よりも高い頻度で重点疾患を発症していると推測された[1]．

さらに，臨床診断登録に加えて，2011 年改定ネフローゼ症候群の定義[3]である尿蛋白排泄量 3.5 g/日以上（未測定の場合は，尿蛋白・クレアチニン比 3.5 g/gCr以上）かつ血清アルブミン値 3.0 g/dl以下もしくは血清総蛋白 6.0 g/dl以下で抽出すると，高齢者ネフローゼ症候群においては，IgA 腎症を含む一次性が 61.9% であり，次いで糖尿病性腎症（9.9%），アミロイド腎（7.6%）と難治性二次性疾患の比率が高かった（図 2）．臨床的には，非高齢成人と比較して尿蛋白・クレアチニン比（g/gCr）と収縮期血圧が高いことが示された．

病理組織診断では，膜性腎症（高齢者 365 例，31.5%：超（後期）高齢者 45 例，28.1%）が最も頻度が高く，次いで微小変化型ネフローゼ症候群（146 例，12.6%：19 例，11.9%），糖尿病性腎症（115 例，9.9%：10 例，6.3%），アミロイド腎（88 例，7.6%：19 例，11.9%），巣状分節性糸球体硬化症（68 例，5.9%：12 例，7.5%）であった（表 1）．65 歳未満の成人と比較すると膜性腎症，膜性増殖性糸球体腎炎I・III型とアミロイド腎が有意に高頻度であった．一方，微小変化型ネフローゼ症候群の頻度は低かったが，ステロイド治療の適応を考える上で重要な診断である．さ

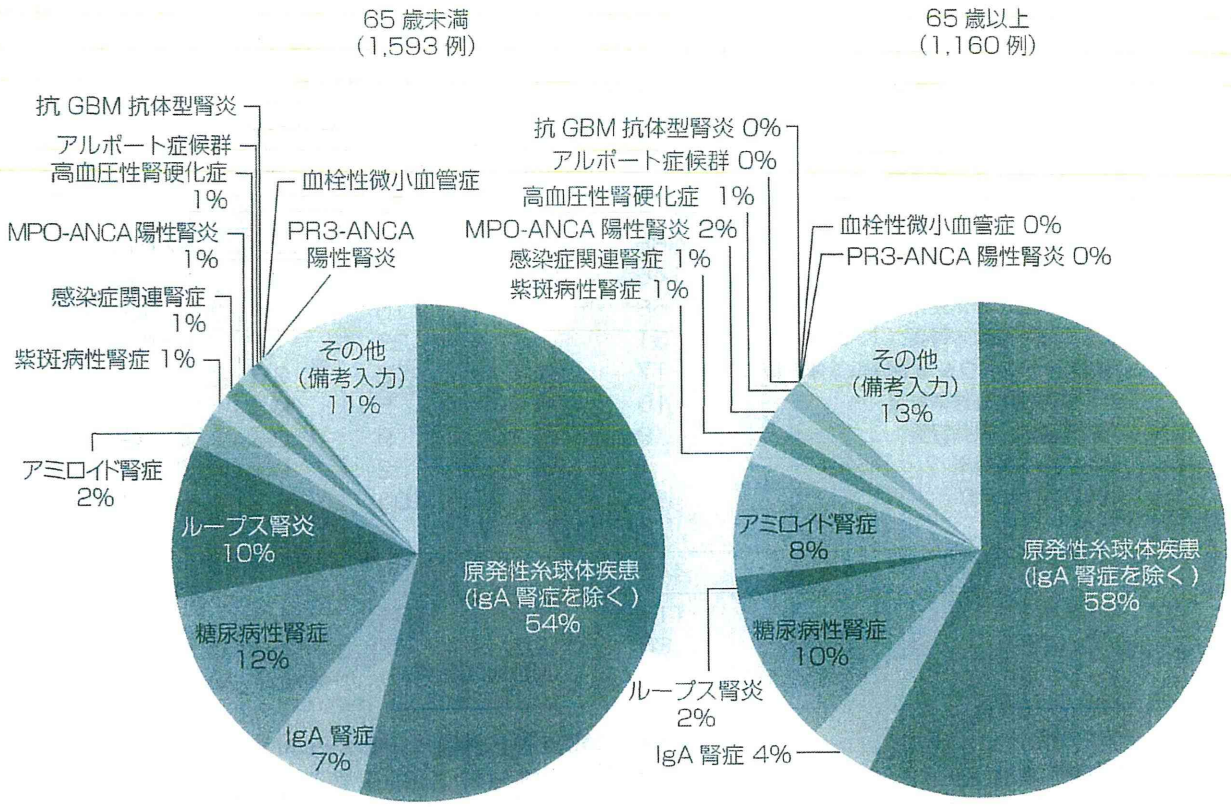

図 2. 高齢者ネフローゼ症候群の病因分類

高齢者ネフローゼ症候群では，IgA腎症を含む一次性が 61.9%（膜性腎症 36.5%，微小変化型 13.4%，巣状分節性糸球体硬化症 5.9%）であり，次いで糖尿病性腎症（9.9%），アミロイド腎（7.6%）と難治性疾患の比率が高い．（文献 1 より引用作図）

らに，年齢層が進むにつれて膜性腎症とアミロイド腎が増加することは，これまでのわが国の報告とも一致している（表 1，2）．

2. 高齢者ネフローゼ症候群における膜性腎症

高齢者ネフローゼ症候群では難治性疾患が多くを占める．中でも重要な膜性腎症について非高齢者を含むレジストリー登録 813 例（腎生検登録の 9.4%）について検討すると，一次性は 633 例（77.9%）であり，二次性が 180 例（22.1%）を占めた．二次性の主な疾患は，ループス腎炎（V 型）9.1%，薬剤性 2.2%，感染症関連 1.2%，悪性新生物あるいは血液疾患関連 1.0%，その他の膠原病 0.9% であった[9]．その生検年齢層別比率をみると 10～30 歳代で二次性が占める割合が約 60% と増加しており，その主体はループス腎炎であった．一方，実数からみると 20 歳以後に年齢層が進むにつれて登録数は増加し，60 歳代でピークを認めた（図 3A）．一次性膜性腎症 633 例では，男女比は 1.3：1（男性 358 例，女性 275 例）と男性の発症頻度が高く，各年齢層による性別比に差はなかった．一方，その平均年齢は 62.2 歳と先の進行性腎障害調査研究班報告の 50.7 歳よりさらに高齢化している[10]．また，推算糸球体濾過率は 76.7（7.6～154.6）ml/1.73 m^2 であり，年齢層が進むにつれて慢性腎臓病ステージ（chronic kidney disease：CKD）G3a，G3b，G4 での腎生検例が増加し，60 歳以後では 20% 以上

表 1. 成人ネフローゼ症候群の原因疾患比較（年齢層比較）

	高齢者群（65 歳以上）		対照群（20-64 歳）		
	n：	%	n：	%	
一次性疾患	718		965		
膜性腎症	365	31.5	284	17.9	p<0.001*
微小変化型ネフローゼ症候群	146	12.6	403	25.3	p<0.001*
巣状分節性糸球体硬化症	68	5.9	110	6.9	NS
膜性増殖性糸球体腎炎（Ⅰ/Ⅲ型）	51	4.4	28	1.8	p<0.001*
非IgAメサンギウム増殖性糸球体腎炎	17	1.5	12	0.8	NS
半月体形成性糸球体腎炎	10	0.9	5	0.3	NS
管内増殖性糸球体腎炎	8	0.7	9	0.6	NS
硬化性糸球体腎炎	1	0.1	2	0.1	NS
IgA腎症（IgAN）	48	4.1	106	6.7	p=0.006*
その他	4	0.3	6	0.4	NS
二次性疾患	442		626		
糖尿病性腎症	115	9.9	184	11.6	NS
アミロイド腎	88	7.6	37	2.3	p<0.001*
ループス腎炎	18	1.6	160	10.1	p<0.001*
感染症関連腎炎	17	1.5	21	1.3	NS
腎硬化症	17	1.5	9	0.6	p=0.016*
紫斑病性腎炎	16	1.4	21	1.3	NS
MPO-ANCA関連腎炎	19	1.6	14	0.9	NS
PR3-ANCA関連腎炎	1	0.1	1	0.1	NS
抗糸球体基底膜抗体型腎炎	0	0.0	3	0.2	NS
Alport症候群	1	0.1	6	0.4	NS
微小血栓性腎症	1	0.1	3	0.2	NS
その他	149	12.8	167	10.5	NS
合計	1160		1591		

（文献 1 より日本語へ翻訳して引用）
*：高齢者 vs. 対照群；NS, not significant

を占めている．尿蛋白量は，平均 3.99 g/日（尿蛋白・クレアチニン比 5.57 g/gCr）と高く，444 例（70.0%）がネフローゼ状態にあり，その割合は年齢層が進むにつれて増加する（60 歳代 147 例，66.7%：70 歳代 104 例，70.2%：80 歳以後 25 例，80%）（図 3B）．

これを他の基礎疾患を含めて一次性ネフローゼ症候群に登録された症例数を年齢層別として 10 歳毎に区別してみるとわが国におけるネフローゼ症候群の登録は 60～70 歳代にピークを認めた（図 4）．さらに，一次性ネフローゼ症候群の各基礎疾患を年齢層別において占める割合でみると，膜性腎症は，50 歳以後の 48.3～61.9% を占めた（図 5）．この中で，ネフローゼ症候群を伴う一次性膜性腎症の 60 歳以上の割合は 71.6% と高く，先の厚生労働省進行性腎障害調査研究班報告（1997～2001 年，1,008 例）において，60 歳以上は有意な腎不全危険因子（相対危険度 1.98，p=0.008）であり，膜性腎症の治療において高齢者の取り扱いはことに重要である[10]．

3. 高齢者ネフローゼ症候群の治療と予後

高齢者ネフローゼ症候群を治療する上での要

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表 2. 日本人高齢者ネフローゼ症候群の比較

研究	J-RBR*[1]		Uezono[5]		Komatsuda[4]		Ozono[3]		Sato[2]	
報告年	2012		2006		1993		1993		1987	
研究期間	2007-2011		2000-2004		1979-1990		1971-1989		1958-1985	
コホートの種類	全国		単施設（宮崎大学）		単施設（秋田大学）		単施設（長崎大学）		単施設（東北大学）	
症例数	10218		406		2088		不明		不明	
高齢者数	2802		61		247		不明		不明	
高齢者の定義	65 歳以上		65 歳以上		65 歳以上		60 歳以上		60 歳以上	
ネフローゼ症候群の症例数・割合（%）	1160	41.4	27	44.3	88	35.6	90	ND	87	ND
一次性疾患	n：	%	n：	%	n：	%	n：	%	n：	%
IgA腎症	48	4.1	2	7.4	6	6.8				
膜性腎症	365	31.5	4	14.8	35	39.8	26	28.9	30	34.5
微小変化型ネフローゼ症候群	146	12.6	5	18.5	9	10.2	6	6.7	7	8.0
巣状分節性糸球体硬化症	68	5.9	6	22.2	5	5.7	1	1.1		
膜性増殖性糸球体腎炎（Ⅰ/Ⅲ型）	51	4.4			3	3.4	8	8.9	7	8.0
半月体形成性糸球体腎炎	10	0.9			3	3.4	1	1.1	1	1.1
非IgAメサンギウム増殖性糸球体腎炎	17	1.5			4	4.5	12	13.3	12	13.8
その他	13	1.1			3	3.4	1	1.1		
小計	718	61.9	17	63.0	68	77.3	55	61.1	57	65.5
二次性疾患	n：	%	n：	%	n：	%	n：	%	n：	%
糖尿病性腎症	115	9.9	3	11.1	7	8.0	8	8.9	12	13.8
アミロイド腎	88	7.6	2	7.4	9	10.2	14	15.6	9	10.3
ループス腎炎	18	1.6								
感染関連腎炎	17	1.5								
腎硬化症	17	1.5	3	11.1						
紫斑病性腎炎	16	1.4			1	1.1				
MPO-ANCA陽性腎炎	19	1.6								
PR3-ANCA陽性腎炎	1	0.1			1	1.1				
Alport 症候群	1	0.1								
微小血栓性腎症	1	0.1								
その他	149	12.8	2	7.4	2	2.3	13	14.4	5	5.7
小計	442	38.1	10	37.0	20	22.7	35	38.9	26	29.9
分類不能									4	4.6

（文献 1 より日本語へ翻訳して引用）
*J-RBR：Japan Renal Biopsy Registry

点として，約 40% を占める二次性疾患，とくに糖尿病性腎症とアミロイド腎の鑑別が重要である．また，加齢およびネフローゼ状態に伴う免疫能の低下状態にあることを考慮する必要がある．ここでは一次性疾患の主要 3 疾患の要点を述べる[8]．

1）微小変化型ネフローゼ症候群

40 歳以後では若年者に比して寛解率に差はないが，寛解までの期間が遷延する傾向があるとされている．実際，50 歳以上（平均年齢 70 歳）の中国人（香港）15 例に対するプレドニゾロン（0.8 mg/kg/日）治療の報告では，寛解までの期間が延長していたが，ステロイド治療への反応

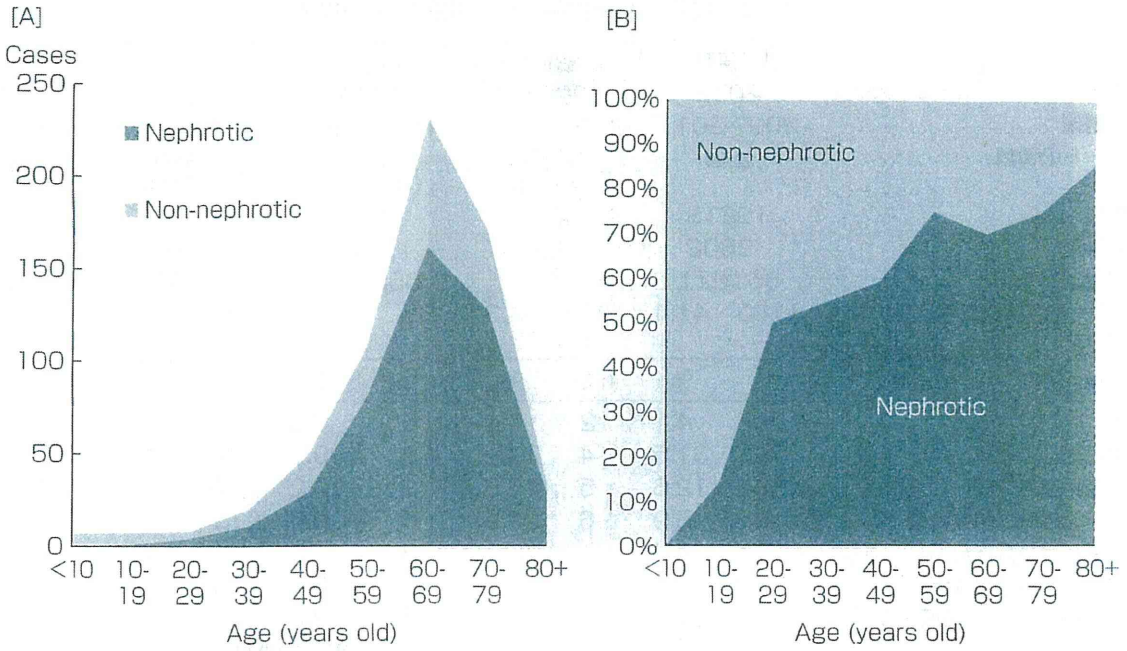

図 3. 特発性膜性腎症の年齢層別登録数［A］とネフローゼ症候群の比率［B］.
（文献 9 より引用）

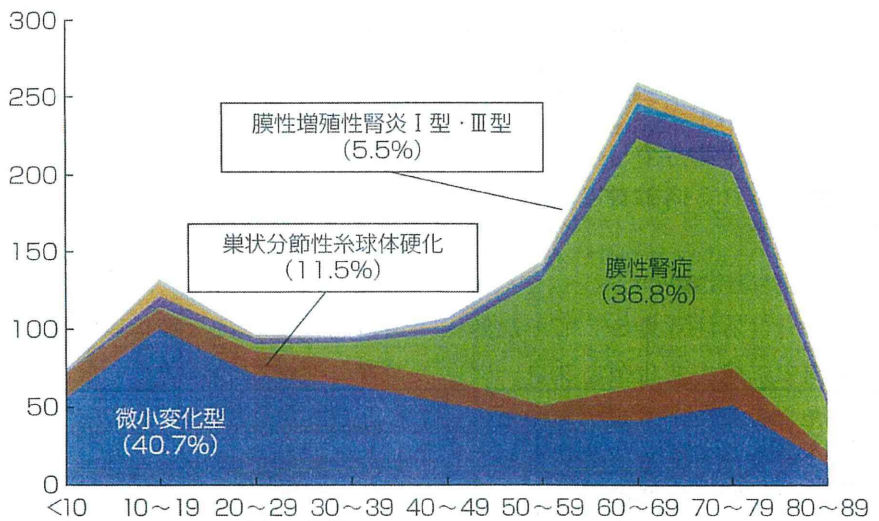

図 4. 一次性ネフローゼ症候群の基礎疾患：年齢層別登録数.
(J-RBR 2007-2010；1,203 例)

性は良好である．さらに，高齢者ネフローゼ症候群の調査でも 75 歳までの高齢者のステロイド反応性は良好であり，中央値 7 日で完全寛解したが，75 歳以上では，寛解が遷延する傾向がみられる．Onokawaらの報告でも，超高齢者微小変化型ネフローゼ症候群 7 例での完全寛解 3 例，不完全寛解 3 例と治療への反応性の低下をみている[6]．このように高齢者においても微小変化型ではステロイド治療が第一選択であるが，反応性の低下とともに副作用（易感染性，耐糖能異

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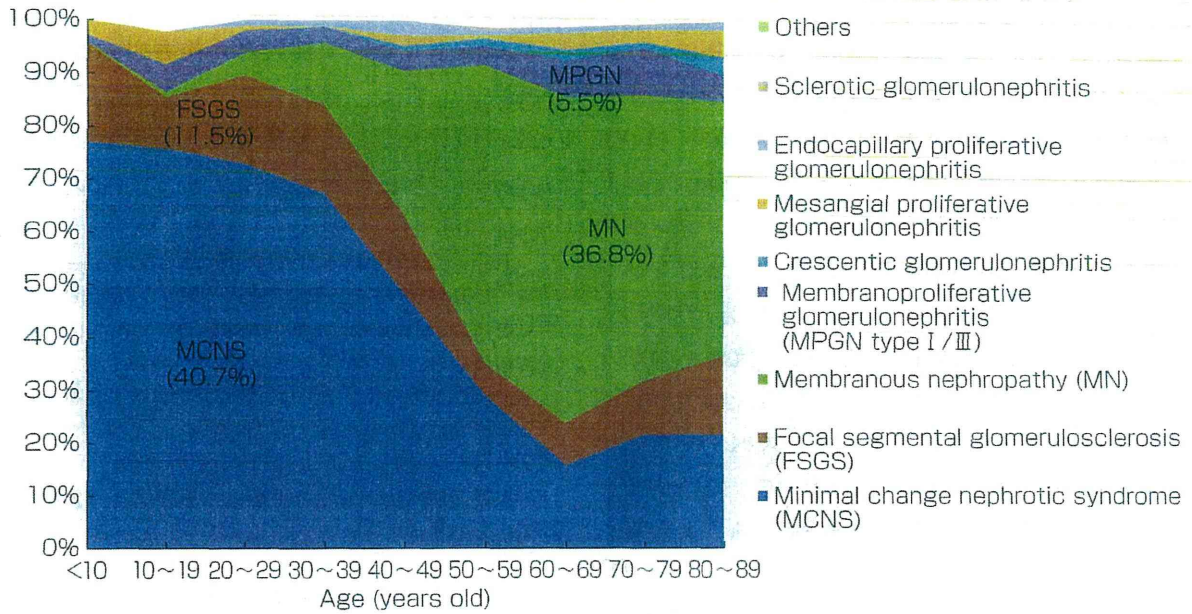

図 5. 一次性ネフローゼ症候群の基礎疾患：年齢層別の病理診断分類の比率．2007-2010 にJ-RBRに登録されたIgA腎症を除く一次性ネフローゼ症候群 1203 例における成績．
（文献 9 より引用）

常，骨粗鬆症など）に十分注意を要する．一方，ネフローゼ状態を早期に改善することにより重症感染症が激減したことが小児では報告されているが，小児に比して高用量ステロイド治療の期間が長くなると考えられる高齢者における今後の検証が必要である．

2）巣状分節性糸球体硬化症

本症の病理診断における注意点として，加齢に伴う分節性硬化病変に微小変化型ネフローゼ症候群が加わった場合の識別が重要であるとの指摘がある．これは治療を考える上でも重要な課題である．高齢者の一次性巣状分節性糸球体硬化症に関する詳細な報告はないが，前回の班研究調査 278 例（12～94 歳）の解析では，年齢（60 歳以上）は腎不全危険因子（相対危険度 1.23，95% 信頼区間 0.50～3.01，p＝0.662）としては有意でないことが報告されている．本症では不完全寛解I型への臨床的改善が腎死を避ける最も重要な治療目標であり，ステロイド（初期投与量：プレドニゾロン 1 mg/kg/日（最大 60 mg/日），重症例では当初からステロイドパルス療法）と反応不良例では，免疫抑制薬が併用される[8, 10]．この免疫抑制薬の使用に関して，班研究調査では本症全体の感染症合併（1.8%），感染による死亡（0.7%）は比較的少ないことが報告されているが，高齢者では加齢とネフローゼに伴う易感染性に注意を要し，高齢者腎移植と同様に使用量の調整が必要と考えられる．また，高齢者ネフローゼ症候群の調査でも治療抵抗性が認められ，その完全寛解率は 67% に留まっている．なお，わが国ではLDLアフェレシスがステロイド抵抗例への保険適用が認められており，より早期の治療において完全寛解あるいは不完全寛解I型への到達率および長期予後の改善が示されている．しかし，高齢者における治療効果に関しては症例報告にとどまっており，今後の検討を要する．

3）膜性腎症

日本人において 60 歳以上は有意な腎不全危険因子であるとともに，欧米でも予後危険因子（50

歳以上，男性，ネフローゼ特に尿蛋白 8～10 g/日以上，血清クレアチニン値上昇）として年齢の要素が確認されており，本症の治療において高齢者の取り扱いは重要である．高齢者では，尿蛋白減少を目的とするアンジオテンシン変換酵素（ACE）阻害薬あるいはアンジオテンシンII受容体（AT1）ブロッカー（ARB）の使用とスタチンなどの高脂血症治療薬，抗血小板薬などによる保存的治療が基本となる．ACE阻害薬あるいはARBの効果について，スペインでの観察研究（GLOSEN研究）において，使用例での2年以内の自然寛解率が32% であることが報告されている．

さらに，ステロイド治療（プレドニゾロン 0.6～0.8 mg/kg標準体重/日相当）を基本とする免疫抑制療法を行う．この治療選択に関して，わが国と欧米との間に異なる部分がある．米国・カナダ（Cattranら）では，保存的治療で6カ月間の観察を行うが，ハイリスク（3カ月以上持続する尿蛋白 8 g/日以上の重度のネフローゼ症状もしくは正常以下の腎機能あるいは持続する腎機能低下）もしくは中等度リスク（腎機能の変化を問わず6カ月以上持続する尿蛋白 4 g/日以上のフローゼ症状）に対しての早期からの免疫抑制治療が勧められている．実際，ネフローゼ症候群を示す高齢者膜性腎症の完全寛解率は56%である．

4. 高齢者ネフローゼ症候群の展望

日本腎臓学会腎臓病総合レジストリーの解析からわが国における難治性疾患を主体とする高齢者ネフローゼ症候群の実態が明確となった．現在，厚生労働科学研究費補助金難治性疾患等克服研究事業「進行性腎障害に関する調査研究」においてネフローゼ症候群の前方視調査および高齢者ネフローゼ症候群の後方視調査が進行している．今後，高齢者ネフローゼ症候群予後調査の結果を基に，早期発見・治療を念頭に置いた診断・診療指針の改訂が期待される．

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文　献

1) Yokoyama H, et al : Clin Exp Nephrol 16 : 903–920, 2012.
2) Sato H, et al : Histologic studies on the nephrotic syndrome in the elderly. Tokoku J Exp Med 53 : 259–264, 1987.
3) Ozono Y, et al : Nephrotic syndrome in the elderly-clinicopathological study. Japnese J Nephrol 36 : 44–50, 1994.
4) Komatsuda A, et al : Kidney diseases among the elderly—A clinicopathological analysis of 247 elderly patients. Intern Med 32 : 377–381, 1993.
5) Uezono S, et al : Renal biopsy in elderly patients : A clinicopathological analysis. Ren Fail 28 : 549–555, 2006.
6) Omokawa A, et al : Renal biopsy in patients aged 80 years and older : a single-center experience in Japan. Clin Nephrol 77 : 461–467, 2012.
7) Sugiyama H, et al : Japan Renal Biopsy Registry : Japan Renal Biopsy Registry : the first nationwide, web-based, and prospective registry system of renal biopsies in Japan. Clin Exp Nephrol 15 : 493–503, 2011.
8) 松尾清一，他：厚生労働省難治性疾患克服研究事業進行性腎障害に関する調査研究班・難治性ネフローゼ症候群分科会　ネフローゼ症候群診療指針．日腎誌　53 : 136–141, 2011.
9) Yokoyama H, et al : Membranous nephropathy in Japan : analysis of the Japan Renal Biopsy Registry (J-RBR). Clin Exp Nephrol 16 : 557–563, 2012.
10) 厚生労働省特定疾患進行性腎障害に関する調査研究班（主任研究者　堺　秀人）：難治性ネフローゼ症候群（成人例）の診療指針　—平成13年度までの調査研究より—．日腎会誌　44 : 751–761, 2002.