APCN2025_Taipei
Dec 5, 2025

Comprehensive Approach to Alport Syndrome

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Agenda

1. What is Alport syndrome
2. Diagnosis
3. Prognosis and the effect of RAS inhibitor treatment
4. Current status in Asian countries

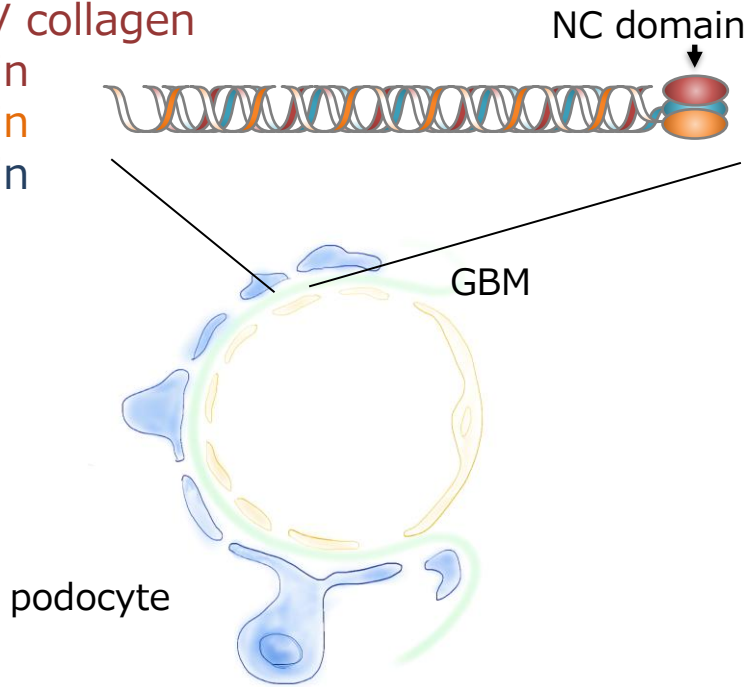
Alport syndrome

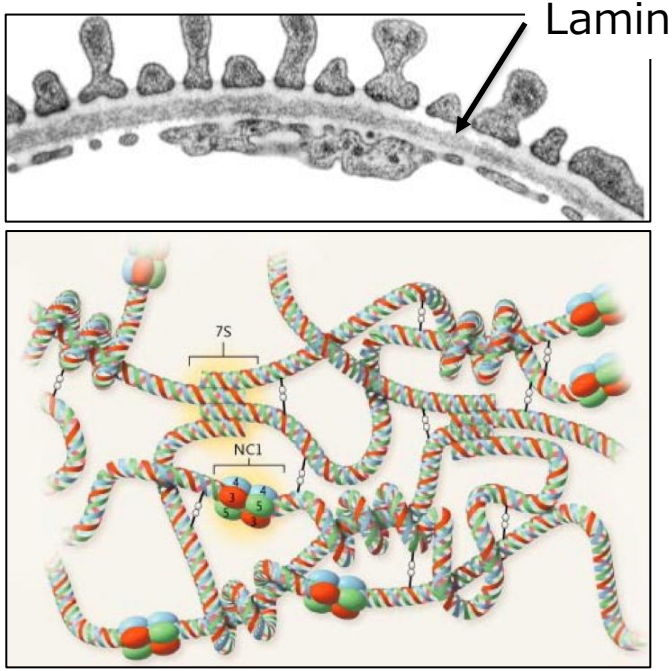
Alport syndrome is characterized by

1. Kidney manifestations
2. Sensorineural hearing loss
3. Ocular manifestations (rare in Japanese, maybe in Asia)

Type IV collagen in GBM

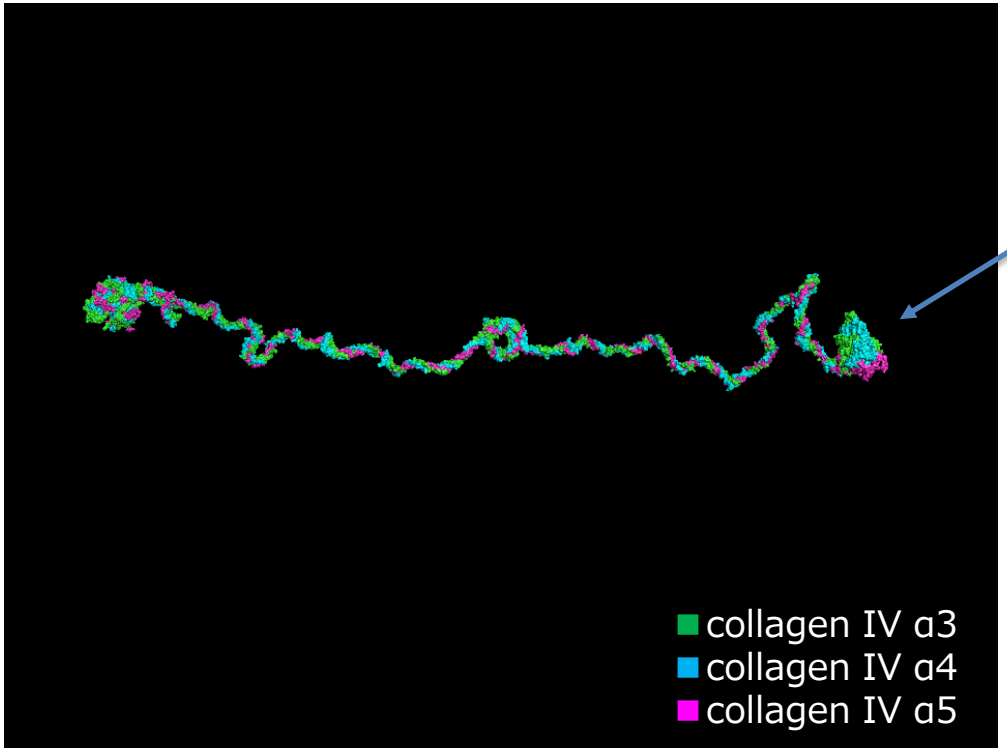
Type IV collagen
α3 chain
α4 chain
α5 chain





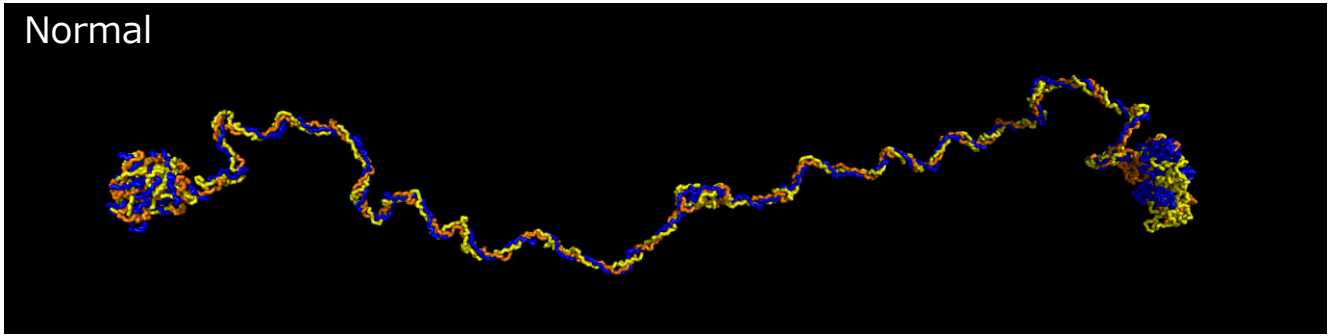
Hudson BG et al. N Engl J Med 2003;348:2543-2556.

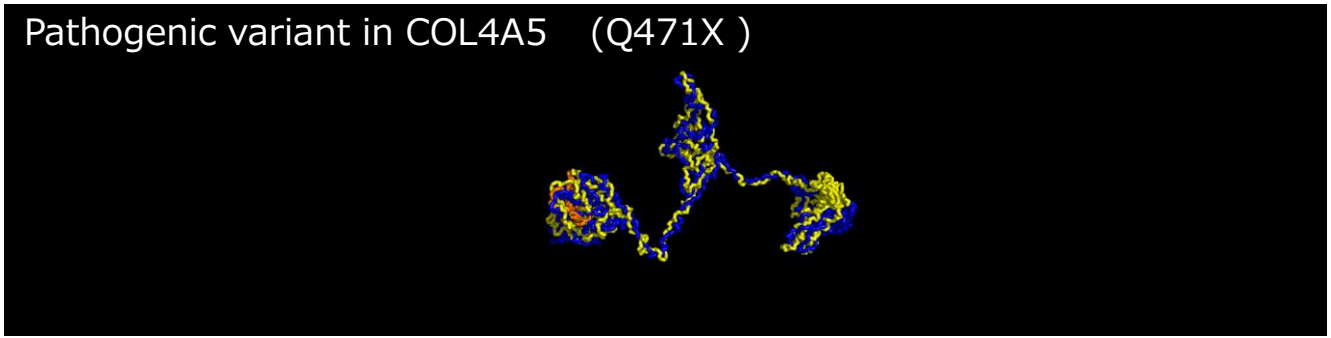
Three-dimensional structural analysis using the K computer



Yamamura T et al, Nature Commun 2020

Three-dimensional structural analysis using the K computer





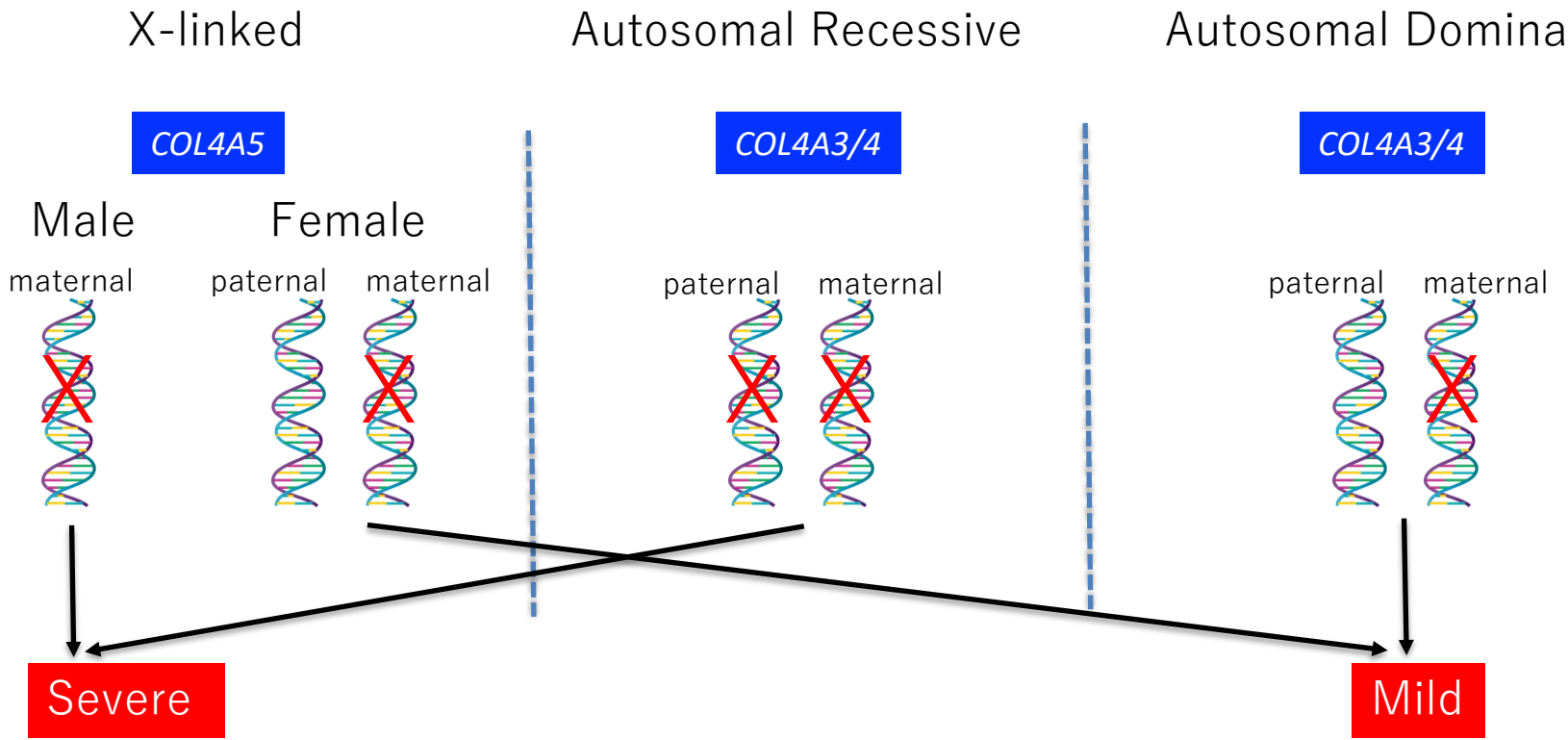
Yamamura T et al, Nature Commun 2020

Genetic Background

	Frequency	Gene	modes
X-linked (XLAS)	74%	*COL4A5*	Hemizygote (men) Heterozygote (women)
Autosomal recessive (ARAS)	9%	*COL4A3* or *COL4A4*	Homozygote or Compound Heterozygote
Autosomal dominant (ADAS)	17%	*COL4A3* or *COL4A4*	Heterozygote

Yamamura et al., MGGM, 2018

Genetic Background



Agenda

1. What is Alport syndrome
2. Diagnosis
3. Prognosis and the effect of RAS inhibitor treatment
4. Current status in Asian countries

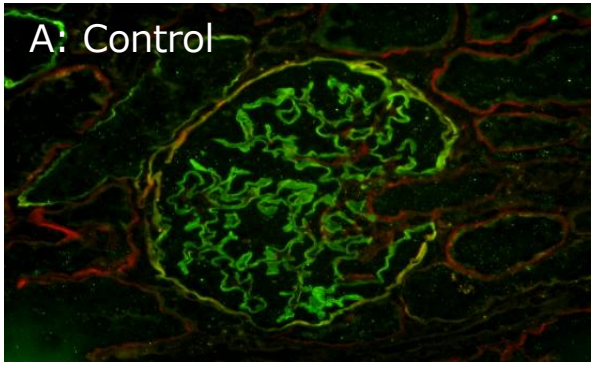
Diagnostic criteria of Alport syndrome

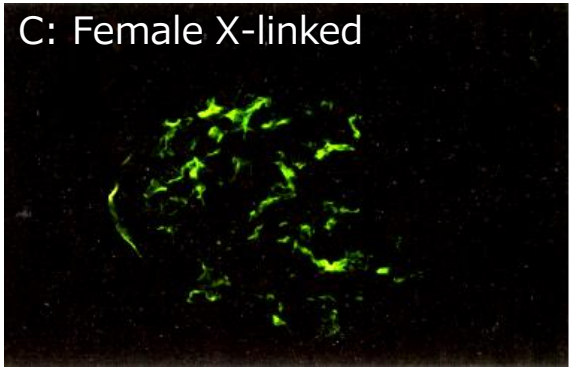
I. Primary feature:
I-1. Persistent hematuria *1
II. Secondary features:
II-1. Mutations in type IV collagen genes *2
II-2. Type IV collagen abnormal expression *3
II-3. Glomerular basement membrane (GBM) -specific abnormalities *4
III. Accessory features
III-1. Family history of kidney diseases
III-2. Bilateral sensorineural deafness
III-3. Ocular abnormalities *5
III-4. Diffuse leiomyomatosis

1.In addition to the primary feature, patients satisfy one or more secondary features
2.In addition to the primary feature, patients should satisfy two or more of the accessory features

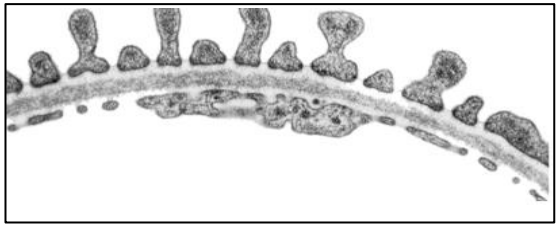
Nozu K, et al, Clin Exp Nephrol, 2019 PMID: 30128941

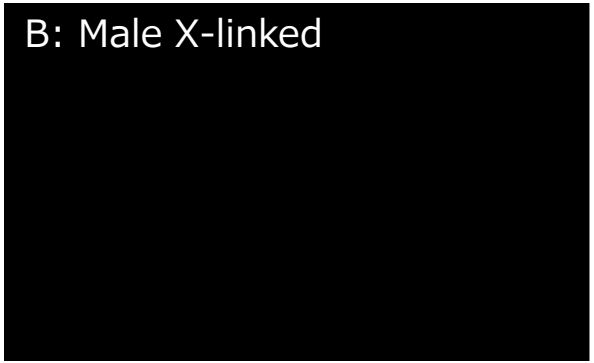
Type IV collagen α5 chain expression

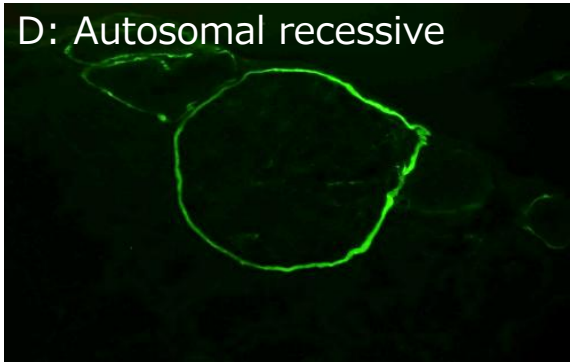




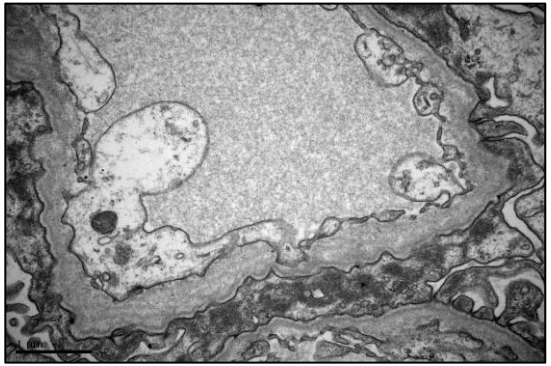
Normal







GBM change



Not all patients with Alport syndrome exhibit these findings.

Diagnostic criteria of Alport syndrome

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I-1. Persistent hematuria *1
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Nozu K, et al, Clin Exp Nephrol, 2019 PMID: 30128941

Diagnostic system of Inherited kidney diseases in Japan

Patients suspected of inherited kidney diseases

Submission of samples to Kobe University

Targeted sequence → (+) Sanger' s sequence

↓ (-)

Copy number variation screening (Pair analysis)

↓ (+)

Custom array CGH or MLPA (-) ↓

Intronic variants search
Whole exome sequence

Free of charge!
(Grant from the government)

Large-scale Data Collection

Gene test results

Alport syndrome (AS) suspected cases
n=1234

No pathogenic variants
n=221

Not all patients can be detected gene variants with the standard genetic test.

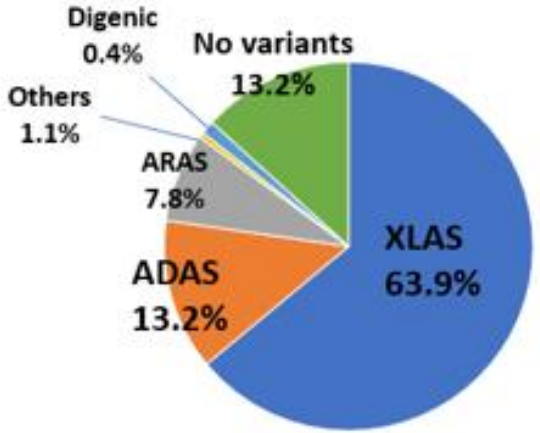
Variants in other genes
n=24

C3,CFB,INF2,MYH9,PAX2,PODXL, WT1,HNF1B,NPHS1,TBC1D8B

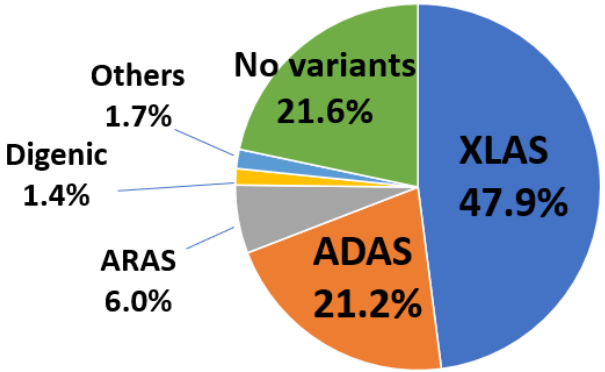
X-Linked AS	n=624
Autosomal Recessive AS	n=71
Autosomal Dominant AS	n=264
Digenic	n=16

Current data in Kobe U.

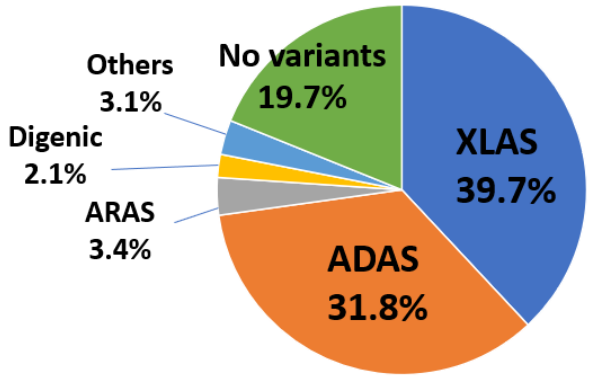
Alport syndrome Inheritance modes



2006-2017
N=422



2017-2020
N=413



2020-2023
N=380

Q: Is the number of cases with ADAS increasing?

A: No, it isn't. The recognition of this disease is increasing among the adult nephrology section.

Current data in Kobe U.

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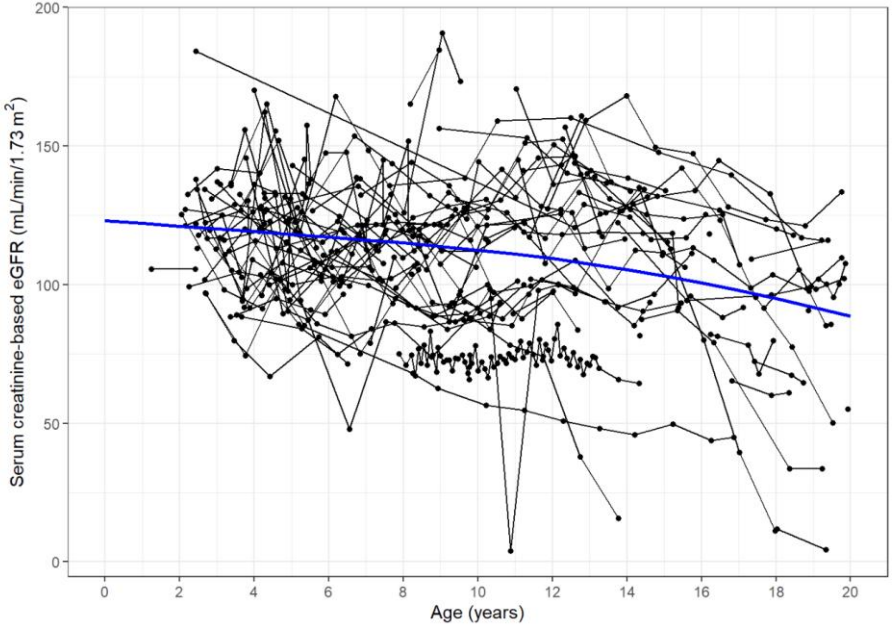
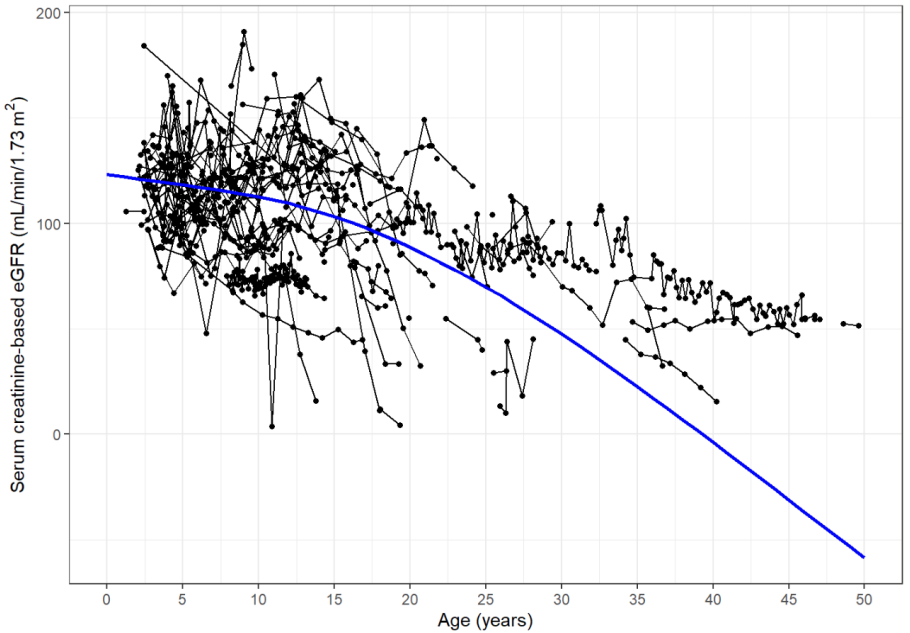
Alport Syndrome National Registry in Japan (JP-ALPS)

329 cases were registered (Mar 17, 2025)

eGFR decline

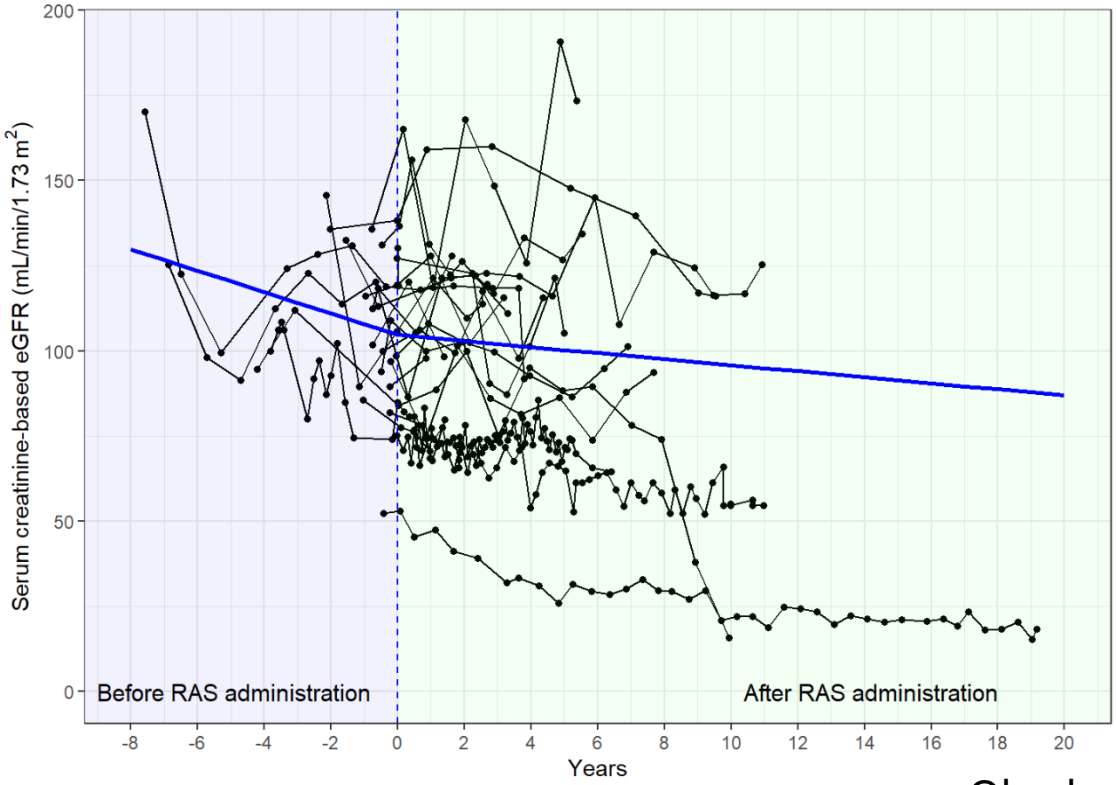




Okuda Y, Nozu K, Clin Exp Nephrol 2025

Alport Syndrome National Registry in Japan (JP-ALPS)

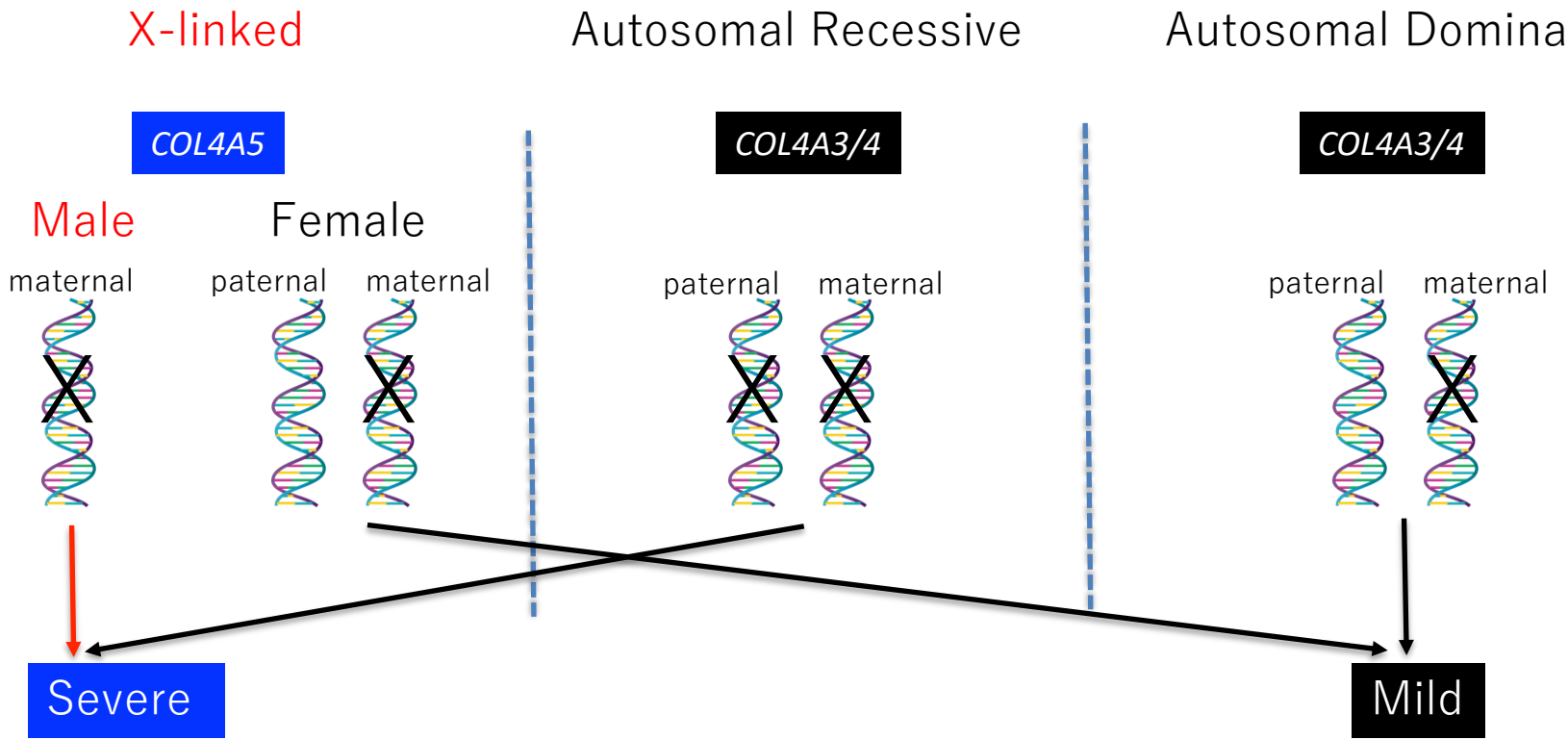
The decline in eGFR before and after the introduction of RAS inhibitors



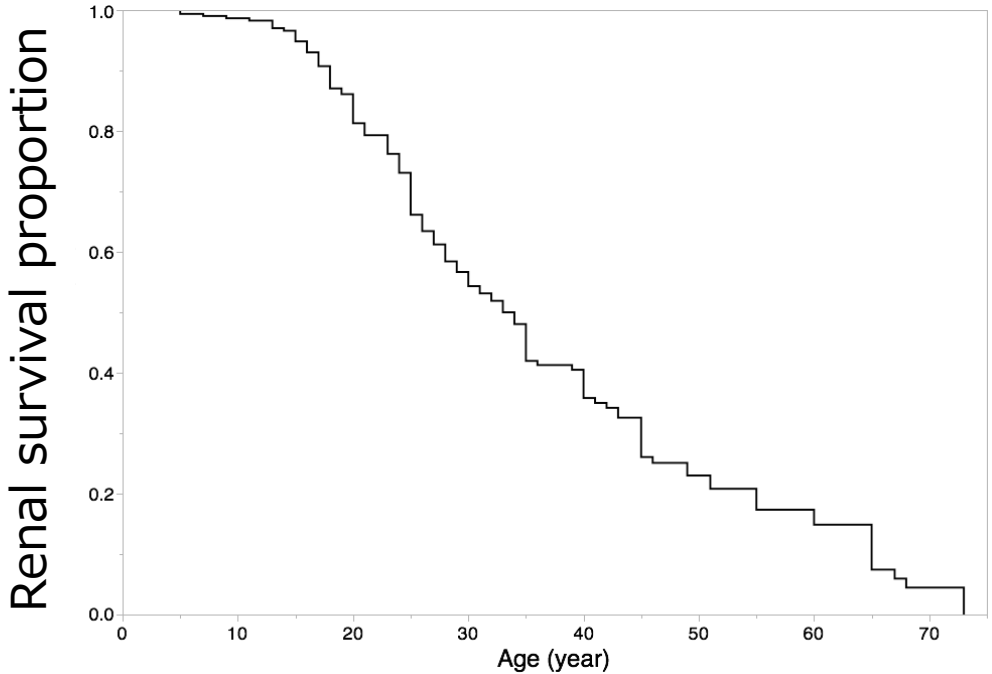
-3.141ml/y→-0.886ml/y

Okuda Y, Nozu K, Clin Exp Nephrol 2025

Genetic Background



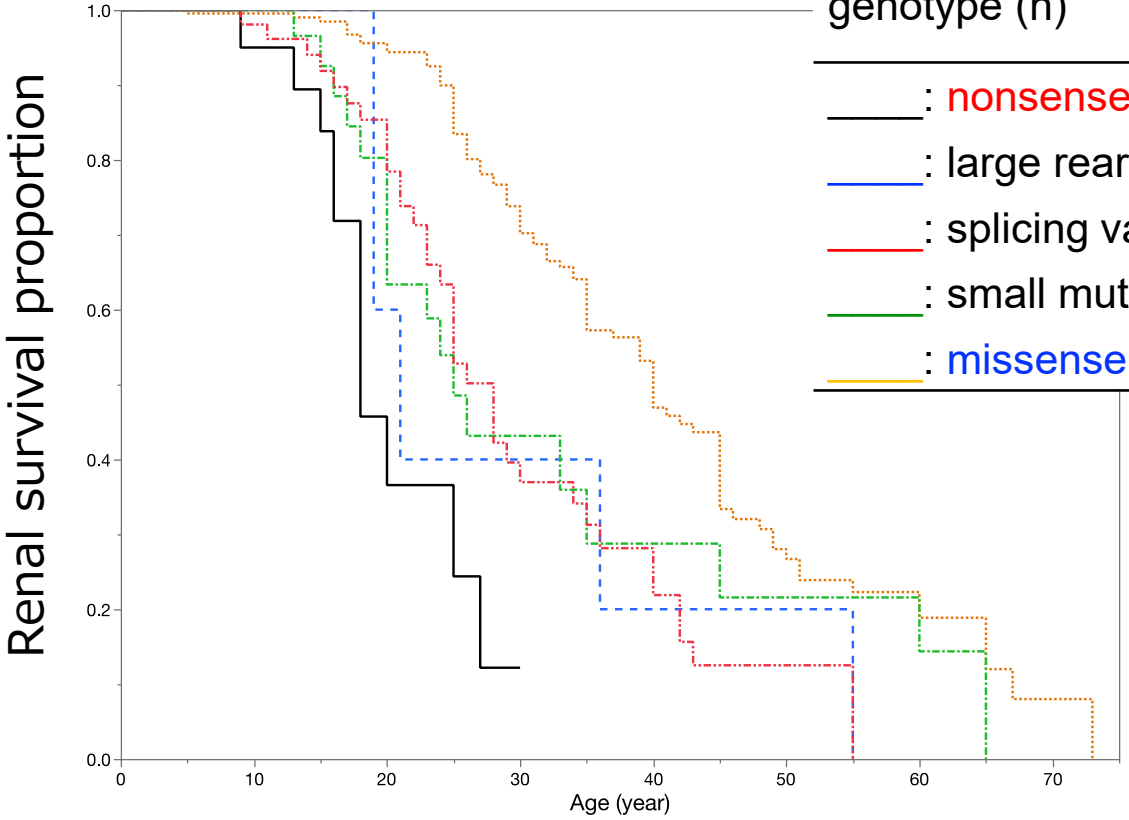
Renal prognosis in **Male X-linked** Alport syndrome



Median age developing ESKD : 35 yo
(n=422)

Yamamura et al. Kidney Int, 2020

Genotype-phenotype in **Male X-linked** Alport syndrome

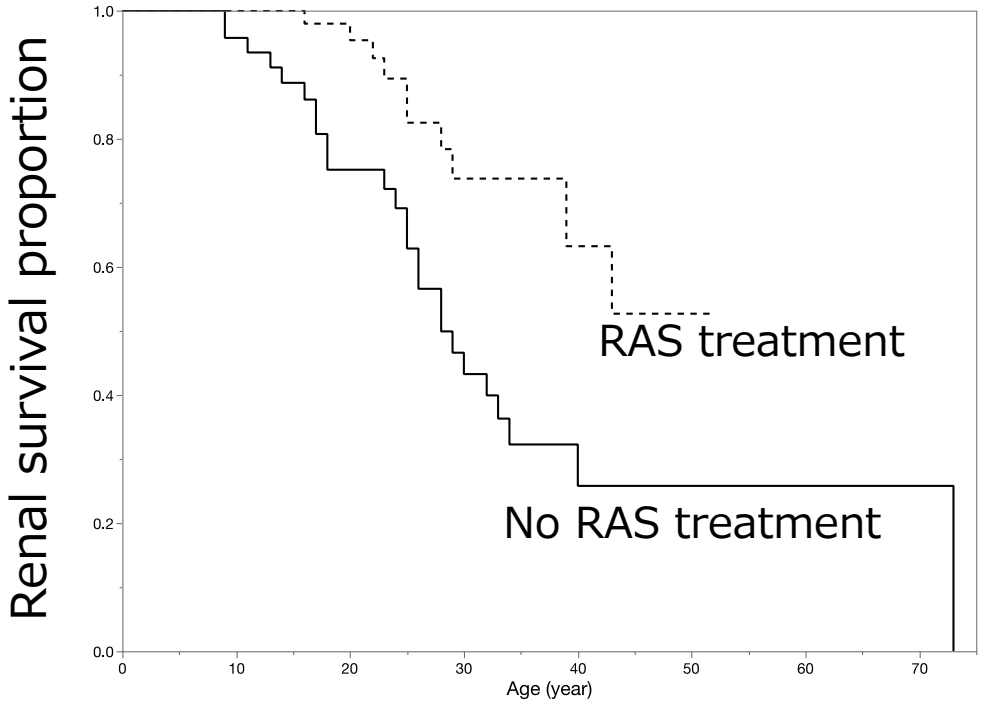


genotype (n)	age at ESKD
____: nonsense (30)	18yo
____: large rearrangement (14)	21yo
____: splicing variant (70)	25yo
____: small mutation (64)	26yo
____: missense (244)	40yo

22yo

Yamamura et al. Kidney Int 2020

RAS inhibitor treatment in **Male X-linked** Alport syndrome



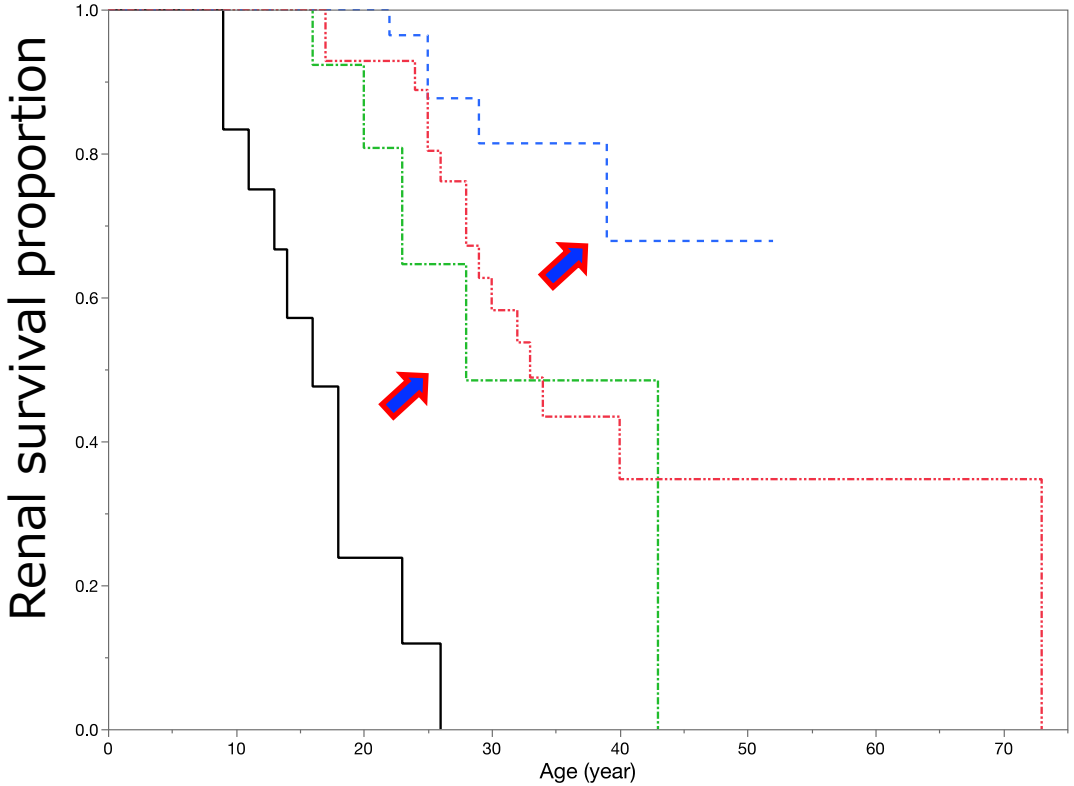
ACEI/ARB treatment (n)	age at ESKD
+ (126)	>50
− (81)	28yo

P=0.0004

RAS inhibitor treatment improves renal prognosis.

Yamamura et al. Kidney Int, 2020

RAS inhibitor treatment in **Male X-linked** Alport syndrome

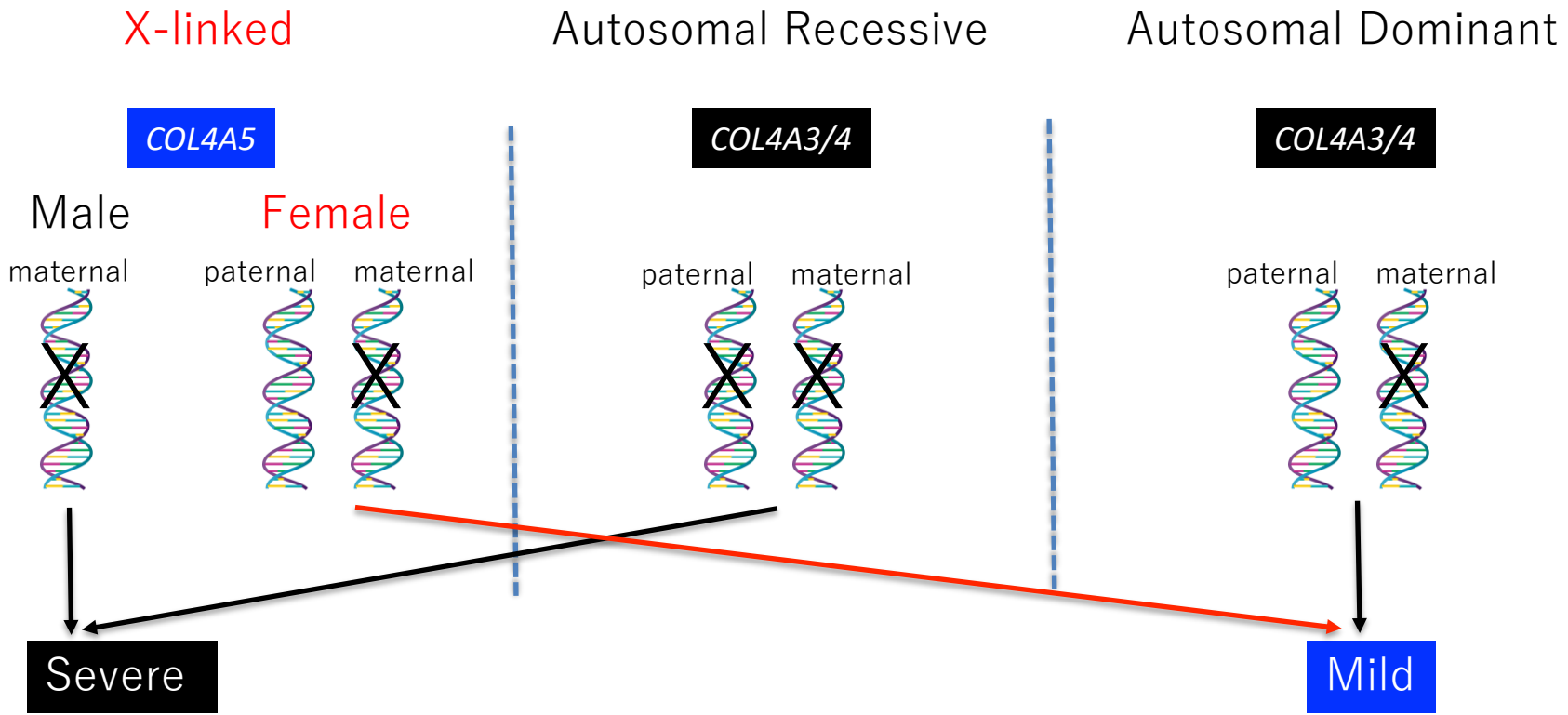


genotype (n)	age at ESKD
: Truncating+RAS(-) (n=50)	16yo
: Truncating+RAS(+) (n=25)	28yo
: Non-truncating+RAS(-) (n=56)	33yo
: Non-truncating+RAS(+) (n=56)	>50yo

For patients with truncating variants, the effect is limited.

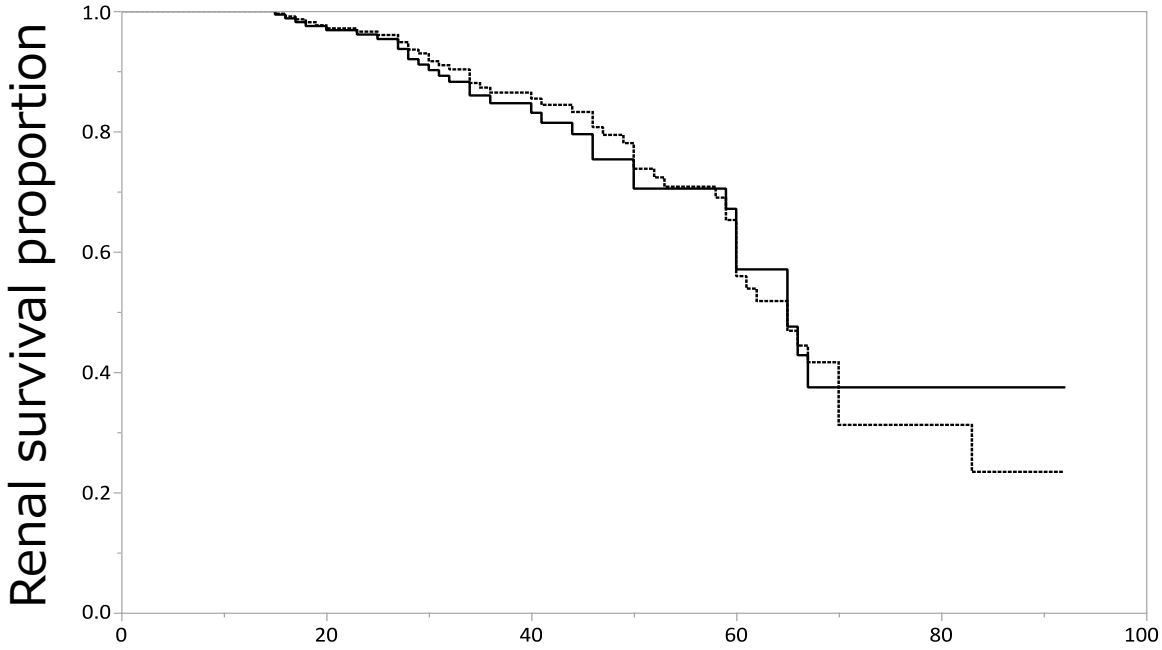
Yamamura et al. Kidney Int, 2020

Genetic Background



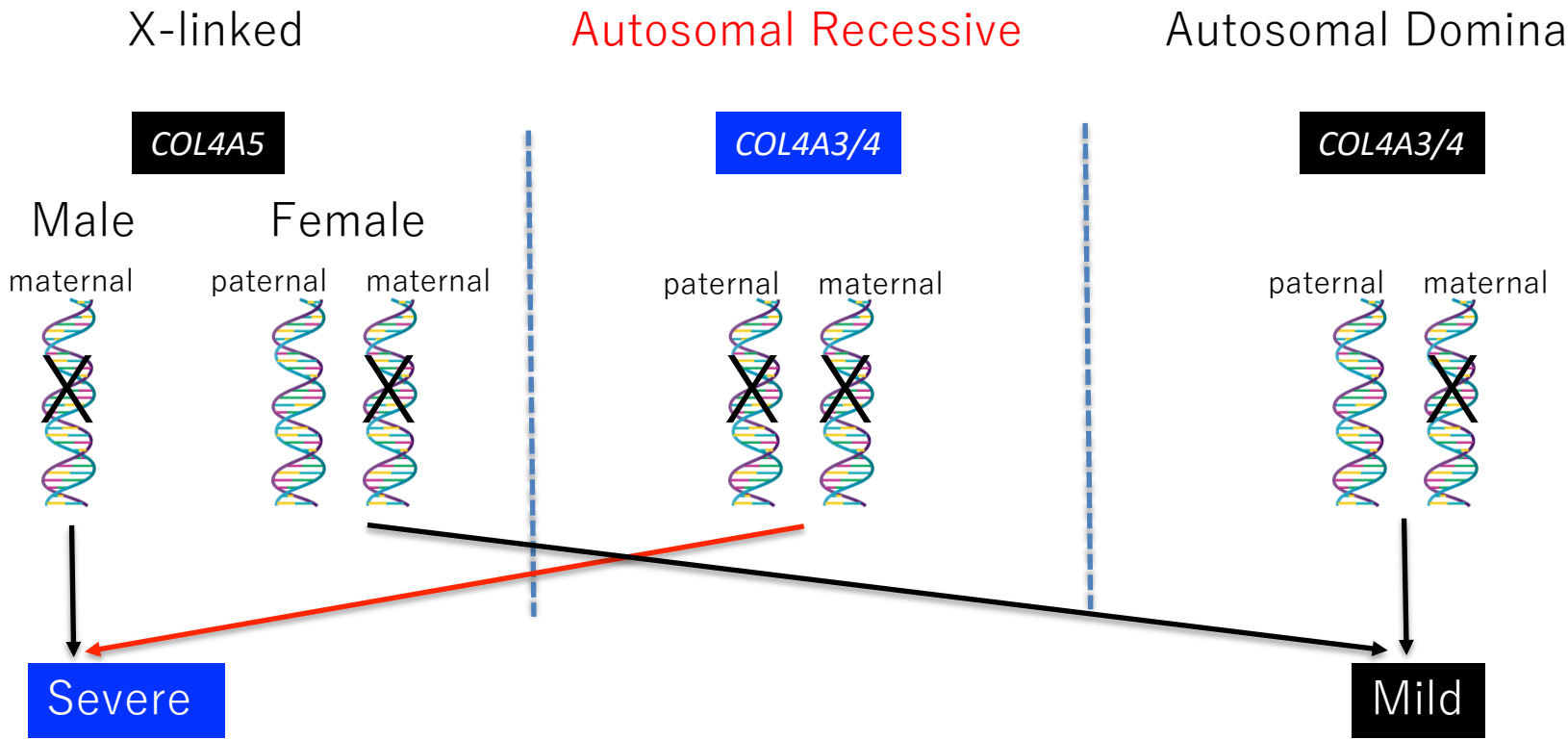
Renal prognosis in **Female X-linked** Alport syndrome

Yamamura et al, KI reports, 2017

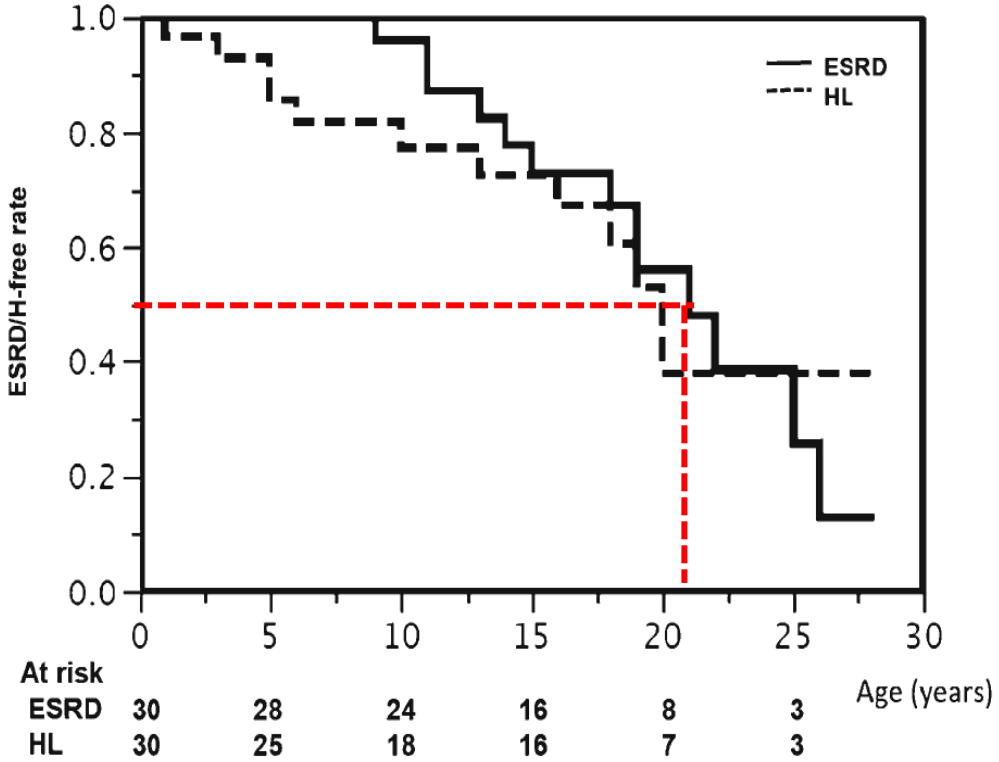


Median age developing ESKD : 65 yo (n=312)

Genetic Background



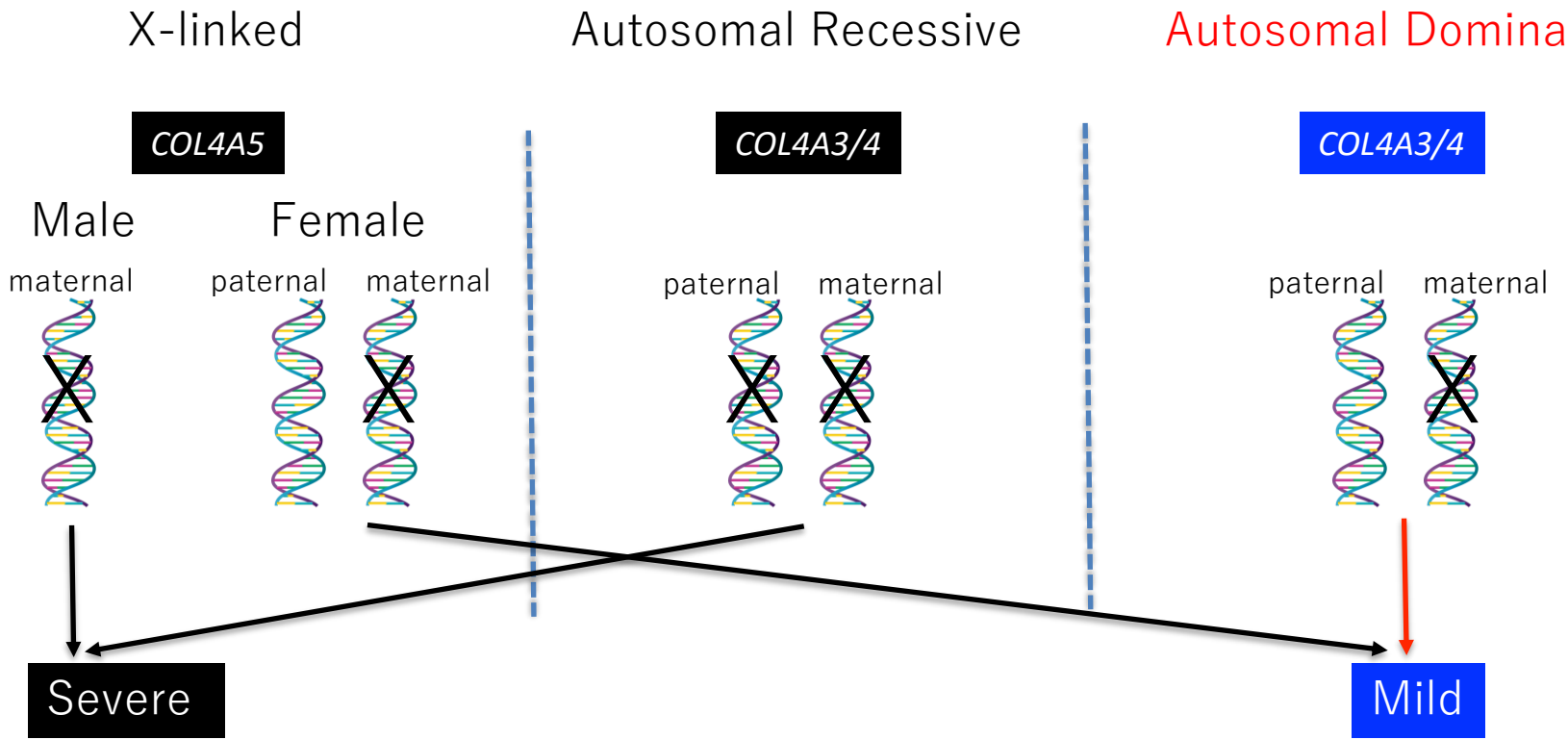
Renal prognosis in **Autosomal Recessive** Alport syndrome



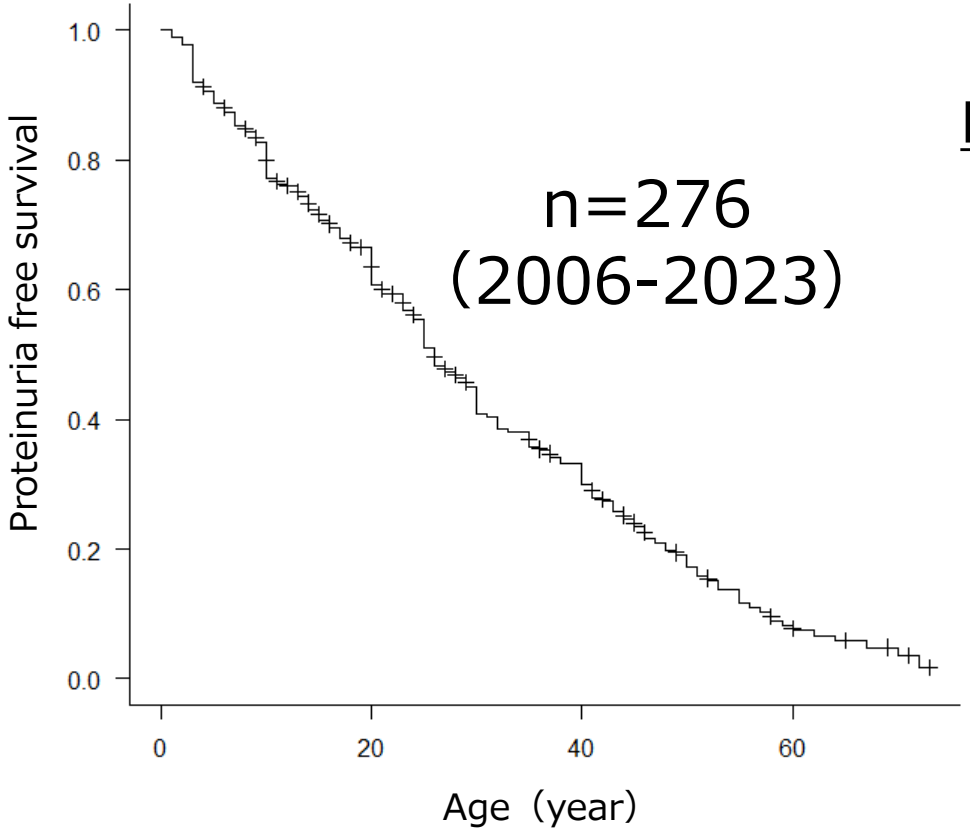
Median age developing ESKD : 21 yo (n=30)

Oka et al. Pediatr Nephrol 2014

Genetic Background



Renal prognosis in **Autosomal Dominant** Alport syndrome

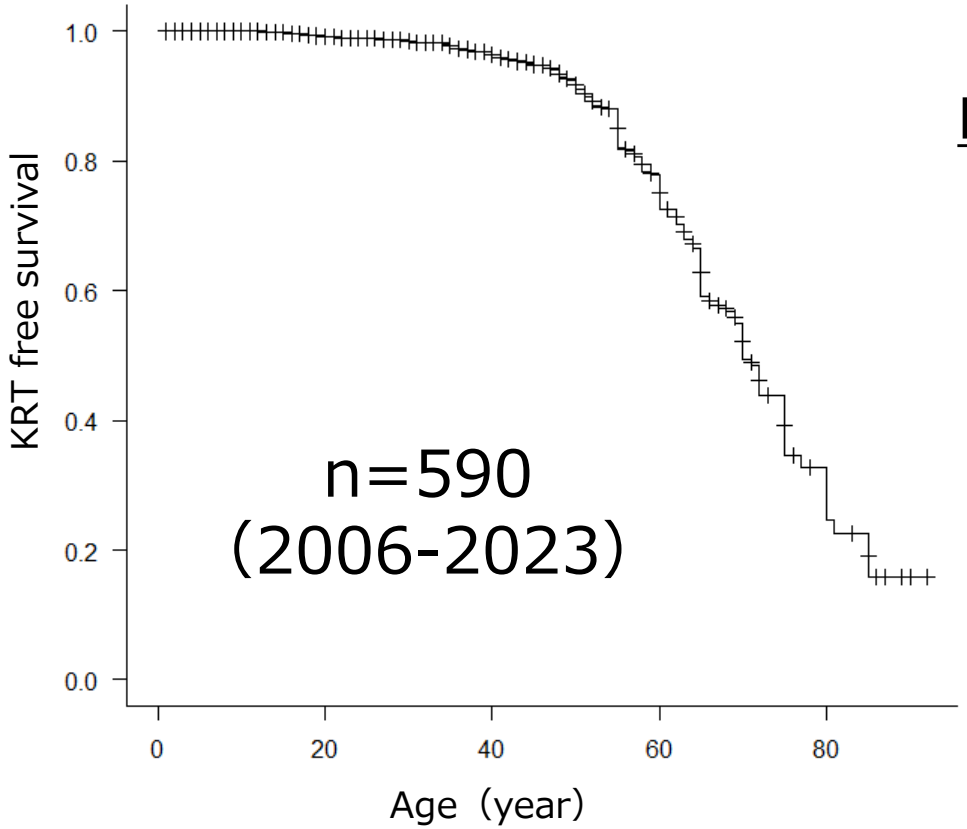


Detection of Proteinuria

26 years
(95%CI:24-30)

On submission

Renal prognosis in **Autosomal Dominant** Alport syndrome



Development of ESKD

70 years
(95%CI:68-75)

On submission

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Clinical and Experimental Nephrology (2023) 27:776–780
https://doi.org/10.1007/s10157-023-02358-6

ORIGINAL ARTICLE

Investigation of the current situation regarding diagnosis and treatment of Alport syndrome in Asian countries: results of survey of the Asian Paediatric Nephrology association (AsPNA) tubular and inherited working group

Kandai Nozu[1] · Lourdes Paula Real Resontoc[2] · Nakysa Hooman[3] · Anil Vasudevan[4] · Jie Ding[5] · Hee Gyung Kang[6]

The group conducted an online survey among the members of AsPNA in 2021–2022.

Institute numbers answered the survey

Patients numbers

Country	Institute number	Patients number	XL (Male)	XL (Female)	AR	AD	Unknown
Bangladesh	3	19	4	0	0	0	15
China	40	501	225	140	25	16	14
Hong Kong, China	1	10	7	0	1	2	0
India	14	41	35	2	5	5	7
Indonesia	1	0	0	0	0	0	0
Iran	4	84	24	9	8	12	9
Japan	55	314	126	124	14	27	24
Jordan	2	10	4	1	4	1	0
Korea	13	155	74	30	33	3	15
Laos	1	0	0	0	0	0	0
Lebanon	2	2	0	0	0	0	2
Malaysia	4	10	4	2	2	3	3
Mongolia	2	48	11	7	7	11	13
Myanmar	2	2	0	0	0	0	0
Nepal	3	6	1	0	0	0	5
Pakistan	3	9	4	1	1	3	4
Philippines	8	6	1	2	1	0	4
Sri Lanka	2	3	0	2	0	0	1
Thailand	1	0	0	0	0	0	0
UAE	3	10	4	1	4	1	1
Vietnam	1	10	8	1	0	0	1
Total	165	1240	532	322	105	84	118

Patients numbers

Country	Institute number	Patients number					nown
Bangladesh	3	19					
China	40	501					
Hong Kong, China	1	10					
India	14	41					7
Indonesia	1	0					0
Iran	4	84	24			12	9
Japan	55	314		24	14	27	24
Jordan	2	10		1	4	1	0
Korea	13	155		30	33	3	15
Laos	1	0		0	0	0	0
Lebanon	2	2		0	0	0	2
Malaysia	4	10		2	2	3	3
Mongolia	2	48		7	7	11	13
Myanmar	2	2			0	0	0
Nepal	3	6			0	0	5
Pakistan	3	9	4	1	1	3	4
Philippines	8	6	1	2	1	0	4
Sri Lanka	2	3	0	2	0	0	1
Thailand	1	0	0	0	0	0	0
UAE	3	10	4	1	4	1	1
Vietnam	1	10	8	1	0	0	1
Total	165	1240	532	322	105	84	118

There are no doubt many more patients in Indonesia. But we did not have access to diagnostic tools for this disease until recently.

Dr. Rini Rossanti

Gene tests availability

Country	Institute number answered the survey	Gene test					
		Availability(%)	In-house test	Different center	Foreign countries(%)	Genetic First approach(%)	Average Cost (USD)
Bangladesh	3	3 (100)	0	0	3(100)	1 (33)	600
China	40	34 (85)	12(35)	22(65)	0	31(78)	700
Hong Kong, China	1	1 (100)	N/A	N/A	N/A	1(100)	N/A
India	14	5 (36)	0	5(100)	0	4(80)	215
Indonesia	1	0 (0)	0	0	0	0	-
Iran	4	2 (50)	1(50)	0	1(50)	0	N/A
Japan	55	50 (91)	1(2)	49(98)	0	22(40)	N/A
Jordan	2	1 (50)	0	0	1(100)	1(50)	free or 300
Korea	13	13 (100)	4(31)	9(69)	0	7(54)	776
Laos	1	1 (100)	0	0	1(100)	0	1300
Lebanon	2	1 (50)	0	0	1(100)	1(50)	650
Malaysia	4	4 (100)	0	0	4(100)	4(100)	438
Mongolia	2	2 (100)	0	0	2(100)	1(50)	100
Myanmar	2	1 (50)	0	0	1(100)	0	2000
Nepal	3	2 (67)	0	0	2(100)	0	350
Pakistan	3	1 (33)	0	0	1(100)	0	N/A
Philippines	8	3 (38)	0	0	3(100)	0	free or 400
Sri Lanka	2	0 (0)	0	0	0	0	-
Thailand	1	1 (100)	0	1(100)	0	0	N/A
UAE	3	3 (100)	0	0	3(100)	2(67)	1017
Vietnam	1	1 (100)	0	0	1(100)	0	N/A
Total	165	129	18	88	24	75	

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China	40	34 (85)	12(35)	22(65)	0	31(78)	700
Hong Kong, China	1	1 (100)	N/A	N/A	N/A	1(100)	N/A
India	14	5 (36)	0	5(100)	0	4(80)	215
Indonesia	1	0 (0)	0	0	0	0	-
Iran	4	2 (50)	1(50)	0	1(50)	0	N/A
Japan	55	50 (91)	1(2)	49(98)	0	22(40)	N/A
Jordan	2	1 (50)	0	0	1(100)	1(50)	free or 300
Korea	13	13 (100)	4(31)	9(69)	0	7(54)	776
Laos	1	1 (100)	0	0	1(100)	0	1300
Lebanon	2	1 (50)	0	0	1(100)	1(50)	650
Malaysia	4	4 (100)	0	0	4(100)	4(100)	438
Mongolia	2	2 (100)	0	0	2(100)	1(50)	100
Myanmar	2	1 (50)	0	0	1(100)	0	2000
Nepal	3	2 (67)	0	0	2(100)	0	350
Pakistan	3	1 (33)	0	0	1(100)	0	N/A
Philippines	8	3 (38)	0	0	3(100)	0	free or 400
Sri Lanka	2	0 (0)	0	0	0	0	-
Thailand	1	1 (100)	0	1(100)	0	0	N/A
UAE	3	3 (100)	0	0	3(100)	2(67)	1017
Vietnam	1	1 (100)	0	0	1(100)	0	N/A
Total	165	129	18	88	24	75	

Kidney biopsy availability

Country	Institute number answered the survey	Kidney biopsy		
		Kidney biopsy availability(%)	Type 4 collagen staining(%)	Electron microscopy(%)
Bangladesh	3	3 (100)	1 (33)	0
China	40	14 (35)	10 (25)	13 (33)
Hong Kong, China	1	1 (100)	1(100)	1(100)
India	14	12 (86)	4(29)	11(79)
Indonesia	1	1 (100)	0	0
Iran	4	3 (33)	1(25)	3(75)
Japan	55	23 (42)	18(33)	22(40)
Jordan	2	2 (100)	0	2(100)
Korea	13	4 (31)	3(23)	4(31)
Laos	1	0 (0)	0	0
Lebanon	2	1 (50)	1(50)	1(50)
Malaysia	4	3 (75)	0	2(50)
Mongolia	2	2 (50)	1(50)	2(100)
Myanmar	2	2 (100)	0	0
Nepal	3	3 (100)	0	0
Pakistan	3	3 (100)	0	1(50)
Philippines	8	6 (75)	1(13)	6(75)
Sri Lanka	2	2 (100)	0	0
Thailand	1	1 (100)	0	0
UAE	3	3 (100)	2(67)	3(100)
Vietnam	1	0 (0)	0	0
Total	165	89	43	71

Treatment

Country	Institute number answered the survey	Treatment			
		RAS treatment (%)	Other medicine	Medicine(institute number)	RAS for Suspected cases (%)
Bangladesh	3	3 (100)	1	Cyclosporine(1)	2(67)
China	40	34 (85)	8	Chinese medicine(4), Cyclosporine(2) , SGLT2(2), Spironolacton(1)	7(18)
Hong Kong, China	1	1 (100)	0		0
India	14	14 (100)	0		3(21)
Indonesia	1	0 (0)	0		1(100)
Iran	4	3 (75)	1	Cyclosporine(1)	3(75)
Japan	55	49 (89)	1	SGLT2(1)	2(4)
Jordan	2	2 (100)	0		2(100)
Korea	13	12 (92)	0		2(15)
Laos	1	1 (100)	0		1(100)
Lebanon	2	1 (50)	0		1(50)
Malaysia	4	4 (100)	0		2(50)
Mongolia	2	2 (100)	1	Dipyridamole, Ascorutin, Vit A,E	2(100)
Myanmar	2	1 (50)	0		0
Nepal	3	2 (67)	0		2(67)
Pakistan	3	2 (67)	0		2(67)
Philippines	8	3 (38)	0		6(75)
Sri Lanka	2	1 (50)	0		2(100)
Thailand	1	1 (100)	0		0
UAE	3	3 (100)	0		1(33)
Vietnam	1	1 (100)	0		0
Total	165	137 (83)	12		41 (25)

Survey Results

1. A total of 299 pediatric nephrologists from 21 countries in Asia participated in the online survey.
2. It is possible to order genetic diagnosis in most countries, but the cost is high and not all patients can afford it.
3. Renal biopsies can be performed in most countries, but only a limited number of centers are able to perform the crucial collagen staining and electron microscopy.
4. Pleasingly, in most countries, patients with Alport syndrome were already being treated with RAS inhibitors.
5. However, treatment was not initiated for suspected Alport syndrome patients without a definitive diagnosis. It should be recommended that RAS inhibitor treatment be initiated in patients with hematuria and proteinuria who have not been confirmed genetically or pathologically.

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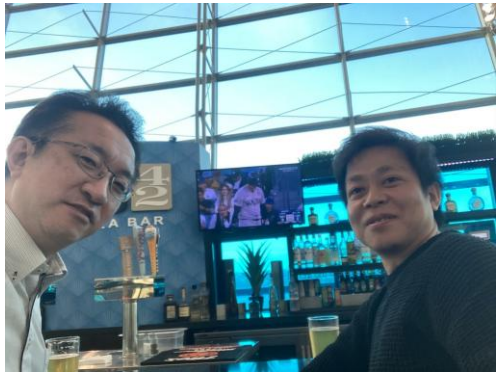

The Department of Pediatrics at Kobe University accepts Japanese government-sponsored international students from ASEAN countries. Don't hesitate to get in touch with me if you are interested!

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