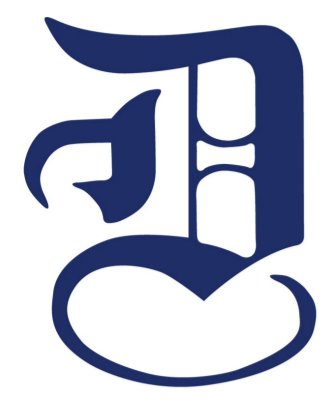# RENAL SURVIVAL AND PROGNOSTIC FACTORS IN 34 PATIENTS WITH ANCA-ASSOCIATED GLOMERULONEPHRITIS

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OBJECTIVES

The incidence of ANCA-associated vasculitis (AAV) has increased during the last three decades[1)-3)]. We evaluated patients and prognostic value of clinical, laboratory, and pathologic features at the time of presentation on patient and renal survival in patients with ANCA-associated glomerulonephritis.

Patients

2011Nov~2015Nov

n=34 (M 15, F 19),   Age: Median 69 yo [66.2-73.7]
Observation period: Median 474days [52.7-927]
Chapel Hill classification
- Microscopic polyangiitis (MPA)   32
- Granulomatosis with polyangiitis (GPA)   1
- Eosinophilic GPA (EGPA)   1

Treatments
- Prednisolone (PSL) only: 16
- PSL+MPT: 15
- PSL+MPT+cyclophosphamide (CY)   2
- PSL+MPT+mizoribine (MZR)   1

METHODS

We set the two end-points:
①death
②CKD5 or HD = CKD5 or hemodialysis except deceased patients

Univariate analyses

Quantitative variables
We compared various parameters between the patients who implemented these endpoints and those who did not with Student's t-test or the Mann–Whitney non-parametric test.

Survival curve analyses
Nominal and quantitative variables (quantitative variables were divided into two groups with an appropriate value) were compared using Kaplan–Meier analysis with the Log rank test to evaluate patient survival.
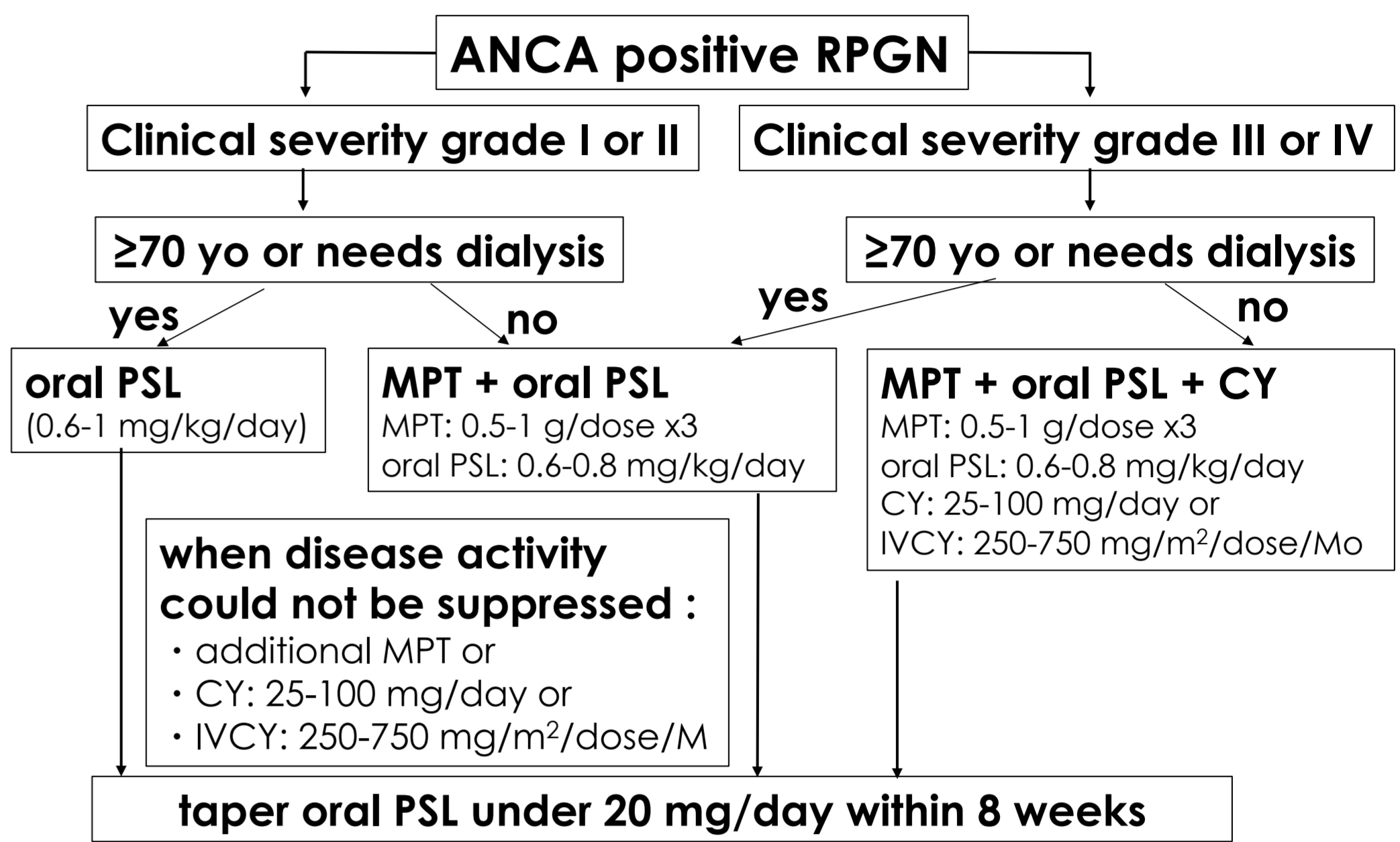
Parameters which had significant differences

Multivariate analyses

Endpoint ①death   Endpoint ②CKD5 or HD

Clinical Severity score J and treatment algorithm of the Japanese practice guideline of RPGN[4)]

Score	S-Cre (mg/dL)	Age	Lung involvement	CRP (mg/dL)	Total score	Clinical severity grade
0	[Cr]<3	<60	-	<2.6	0~2	Grade Ⅰ
1	3≦[Cr]<6	60~69		2.6~10	3~5	Grade Ⅱ
2	6≦[Cr]	≧70	+	>10	6~7	Grade Ⅲ
3	dialysis				8~9	Grade Ⅳ

ANCA positive RPGN

Clinical severity grade I or II → ≥70 yo or needs dialysis
- yes → oral PSL (0.6-1 mg/kg/day)
- no → MPT + oral PSL MPT: 0.5-1 g/dose x3 oral PSL: 0.6-0.8 mg/kg/day

Clinical severity grade III or IV → ≥70 yo or needs dialysis
- yes → MPT + oral PSL
- no → MPT + oral PSL + CY MPT: 0.5-1 g/dose x3 oral PSL: 0.6-0.8 mg/kg/day CY: 25-100 mg/day or IVCY: 250-750 mg/m²/dose/Mo

when disease activity could not be suppressed :
· additional MPT or
· CY: 25-100 mg/day or
· IVCY: 250-750 mg/m²/dose/M

taper oral PSL under 20 mg/day within 8 weeks

RESULTS

Univariate analyses

Patient variables for survival analyses
(the numbers of quantitative variables are as follows: we divided into two groups which contains that number and over, and under that number)
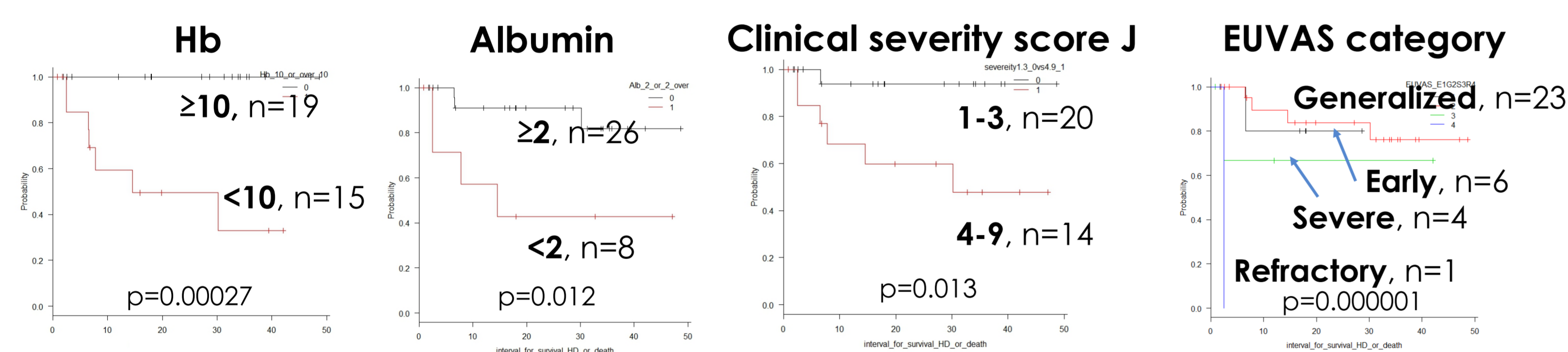
Clinical findings (at first visit)
type of treatment, sex, diabetes mellitus complication, lung involvement
age 65, 70 yo, Hb 9, 10 mg/dL, eGFR15, 30 mL/min/1.73 m², PCT 0.1, 0.15, 0.2 ng/mL, CRP5, 7, 10 mg/dL, BVAS 16, 18, 20 points, U-β2MG/Cr15, 20(μg/mg・Cr)、Alb 2, 2.5, 3, 3.5mg/dL
Clinical severity score J 3,4,5,6,7 points[4)], Clinical severity grade[4)], EUVAS disease category[5]
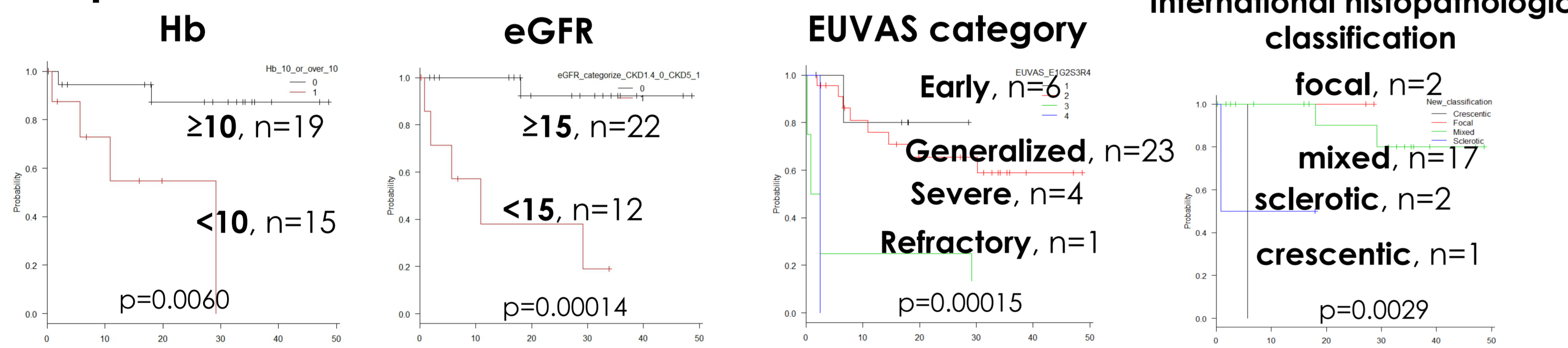
Pathological findings (at first visit)
crescents formation, 50%, global sclerosis, 30%, interstitial infiltration, vascular necrosis, basement membrane breakdown, interstitial fibrosis(with or without and severity), International histopathologic classification of ANCA related nephritis[6)]

Endpoint : ①death

Hb: ≥10, n=19; <10, n=15; p=0.00027
Albumin: ≥2, n=26; <2, n=8; p=0.012
Clinical severity score J: 1-3, n=20; 4-9, n=14; p=0.013
EUVAS category: Generalized, n=23; Early, n=6; Severe, n=4; Refractory, n=1; p=0.000001

Endpoint: ②CKD5 or HD

Hb: ≥10, n=19; <10, n=15; p=0.0060
eGFR: ≥15, n=22; <15, n=12; p=0.00014
EUVAS category: Early, n=6; Generalized, n=23; Severe, n=4; Refractory, n=1; p=0.00015
International histopathologic classification: focal, n=2; mixed, n=17; sclerotic, n=2; crescentic, n=1; p=0.0029

Stratified Analyses

Endpoint: ①death
Hb was the only independent risk factor.
stratified by eGFR data: Chisq= 9.9, p= 0.00169
stratified by Alb: Chisq= 10.9, p= 0.0009,
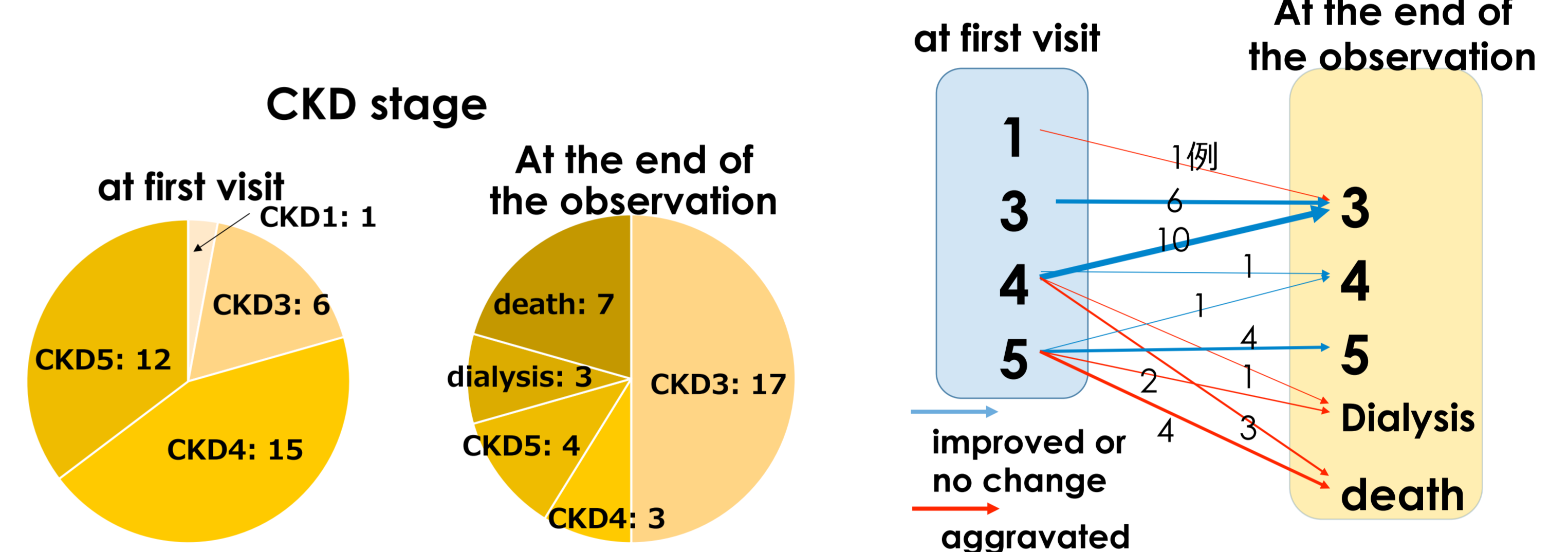stratified by clinical severity score J: Chisq= 9.9, p= 0.00169

Endpoint: ②CKD5 or HD
eGFR and EUVAS category were the independent risk factors
eGFR: stratified by Hb data: Chi-sq = 9.1, p= 0.0025, International classification: Chi-sq = 10, p= 0.0153, EUVAS: Chi-sq = 11.8, p= 0.0025
EUVAS: stratified by eGFR data: Chi-sq = 14, p= 0.0029, Hb: Chi-sq = 9.2, p= 0.027, International classification: Chi-sq = 6.3, p= 0.043

1-year survival rate: 82.9%
1-year renal survival rate: 76.9%

CKD stage

CKD stage at first visit: CKD1: 1; CKD3: 6; CKD4: 15; CKD5: 12
At the end of the observation: death: 7; dialysis: 3; CKD5: 4; CKD4: 3; CKD3: 17

CKD stage at first visit → At the end of the observation
improved or no change / aggravated

The parameters which analyzed with Cox proportional-hazard model

Endpoint: ①death
- eGFR≧15 or <15
- Hb≧10 or <10
- Albumin ≧2.0 or <2.0
- Clinical severity score J 1-3 or 4-9
- EUVAS category

Endpoint: ②CKD5 or HD
- eGFR≧15 or <15
- Hb≧10 or <10
- International histopathologic classification
- EUVAS category

Multivariate analyses

The Results of Cox Proportional-hazard Model Analyses
(stepwise elimination method using p value)

Endpoint: ①death
R^2= 0.383 (max possible= 0.727), Likelihood ratio test= 16.41, p=0.00093
eGFR<15mL/min/1.73m² at first visit and
hazard ratio: 5.22, 95%CI: 1.04-26.2, p=0.044
Albumin <2.0 at first visit were unchanged.
hazard ratio: 6.88, 95%CI: 1.43-32.9, p=0.015

Endpoint: ②CKD5 or HD
R^2= 0.443 (max possible= 0.617), Likelihood ratio test= 12.89, p=0.024
eGFR<15mL/min/1.73m² at first visit was unchanged.
hazard ratio: 17.18, 95%CI: 3.142-93.91, p=0.0010

DISCUSSION

- The prognosis analysis indicated that renal function could be improved if the patient's renal function at the first visit was in the CKD 3-4 category.
- In the deceased patients analysis, more than half of the patients died due to infectious diseases. This result was similar to previous reports.
- eGFR and albumin at first visit were predictors of death.
- Although eGFR and CRP at the first visit was a risk factor for death and poor renal outcome in the Japanese practice guideline of RPGN, CRP was not a risk factor in our analysis.
- Hb at the first visit could be a potential risk factor for death. This was not suggested in the previous reports.

CONCLUSIONS

- eGFR and albumin were predictors of death.
- eGFR was a predictor of poor renal outcome.
- Hb could be a potential risk factor for death.

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