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Genotype-phenotype analyses in Korean X-linked Alport syndrome: a multicenter study

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Objectives: Many clinical studies have elucidated the correlation between genotype and phenotype in male X-linked Alport syndrome (XLAS), whereas no association has been found in female XLAS. Here, we analyzed genotype-phenotype correlation in Korean XLAS.

Methods: In this multicenter, retrospective study, we recruited a total of 138 Korean patients (male : female = 96 : 42) with XLAS from 121 families who had been diagnosed from Jan 1985 to Jan 2021 in 13 tertiary centers in Korea. The genetic diagnosis was confirmed by Sanger or next-generation sequencing. The patients were divided into three groups according to the genotypes: Group (GP) 1=missense (n=45; Gly:non-Gly=36:9) or in-frame mutations (n=1); GP 2=splicing mutations (n=12); GP 3=frame-shifting or nonsense mutations (n=38).

Results: In 96 male, the median age of presentation was 5.1 years and the presenting symptoms were asymptomatic urinary abnormality (n=25), gross hematuria (n=24) or nephrotic syndrome (n=19). During follow-up, 54 (56%) developed chronic kidney disease grade 5 (CKD G5) by the median age of 20.0 years despite using renin-angiotensin system inhibitors in nearly all the patients. SNHL was detected in 50%. Although the ages of developing CKD G5 showed no significant difference among the three groups, kidney survival rates were significantly different (the median age of GP 1, 29.0 years; GP 2, 21.4 years; GP 3, 20.6 years, P=0.014). The frequency of SNHL was 33% in GP 1, 58% in GP 2, and 68% in GP 3 (P=0.002). In 42 female, the median age of presentation was 3.0 years, and 9 (21%) developed CKD G5 by the median age of 29.2 years. SNHL was accompanied in 14%. The kidney survival of the female patients was not correlated with genotypes.

Conclusions: Kidney survival rate and frequency of SNHL showed correlation with genotype in male patients but not in female patients, consistent with previous reports.

Fig 1. Kidney survival proportion according to mutant types in X-lined male patients (p=0.014)

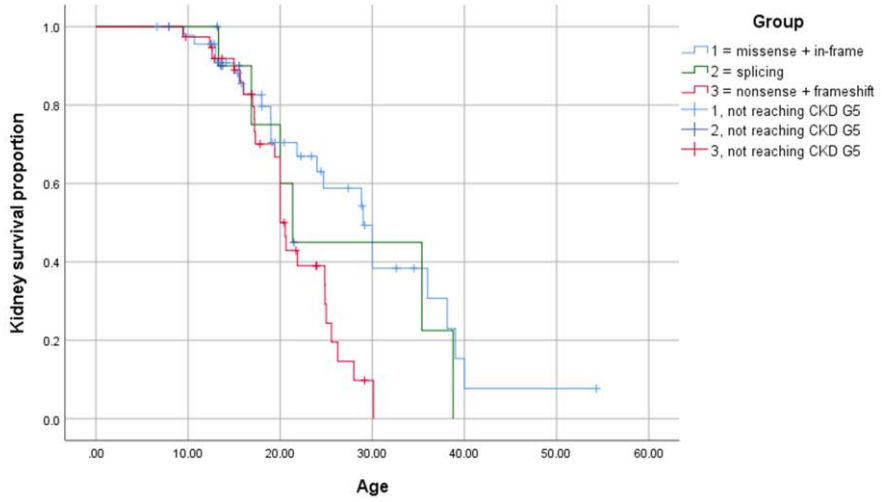

Fig 2. Kidney survival proportion according to mutant types in X-lined female patients (p=0.33)