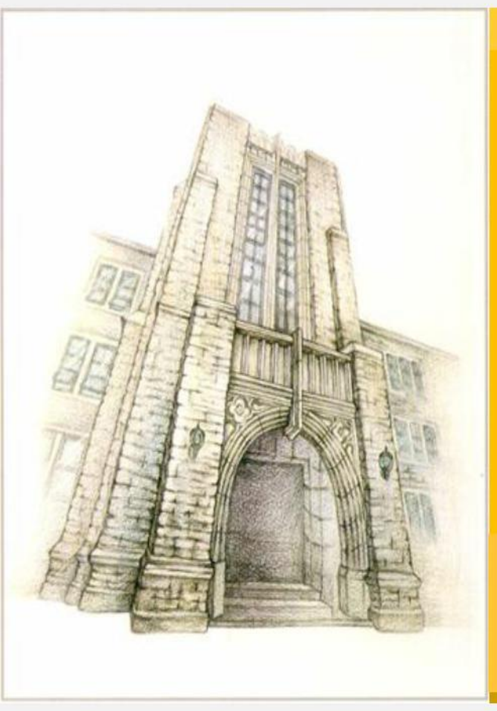

Value of Goal-Directed Urate Lowering Therapy in Slowing the Progression of Renal Disease in Hyperuricemic Patients

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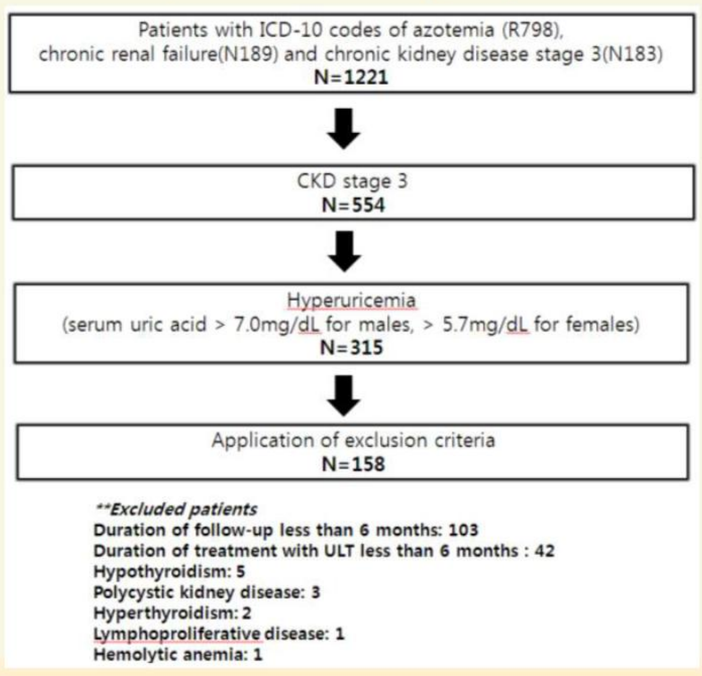
Background

Hyperuricemia associated with chronic kidney disease (CKD) has been traditionally thought to be an epiphenomenon of CKD. However, recent studies revealed that hyperuricemia itself may have a pathogenic role in the progression of renal disease. In this regard, it is expected that urate lowering therapies (ULT) would be beneficial in preventing the progression of renal disease in CKD patients with hyperuricemia. However, most of the relevant studies were relatively small in sample size, used different ULT treatment protocols and some studies did not observe CKD patients long enough to see the progression of renal disease. Currently, more data is needed in order to establish the value of ULT in CKD patients with hyperuricmia. In this study, we aimed to determine whether ULT could delay the progression of renal function decline in hyperuricemic patients with CKD and to evaluate the value of goal directed ULT.

Materials and Methods

We retrospectively reviewed the medical records of patients who were diagnosed as CKD and concurrent hyperuricemia from September 2005 to July 2014. After searching for relevant cases and applying the inclusion and exclusion criteria, we finally found a total of 158 eligible patients, and 65 of whom were treated with ULT during the follow-up period. In order to assess the effect of ULT in slowing the progression of renal disease, we divided the patients into 2 groups: ULT group (n=65) and non-ULT group (n=93) and compared the changes of renal function from baseline to the time point of last follow-up between the 2 groups.



Results

Table 1. Baseline characteristics

	Non-ULT treatment (n=93)	Treatment with ULT (n=65)	*P* value
Age (mean ± SD, years)	70.57±12.41	66.92±14.06	0.087
Male sex [n(%)]	66(70.21)	54(84.38)	0.064
Duration of follow-up (mean ± SD, days)	1066.35±749.70	1027.56±779.26	0.754
Baseline eGFR (mean ± SD, mL/min/1.73m²)	44.94±8.09	44.70±9.03	0.859
Systolic BP (mean ± SD, mmHg)	138.16±24.96	129.54±17.75	0.019
Diastolic BP (mean ± SD, mmHg)	79.51±17.00	80.51±13.79	0.699
Associated disease (%)			
HTN [n(%)]	86(91.49)	50(78.13)	0.032
CVD [n(%)]	20(21.28)	20(31.25)	0.219
DM [n(%)]	40(42.55)	20(31.25)	0.204
Dyslipidemia [n(%)]	57(60.64)	43(67.19)	0.503
Baseline BMI (mean ± SD, kg/m²)	26.40±15.91	27.78±17.78	0.617
Concomitant medications			
ACEi [n(%)]	5(5.32)	7(10.94)	0.316
ARB [n(%)]	44(46.81)	22(34.38)	0.164
Low dose aspirin [n(%)]	45(47.87)	27(42.19)	0.588
Diuretics [n(%)]	31(32.98)	21(32.81)	1
Serum uric acid level (mean ± SD, mg/dL)	8.00±1.16	9.05±1.91	<0.0001
Etiology of CKD [n (%)]			
Hypertensive	27(28.72)	21(32.81)	
Diabetic	39(41.49)	17(26.56)	
Glomerulonephritis	5(5.32)	5(7.81)	0.113
Others	4(4.26)	9(14.06)	
Unknown	19(20.21)	12(18.75)	
Gout [n(%)]	0(0)	42(65.63)	<0.0001

Table 2. Clinical outcomes

	Non-ULT treatment (n=93)	Treatment with ULT (n=65)	*P* value*
Baseline eGFR (mean ± SD, mL/min/1.73m²)	44.94±8.09	44.70±9.03	0.859
Last eGFR (mean ± SD, mL/min/1.73m²)	37.57±12.01	43.51±13.77	0.005
eGFR Change from baseline (mean ± SD, mL/min/1.73m²)	-7.37±11.17	-1.19±12.07	0.001
Renal disease progression [n (%)]	26 (27.90)	8 (12.30)	0.019
Elapsed time from baseline to renal disease progression (mean ± SD, weeks)	147.76±107.94	154±125.40	0.892
Serum uric acid (baseline) (mean ± SD, mg/dL)	8.00±1.16	9.05±1.91	<0.0001
Serum uric acid (last) (mean ± SD, mg/dL)	8.00±1.39	6.05±1.71	<0.0001
Mean serum uric acid (mean ± SD, mg/dL)	7.90±0.87	7.02±1.25	<0.0001
Systolic BP (baseline) (mean ± SD, mmHg)	138.16±24.96	129.54±17.75	0.019
Systolic BP (last) (mean ± SD, mmHg)	127.41±15.98	121.19±17.67	0.024
Diastolic BP (baseline) (mean ± SD, mmHg)	79.51±17.00	80.51±13.79	0.699
Diastolic BP (last) (mean ± SD, mmHg)	72.65±11.08	72.17±10.49	0.791

ULT: urate lowering therapy, eGFR: estimated glomerular filtration rate, SD: standard deviation, BP: blood pressure

Table 3. Subgroup analysis of clinical outcome

	Goal directed treatment (n=42)	Initial dose maintenance (n=23)	Non-ULT group (n=93)
eGFR change from baseline (mean±SD, mL/min/1.73m²)	-0.48±13.03, *P*=0.002*	-2.54±9.90, *P*=0.06*	-7.41±11.22
CKD progression [n (%)]	5/42 (11.9), *P*=0.047*	3/23, (13.0), *P*=0.183*	26/93 (27.9)
Mean serum uric acid (mean±SD, mg/dL)	6.72±1.29, *P*<0.001*	7.59±0.92, *P*=0.148*	7.89±0.87

*: *P* values for the comparison with non-ULT group, eGFR: estimated glomerular filtration rate, SD: standard deviation, CKD: chronic kidney disease, ULT: urate lowering therapy

Table 4. Multivariate analysis of factors associated with renal disease progression

Variable	OR	95% CI	*P* for trend
DM	3.368	1.399 ~ 8.109	
Mean uric acid			
>=8.0 mg/dL (reference)	1.0		
<8.0 mg/dL	0.471	0.178 ~ 1.242	0.04
<7.0 mg/dL	0.306	0.089 ~ 1.059	

OR: odds ratio, CI: confidence interval, DM: diabetes mellitus

Conclusion

ULT significantly lowered the serum uric acid levels and clearly showed a clinical benefit in slowing the progression of renal disease in CKD patients with hyperuricemia. Goal-directed ULT aiming at serum uric acid level < 6mg/dL seems to be better than maintaining the initial dose of ULT. Further studies are needed to establish the value of ULT in CKD patients with asymptomatic hyperuricemia.

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