SAT0372

INCREASED CAROTID INTIMA-MEDIA THICKNESS IN HYPERURICEMIC INDIVIDUALS MAY BE EXPLAINED BY HYPERHOMOCYSTEINEMIA ASSOCIATED WITH RENAL DYSFUNCTION

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Background: Both hyperuricemia and hyperhomocysteinemia are known to be associated with the deterioration of vascular endothelial function and are regarded as important risk factors for atherosclerotic vascular diseases. However, there has been no report about the relationship between homocysteine (Hcy) and atherosclerosis in patients with hyperuricemia.

Objectives: In this study, we evaluated the relationship between the carotid IMT and various clinical parameters including renal function and serum Hcy level in patients with hyperuricemia, and investigated the possible mechanism of how hyperuricemia is related with the increase of carotid IMT.

Methods: A total of 1228 subjects who visited the health promotion centre of hospital were enrolled in this study. All subjects completed both carotid ultrasonography and laboratory measurement, including serum Hcy levels and renal function. Serum Hcy levels were measured by a competitive immunoassay using direct chemiluminescent. Carotid IMT was evaluated by B-mode carotid ultrasonography.

Results: Hyperuricemic patients showed higher carotid IMT values compared with normouricemic patients (1.12±0.64 mm vs. 1.02±0.50 mm, p=0.043). The serum Hcy levels were significantly higher in the hyperuricemic group than in the normouricemic group (13.39±4.42 µmol/L vs. 11.69±3.65 µmol/L, p<0.001). In patients with hyperuricemia, serum uric acid levels were negatively correlated with estimated glomerular filtration rates (eGFR) ($\gamma=-0.334$, p<0.001), and eGFR were negatively correlated with serum Hcy levels ($\gamma=-0.490$, p<0.001). Carotid IMT was correlated with serum Hcy levels ($\gamma=0.196$, p=0.008), and atherosclerotic changes of carotid artery measured by carotid ultrasonography increased 1.09-fold (OR, 95% CI 1.006–1.185, p=0.036) per 1 µmol/L difference in serum homocysteine levels. In multivariate linear regression analysis, carotid IMT was affected by reduced eGFR ($\beta=-0.263$, p=0.002).

Conclusions: Carotid IMT was higher in patients with hyperuricemia than in normouricemic individuals. This study suggests that impairment of the renal function in patients with hyperuricemia may induce the increase in carotid IMT via increased serum Hcy levels.

Disclosure of Interest: None declared

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SAT0373

PREVENTING A LARGE MAJORITY OF INCIDENT GOUT CASES BY MODIFYING KEY RISK FACTORS: FINDINGS FROM A PROSPECTIVE COHORT OF 44,629 MEN OVER 26 YEARS

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Background: Many modifiable risk factors have been found to be independently associated with the risk of developing gout, including dietary factors (e.g., intakes of red meat and fructose), adiposity, alcohol intake, and diuretic use. Conversely, healthy dietary patterns (e.g., Dietary Approaches to Stop Hypertension [DASH]) and a high intake of vitamin C have been shown to be independently associated with lower gout risk. However, the potential combined impact of these factors on the risk of developing gout is unknown.

Objectives: We aimed to estimate the proportion of incident gout cases that could theoretically be avoided through the simultaneous adoption of multiple low-risk behaviours, including low body mass index (BMI), consumption of a DASH-style eating pattern, no alcohol intake, vitamin C supplementation, and no diuretic use.

Methods: From 1986 to 2012, we prospectively followed 44 629 men free from gout at baseline in the Health Professionals Follow-up Study. Lifestyle, anthropometric, and medical information was collected at baseline and updated biennially. Dietary data were obtained using validated food frequency questionnaires at baseline and approximately every 4 years during follow-up. We ascertained incident cases of gout using the American College of Rheumatology survey criteria for gout. We defined low-risk groups according to combinations of the following

five factors: a low BMI (<25 kg/m²), adherence to a DASH-style diet, no alcohol intake, vitamin C supplementation (≥ 1500 mg), and no diuretic use. Cox proportional hazard regression models were used to estimate the association of each risk factor with the development of gout and calculate the population attributable risk percent (PAR%).

Results: During 9 50 086 person-years of follow-up, incident gout developed in 1687 participants. All five modifiable risk factors were independently associated with incident gout. Obesity was the single most important predictor of gout; all other risk factors were also associated with a statistically significant increased risk of gout, even after adjustment for BMI. As compared with the rest of the cohort, men in the low-risk group (comprised of all five low-risk factors; 4.4% of men) had a relative risk of gout of 0.30 (95% confidence interval [CI], 0.12 to 0.72) (table 1). Accordingly, the PAR% for all five risk factors combined was 70% (table 1). The PAR% for four and three risk factors was 64% and 50%, respectively (table 1).

Abstract SAT0373 – Table 1. Relative and Population Attributable Risks of Gout for Groups Defined by Combinations of Modifiable Risk Factors

	Percentage of Men (%)	Number of Gout Cases	Relative Risk (95% CI)	PAR%
3 factors in low-risk category ^a	11.0	24	0.49 (0.33, 0.74)	50
4 factors in low-risk category ^b	10.3	15	0.35 (0.21, 0.59)	64
5 factors in low-risk category ^c	4.4	5	0.30 (0.12, 0.72)	70

Abbreviations: BMI, body mass index. CI, confidence interval. DASH, Dietary Approaches to Stop Hypertension. PAR%, Population attributable risk percent.

Relative risks were adjusted for total energy intake, coffee intake, and histories of renal failure and hypertension.

^aLow BMI, highest quintile of DASH diet score, and no alcohol intake.

^bLow BMI, highest quintile of DASH diet score, no alcohol intake, and no diuretic use.

^cLow BMI, highest quintile of DASH diet score, no alcohol intake, no diuretic use, and vitamin C supplementation.

Conclusions: Five modifiable risk factors accounted for 70% of incident gout cases in this large prospective cohort of male health professionals. Assuming a causal relation, our findings support the hypothesis that the vast majority of cases of gout could be prevented by modifying key risk factors.

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SAT0374

LESINURAD (LESU) ADJUNCTIVE THERAPY WITH ALLOPURINOL (ALLO) IN PATIENTS NOT RESPONDING TO ALLO MONOTHERAPY: POOLED POST HOC SAFETY AND EFFICACY ANALYSIS IN A PATIENT SUBGROUP USING CONCOMITANT DIURETICS AT BASELINE (BL)

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Background: LESU is approved as adjunctive therapy in combination with xanthine oxidase inhibitors (XOI) for gout PT not responding to XOI alone¹. Gout PT often have hypertension (HT) for which diuretics especially thiazide and thiazide-like diuretics (TTLD) are prescribed. TTLD contributes to hyperuricemia² by acting on OAT4 transporter, which is inhibited by LESU.

Objectives: To assess the efficacy and safety of LESU+ALLO in the subgroup of PT using concomitant diuretics at BL in CLEAR 1 and CLEAR 2, two randomised, double-blind, placebo-controlled Phase 3 studies that evaluated LESU200/400 mg daily in combination with ALLO vs ALLO+placebo.^{3&4}

Methods: Data from both trials of 1,213 PT, was pooled and PT group using diuretics at baseline was compared to non-users with respect to sUA target and TEAE.

Results: Totally 221 PT received diuretics, >90% due to HT and ~80% being TTLD. In both groups, LESU +ALLO doubled the number of PT reaching sUA target of <6.0 mg/dL vs ALLO +PBO at month 6 (m-6) and 12 (m-12) (table 1). At m-12, the response rate in PT receiving TTLD was 60.8%, 61.5% in the LESU 200 and 400 mg group, and 26.6% in the ALLO alone group, and 47.5%, 50.5%, and 25.7% in PT not receiving TTLD respectively. The safety profile was comparable