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Crystal diseases

OP0202

DOES EXCESS WEIGHT AFFECT GOUT RISK DIFFERENTLY AMONG GENETICALLY PREDISPOSED INDIVIDUALS? – SEX-SPECIFIC PROSPECTIVE COHORT FINDINGS OVER >26 YEARS

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Background: Global burden of gout has increased substantially, particularly among women.^{1,2} Addressing obesity, a major modifiable risk factor for gout, may alleviate this burden; however, there is also a significant genetic contribution to gout risk according to the genome-wide association studies (GWAS).^{3,4} Genetic predisposition may modify the excess weight effect on gout risk.

Objectives: To investigate the potential role of genetic predisposition on the association between excess weight (i.e., BMI \geq 25 kg/m²) and gout risk in two US prospective longitudinal cohorts over >26 years, stratified by sex.

Methods: We examined the association between excess weight and risk of incident gout meeting the ACR survey criteria,⁵ according to genetic risk, in 18,512 women from the Nurses' Health Study (NHS) over 32 years, and 10,917 men from Health Professionals Follow-Up Study (HPFS) over 26 years. We derived a genetic risk score (GRS) using 114 serum urate single nucleotide polymorphisms from the latest GWAS.³ We also calculated the population attributable risk (PAR) for excess weight according to GRS stratum.

Results: We ascertained 530 incident gout cases in NHS and 983 in HPFS. While the relative risks (RRs) due to excess weight (overweight or obesity) appeared larger among women above the mean than below the mean, the RRs among men appeared similar according to genetic predisposition (Table 1). The RRs among women for excess weight compared to normal were 1.66 (95% CI, 1.17 to 2.37) and 2.55 (1.95 to 3.34) below and above the mean GRS, respectively (P for multiplicative interaction = 0.06), whereas corresponding RRs among men were 1.68 (95% CI, 1.31 to 2.16) and 1.76 (1.47 to 2.10) (P for multiplicative interaction = 0.8). The risk differences (RD) among women for excess weight were 0.69 and 2.38 with GRS below and above the mean, respectively, resulting in the relative excess risk due to interaction (RERI) of 1.69 (95% CI, 1.03 to 2.35, P for additive interaction = 5.4x10⁻⁷); for men, the corresponding RDs were 0.70 and 1.46, with RERI = 0.76 (0.26, 1.25; P for additive interaction = 2.6x10⁻³). Excess weight accounted for a larger proportion of incident gout cases among women with GRS above the mean (PAR, 48.5% [95% CI, 38.8 to 55.9]) compared to those with GRS below the mean (PAR, 29.0% [95% CI, 10.5 to 42.1]), whereas the PARs among men were similar (31.6% vs 29.7%, respectively).

Conclusion: These large scale longitudinal prospective cohorts suggest maintaining healthy weight is an important gout prevention strategy, regardless of underlying genetic risk. In genetically predisposed individuals, addressing excess weight may prevent a large proportion of gout cases, especially among women.

REFERENCES:

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Table 1. Relative Risk of Gout by Body Mass Index, Stratified by Mean Genetic Score

BMI	HPFS (men)							
	Overall	Below Mean			Above Mean			
		<25	25-30	>30	Overall	<25	25-30	>30
No. Cases	333	88	172	73	650	172	349	129
Person-Years	104055	43314	49253	11488	98634	41994	46096	10544
Age-Adjusted RR	-	1.0 (ref)	1.71 (1.32, 2.22)	3.00 (2.18, 4.12)	-	1.0 (ref)	1.80 (1.50, 2.16)	2.87 (2.27, 3.62)
MV Adjusted* RR	-	1.0 (ref)	1.53 (1.18, 1.99)	2.31 (1.66, 2.21)	-	1.0 (ref)	1.63 (1.35, 1.96)	2.38 (1.87, 3.03)
BMI	NHS (women)							
	Overall	Below Mean			Above Mean			
		<25	25-30	>30	Overall	<25	25-30	>30
No. Cases	173	47	40	86	357	72	120	165
Person-Years	244392	123849	76414	44129	239259	120229	76123	42907
Age-Adjusted RR	-	1.0 (ref)	1.23 (0.81, 1.88)	4.46 (3.10, 6.41)	-	1.0 (ref)	2.41 (1.79, 3.23)	5.68 (4.82, 7.52)
MV Adjusted* RR	-	1.0 (ref)	1.00 (0.65, 1.53)	2.84 (1.92, 4.20)	-	1.0 (ref)	1.97 (1.46, 2.65)	3.61 (2.68, 4.87)

*Adjusted for age (continuous), menopause, use of hormone therapy (never, past or current), history of hypertension, and systolic and diastolic blood pressure, alcohol, total energy intake and intake of meat, seafood and dairy foods (all continuous).

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OP0203

GENE-DIET INTERACTION ON THE RISK OF INCIDENT GOUT AMONG WOMEN – PROSPECTIVE COHORT STUDY OVER 32 YEARS

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Background: Although gout is conventionally known as a male condition, the recent Global Burden of Disease (GBD) Study found disproportionate worsening among women.¹ We have found Dietary Approaches to Stop Hypertension (DASH) diet is independently associated with a lower risk of incident gout, while Western diet is associated with increased risk.² Whether these risks vary according to genetic risk remains unknown.

Objectives: To investigate the influence of genetic predisposition on the relation between diets (one protective and another hazardous) and gout risk in a large prospective US cohort of women over 32 years.

Methods: We examined the role of genes on the association between two dietary patterns (DASH and Western) on the risk of incident gout in 18,512 women from the Nurses' Health Study. Using validated food frequency questionnaires, for each participant we derived: 1) DASH score emphasizing fruits, vegetables, nuts, legumes, whole grains, low-fat dairy, and reduced intake of saturated fat and sugar-sweetened beverages (SSBs) and 2) Western diet score characterized by high intake of red and processed meats, SSBs, desserts, French fries, and refined grains. A genetic risk score (GRS) was derived using 114 serum urate single nucleotide polymorphisms from the latest GWAS consortium.³

Results: There were 523 incident gout cases meeting ACR survey criteria⁴ (170 vs. 353 in GRS below and above the mean, respectively) (Table 1). Among women with GRS below and above the mean, the multivariable relative risks (RRs) of gout were 1.0, 1.56, 1.32, 0.89, and 0.61 (0.34 to 1.09) and 1.0, 1.0, 0.85, 0.51, and 0.68 (0.49 to 0.96), for quintiles (Q) 1 through 5 of DASH score, respectively (p for interaction = 0.69) (Table 1). For the Western diet, RRs for Q1 through 5 were 1, 1.34, 1.07, 1.33, and 1.63 (0.91 to 2.93) for those with GRS below the mean and 1.0, 1.17, 0.93, 1.27, and 1.77 (1.19 to 2.61) among those with GRS above the mean, respectively (p for multiplicative interaction = 0.64).

Conclusion: In this prospective female cohort that ascertained gout with standardized criteria over 32 years, regardless of genetic predisposition, DASH diet was similarly associated with lower risk of incident gout while Western diet was associated with a higher risk. The anticipated absolute impact of diet among