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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 ≥ 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 = 5.4×10^{-7}); for men, the corresponding RDs were 0.70 and 1.46, with RERI = 0.76 (0.26, 1.25; P for additive interaction = 2.6×10^{-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.

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

BMI	HPFS (men)							
	Below Mean				Above Mean			
	Overall	<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)							
	Below Mean				Above Mean			
	Overall	<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 (2.17, 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

Table 1. Relative Risk of Gout by Quintiles of DASH and Western Diet Score, Stratified by Mean GRS

DASH											
Below Mean						Above Mean					
	Q1	Q2	Q3	Q4	Q5	Q1	Q2	Q3	Q4	Q5	P Interaction
No. Cases	27	49	51	21	22	75	89	90	34	65	
Person-Years	39208	47247	57227	34953	58764	39815	45853	55401	34733	56521	
Age-Adjusted RR	1.0 (ref)	1.43 (0.89, 2.29)	1.22 (0.76, 1.96)	0.8 (0.45, 1.42)	0.5 (0.28, 0.88)	1.0 (ref)	0.97 (0.72, 1.33)	0.79 (0.58, 1.07)	0.47 (0.31, 0.70)	0.54 (0.39, 0.76)	0.73
MV-Adjusted* RR	1.0 (ref)	1.56 (0.97, 2.51)	1.32 (0.82, 2.12)	0.89 (0.50, 1.59)	0.61 (0.34, 1.09)	1.0 (ref)	1.0 (0.73, 1.37)	0.85 (0.63, 1.17)	0.51 (0.33, 0.76)	0.68 (0.49, 0.96)	0.69
Western											
	Below Mean					Above Mean					
No. Cases	Q1	Q2	Q3	Q4	Q5	Q1	Q2	Q3	Q4	Q5	P Interaction
Person-Years	21	36	28	39	46	52	70	56	76	99	
Age-Adjusted RR	47397	49348	47837	47589	45283	45529	47913	47357	46	44785	
Age-Adjusted RR	1.0 (ref)	1.49 (0.86, 2.56)	1.26 (0.71, 2.23)	1.71 (1.00, 2.93)	2.22 (1.31, 3.74)	1.0 (ref)	1.21 (0.85, 1.74)	0.98 (0.67, 1.43)	1.35 (0.94, 1.93)	1.88 (1.34, 2.65)	0.72
MV-Adjusted* RR	1.0 (ref)	1.34 (0.78, 2.32)	1.07 (0.60, 1.90)	1.33 (0.76, 2.34)	1.63 (0.91, 2.93)	1.0 (ref)	1.17 (0.81, 1.68)	0.93 (0.63, 1.38)	1.27 (0.87, 1.84)	1.77 (1.19, 2.61)	0.64

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

genetically predisposed females was larger with greater absolute risk difference. These data agree with the recent GBD Study's recommendation for intensive dietary and anti-obesity measures for gout prevention, especially in females.¹

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OP0204

URATE CRYSTAL DEPOSITIONS ARE ASSOCIATED WITH INFLAMMATORY MARKERS AND CAROTID PLAQUES INDICATING SUBCLINICAL INFLAMMATION IN GOUT; BASELINE RESULTS FROM THE NOR-GOUT STUDY

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Background: In gout patients the extent of monosodium urate (MSU) crystal depositions can be quantitated by use of ultrasound. Gout may be associated with atherosclerotic disease which might be related to low-grade inflammation. Calprotectin is a major granulocyte protein reflecting the level of systemic inflammation.

Objectives: To explore whether the extent of MSU crystal depositions is associated with low grade systemic inflammation as assessed by calprotectin/C-reactive protein (CRP) and with carotid pathologies in asymptomatic gout patients.

Methods: The baseline data from NOR-GOUT, a prospective study of patients with crystal-proven gout with increased serum urate levels (>360 µmol/L), were used. All patients were assessed by ultrasound (GE Logiq E9 machine) to assess MSU depositions (OMERACT definitions; double contour (DC), tophi and aggregates) with bilateral assessment of wrist, MCP2, knee, ankle, MTP1 and insertions of triceps, quadriceps, proximal/distal patellar and Achilles tendons, all scored semi-quantitatively 0-3. Bilateral B-mode ultrasound assessments of the carotid arteries examined carotid intima-media thickness (cIMT; increased thickness >0.9mm). Atherosclerotic plaques were identified as protrusions of ≥1.5 mm or ≥ 2 times the adjacent IMT. Sum scores of each of the ultrasound elementary lesions for MSU depositions were calculated and the associations with calprotectin (plasma assessed by ELISA (Calpro), normal levels <910 µg/L), CRP (routine assessment, normal levels <4mg/L) as well as cIMT and presence of carotid plaque were explored. Correlations were performed by use of Spearman and differences between group was investigated by Mann-Whitney test.

Results: A total of 202 gout patients without flare were included (95.5% men, mean (SD) age of 56.5 (13.8) years, 7.9 (7.7) years since first flare). The mean (SD) sum score of DC was 4.4 (3.5), tophi 6.6 (6.6), aggregates 9.3 (5.6), calprotectin 801 (525) µg/L, CRP 7 (14) mg/L and serum urate (SUA) 499 (77) µmol/L. Carotid examinations were performed in 122 (60.4%) of the patients. Significant correlations were found between the MSU depositions and the inflammatory markers as well as cIMT. The 27% patients with increased calprotectin had the highest levels of each of the three elementary lesions (p=0.001) (Figure), and the 39% with elevated CRP levels had the highest levels of tophi and aggregates (p<0.05). The 18% with increased thickness of cIMT and the 53% of patients with carotid plaque had the highest levels of aggregates (p=0.003 and p=0.037, respectively).

Conclusion: In asymptomatic gout patients, higher load of MSU crystal depositions was associated with increased levels of inflammatory markers, cIMT and presence of atherosclerotic plaques in the carotid arteries. This may indicate that crystal depositions cause subclinical inflammation with subsequent systemic implications, but future longitudinal studies are needed to confirm such causal relationships.

	Sum score double contour	Sum score tophi	Sum score aggregates
Calprotectin	0.26**	0.32**	0.28**
CRP	0.20*	0.25**	0.18*
Right IMT	NS	NS	0.18*
Left IMT	NS	NS	0.21*
Sum bilateral IMT	NS	NS	0.22*

Spearman's correlations. NS; Not significant, *p<0.05, **p<0.001

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OP0205

ULTRASOUND-DETECTED CALCIUM PYROPHOSPHATE CRYSTAL DEPOSITION: WHICH SITES SHOULD BE SCANNED?

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Background: In recent years, ultrasonography (US) has emerged as an accurate and reliable tool for the diagnosis of calcium pyrophosphate (CPP) deposition disease (CPPD) in daily practice. Previous studies analyzed the diagnostic value of US findings in different tissues and joints. However, no studies have investigated the optimal US scanning protocol in the diagnosis of CPPD at patient level.

Objectives: To assess the diagnostic value of the combinations of OMERACT-defined US findings of CPPD in the upper and lower limbs and to select the best minimal combination of anatomic structures to be scanned for diagnosing CPPD in inter-critical periods.