FRI0227

RISK FACTORS FOR SKIN REACTIONS TO ALLOPURINOL IN THE KINH POPULATION OF VIETNAM

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Background: Allopurinol (ALLO) exposes to mild (M) and severe (S) cutaneous adverse reactions (CARs). SCARs have been associated with HLA*B58 01 with various strength of across ethnicities. Little is known about ALLO tolerance in Vietnam (VN).

Objectives: The aim of this ongoing prospective study was to investigate risk factors, including HLA*B-58 01, for MCARs and SCARs in the predominant Kinh ethnicity of VN

Methods: All included patients were Kinh Vietnamese. SCARs were recruited at Ho Chi Minh City hospitals, MCARs from the same departments and from the Vien Gut clinic at HCMC (specialised in gout care), and tolerant gouty patients (no skin reaction after at least 3 months from the last increment in ALLO dose) at the Vien Gut clinic. Clinical data were prospectively collected and HLA*B-58 01 typing used the PG5801 DNA detection kit (Pharmigene-Taiwan). Fisher exact test for categorical variables and Kruskal/Wilkinson test for quantitative variables were used for statistics.

Results: 10 patients experienced a non-fatal SCAR. Toxic necrotic epidermolysis, Stevens-Johnson syndrome and mixed syndrome were diagnosed in 1, 8 and 1 patients respectively. 54 patients stopped ALLO because of MCAR. 112 ALLO tolerant patients were recruited. Table 1 shows the main features of interest in the 3 groups. The Odds ratio of HLA*B-58 01 positive patients to develop SCARs was calculated at 171.2 (95% CI: 20; 7889)

Abstract FRI0227 – Table 1. Features associated with MCARs and SCARs

	SCARs (n=10)	MCARs (n=54)	Tolerant (n=112)	P value Global test	P value SCARs vs tolerant	P value MCARs vs tolerant
No Gout n (%)	5 (50%)	53 (98%)	112 (100%)	p<0,0001	p<0,0001	p=0,33
Females n (%)	2 (20%)	0	0	p=0003	p=0006	p=1
Age Mean (CI)	55 (CI :12)	47 (CI :12)	46 (CI :12)	p=0012	p=0,04	p=0,73
History of MCAR to ALLO	1/7 (14%)	1/52 (2%)	0	p<0,0001	p=0006	p=0,32
Diuretic intake n/known (%)	2/9 (22%)	1/52 (2%)	0	p=0002	p=0.005	p=0,32
ALLO dose/d Mean (CI)	345 mg/j (CI :142)	259 mg/j (CI :119)	356 mg/j (CI :114)	p<0,0001	p<0,0001	p=0.51
ALLO titration n (%)	0	49 (91%)	112 (100%)	p<0,0001	p<0,0001	p<0,0001
GFR<60 ml/ min n/known (%)	2/6 (33%)	1/51 (0.2%)	1/88 (0.01%)	p=0008	p=0,01	p=1
HLA-B*5801	10 (100%)	3 (5,6%)	6 (5,3%)	p<0,0001	p<0,0001	p=1

Conclusions: HLA*B-58 01 was significantly associated with SCARs to ALLO in the VN Kinh population. Other known factors but not high ALLO dose were also associated. The only association with MCARs was lack of ALLO titration.

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FRI0228

URATE CORRELATES TO CORONARY ARTERY CALCIFICATION BUT NOT TO INTIMA MEDIA THICKNESS

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Background: Hyperuricemia is closely associated to cardiovascular disease (CVD) although it has not been definitively established whether it is a marker or a causative agent. Serum urate (SU) is strongly linked to the metabolic syndrome, hypertension, hyperlipidemia, kidney failure and higher BMI and higher levels are seen in men compared to women. Coronary artery calcification (CAC) is associated with future risk of atherosclerotic CV events in addition to the traditional cardiovascular risk factors (CVRF). CACs are present in atherosclerotic arteries and can be quantified and scored non-invasively by computed tomography. Carotid intima media thickness (CIMT) is a method of estimating atherosclerosis by assessing the level of arterial thickening present. CIMT can be used as a noninvasive marker of atherosclerotic disease with increasing CIMT linked to an increased risk of subsequent CV events. In the present study we have examined the relation between CACs, CIMT and SU in 1040 male and female with no history of myocardial infarction or stroke.

Objectives: To examine the association between SU and CAC and CIMT respectively in men and women separately.

Methods: We identified 1106 (552 males) individuals who were screened for traditional CVRFs, such as hypertension (HT), dyslipidemia (DL), diabetes mellitus (DM), smoking, physical activity (PA), educational level (EDU), socioeconomic status (SES), BMI, high sensitive CRP (hsCRP), kidney function by eGFR (eGFR). CACs, reflecting calcification of coronary arteries, was determined according to Agatston¹. CIMT was calculated as the mean of CIMT of the left and right coronary artery. We measured SU and related quartiles of it to CACs and CIMT with multiple logistic regression analyses adjusting for traditional CVRFs. CAC was defined positive if ≥ 1 . CIMT was defined positive for ≥ 75 percentile. All study participants with a history of CVD (n=68, 44 male) were excluded.

Results: Of the 1106 participants, 68 were excluded due to history of CVD rendering a study population of 1040 individuals (508 males) with a mean age of 57.7 and 57.5 for male and female respectively. Age, BMI, EDU, SES, smoking status, PA, hsCRP, HT and DL showed no differences between sex while presence of CAC and diabetes was twice as common in men (table 1) and 65% of men displayed an eGFR below 90 mL/min compared to 12% of women (table 1a b). The three upper quartiles of SU (>306 $\mu\text{mol/L}$) all significantly ($p<0.05$) predicted presence of CACs in male when adjusting for HT, DL, DM, smoking, PA, EDU, SES, BMI, hsCRP, eGFR and age in multivariate logistic regression, but not in women (table 2). CIMT showed no correlation to SU in men nor women.

Abstract FRI0228 – Table 1. Prevalence of gout I WSHCR by 2012–12–31, age above 20 years in total and by age and sex

Variables	Male, n=508	Female, n=532
Age, years, mean, (SD)	57.7(4.4)	57.5(4.3)
BMI, mean, (SD)	27.7(4.1)	26.8(4.9)
hsCRP, (mean, SD)	2.2(3.4)	2.4(3.8)
CAC positive, (%)	293(58%)	137(26%)
eGFR >90 ml/min	180(35%)	467(88%)
eGFR 60-90 ml/min	316(62%)	60(11%)
eGFR <60 ml/min	12(2%)	5(1%)
Smoking status, never	215(42%)	237(45%)
Smoking status, previous	206(41%)	191(36%)
Smoking status, active	86(17%)	102(19%)
Hypertension (%)	160(32%)	178(33%)
Diabetes mellitus (%)	39(8%)	21(4%)
Dyslipidemia (%)	144(28%)	121(23%)

Abstract FRI0228 – Table 2. Quartiles of sUA and age as predictors for presence of CAC (>0 CACs score) in male and female in multivariate logistic regression analyses adjusted for age, smoking, BMI, DM, DL, HT, hsCRP, EDU and PA.

	Male			Female	
	Odds ratio, multivariate*, (CI)	p-value		Odds ratio, multivariate*, (CI)	p-value
sUA, $\mu\text{mol/L}$			sUA, $\mu\text{mol/L}$		
31-305, Ref			143-229, Ref		
306-350	2.1 (1.2-3.7)	0.01	230-262	0.9 (0.5-1.7)	0.7
351-404	1.8 (1-3.3)	0.04	263-305	1 (0.5-2)	0.9
405-665	2 (1-3.8)	0.04	306-702	1.2 (0.6-2.3)	0.6

Conclusions: Higher levels of SU is associated with presence of CACs in men but not with CIMT. This could suggest that SU is an innocent bystander that covariates with many, but not all, CVRFs. However, it could also imply biological differences in the effect of SU on calcification of coronary arteries compared to carotid intima thickening. Furthermore, SU may exert different effects depending upon biological age and degree of CVD development.

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FRI0229 THE VALIDITY OF THE OMERACT ULTRASOUND DEFINITIONS OF GOUT ELEMENTARY LESIONS IN THE DIAGNOSIS OF GOUT

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Objectives: The aim was to evaluate ultrasound (US) as a diagnostic tool for gout using the OMERACT US Working Group's 2015 US definitions for elementary lesions in gout using a) positive urate crystal microscopy or b) clinical diagnosis of gout blinded to the US assessment as gold standard for determining the sensitivity and specificity of each elementary lesion.

Methods: US examination (28 joints, 26 tendons) were performed in patients with clinically suspected gout. Joints were evaluated for the four OMERACT elementary lesions of gout (Double contour (DC), Tophus, Aggregates and Erosions) and tendons for aggregates and tophus. The lesions were registered as either present or absent for each patient. The US assessment was compared to 2 different gold standard references: 1) presence/absence of monosodium-urate (MSU) crystals by joint fluid microscopy and 2) the final clinical diagnosis based on the clinical assessment by a rheumatologist, blinded to US findings but not microscopy findings (table 1).

Results: 51 patients (44 males, 7 female), mean age of 62(30 – 89) years were included. 34 of these had a positive microscopy for MSU crystals whereas 15 patients had a negative microscopy and in 2 patients joint aspiration was not possible. Of the patients without positive microscopy 3 were clinically diagnosed as having gout by a US blinded assessor whereas 14 were diagnosed with other diseases.

DC, tophus and aggregates were found to be statistically significantly more frequent in both patients with positive MSU microscopy and in patients with clinically diagnosed gout (p-values range from 0.003 to <0.0001), compared to patients with negative MSU microscopy and other clinical diagnoses, respectively. All four elementary lesions were found to have high sensitivity (ranges from 0.74–0.88) for gout, both when MSU microscopy and when clinical diagnosis was used as gold standard reference. DC and aggregates had the highest sensitivities (0.85–0.88). Low specificity (0.33–0.64) was found for both aggregates and erosions, both when microscopy and clinical diagnosis was considered the gold standard. In contrast, DC and tophus showed high specificities for patients with microscopically proven gout (0.73 and 0.87, respectively) and particularly patients with clinically diagnosed gout (both 0.93).

DC and tophi were also found to have high positive predictive values (PPV) for gout for patients with microscopically proven gout (0.88 and 0.93, respectively) and especially for patients with clinically diagnosed gout (both 0.97). In contrast negative predictive values (NPV) were relatively low for all lesions (ranges from 0.36–0.72).

Abstract FRI0229 – Table 1. US findings in patients with microscopically proven or clinically defined gout.

		Microscopy gold standard reference						Clinical diagnosis gold standard reference					
		No. 49						No. 51					
		Microscopy positive	Microscopy negative	Sensitivity	Specificity	PPV	NPV	Fisher's exact test	Clinical gout	Clinical no gout	Sensitivity	Specificity	PPV
US lesions**	No.	34	15					P-value*	No.	37	14		
DC	Present	33	4	0.85	0.73	0.85	0.69	0.0001	33	32	1	0.85	0.93
	Absent	1	11						1	5	13		0.97
Tophi	Present	29	2	0.79	0.87	0.93	0.65	<0.0001	30	29	1	0.78	0.93
	Absent	7	13						7	8	13		0.62
Aggregates	Present	37	7	0.88	0.53	0.61	0.67	0.003	37	32	5	0.85	0.64
	Absent	12	8						14	5	9		0.64
Erosions	Present	35	10	0.74	0.33	0.71	0.36	0.73	36	28	8	0.75	0.43
	Absent	14	5						15	9	6		0.40

*P-values are calculated using Fisher's exact test, two-sided p-values.

**Joints evaluated by US: Metacarpophalangeal, wrist, elbow, metatarsophalangeal, tibiotaral and knee joints. Tendon compartments evaluated by US: Extensor tendons of the wrist, flexors, peroneus, tibialis posterior, quadriceps and patella tendons.

Conclusions: The OMERACT US definitions of gout elementary lesions seem to be a valid tool for diagnosis of gout in clinical practice. Particularly, DC and tophi seem to have a high specificity and high PPV for the disease.

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FRI0230 CROWNED DENS SYNDROME, YET ANOTHER RHEUMATIC DISEASE IMPOSTER

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Background: Crowned Dens Syndrome (CDS) is defined as acute cervical or occipital pain, usually associated with elevated acute phase reactants, due to local inflammatory reaction related to calcifications in the ligaments surrounding the odontoid process. Virtually all previous descriptions of CDS have been related to calcium pyrophosphate dehydrate (CPPD) arthropathy.

Objectives: To evaluate patients admitted with acute neck pain and/or headache for CDS not only in those with CPPD arthropathy but also in patients with other rheumatic diseases

Methods: Twenty four cases of CDS treated in Zion Medical Centre in 2016–2017 were prospectively reviewed. Patients were evaluated according to clinical and laboratory features, background rheumatic disease, response to treatment and invasive investigational procedures undertaken.

Results: All patients (age range 54 to 87 years, 67% females) presented with acute onset pain in upper neck and/or occiput accompanied with extreme neck stiffness. Nineteen of 24 patients (79%) had elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Five patients (21%) complained on concomitant severe diffuse headache. Four of those underwent temporal artery biopsy, which was negative for arteritis in all cases, and one was subjected to lumbar puncture, which was non-contributory.

The diagnosis of CDS was based on computed tomography imaging in all patients, with precipitations of calcium pyrophosphate dehydrate seen most often in transverse ligament (figure 1) or in alar ligaments.

Seventeen patients (71%) had known rheumatic disease on presentation: 10 patients had the diagnosis of CPPD arthropathy, 3 patients had ankylosing spondylitis, 2 patients had rheumatoid arthritis, 1 patient had Behcet's disease and 1 suffered from Familial Mediterranean Fever (table 1). In 4 more patients CDS was the presenting symptom of CPPD disease, diagnosed during hospitalisation.

All patients were treated with glucocorticoids as 0.5 mg/kg prednisone plus colchicine 0.5 mg bid resulting in dramatic improvement in both clinical (head/neck pain alleviated and cervical spinal mobility regained) and laboratory measures.

Abstract FRI0230 – Table 1. Clinical and laboratory feature of 24 patients with crowned dens

Age, median(range)	71(44-87)
Female (ratio)	16/24 (66%)
Presentation symptoms:	No. (%)
Neck pain	24 (100%)
Headache/Fever	5 (20.6%) 1 (4%)
Antecedent rheumatologic diagnosis:	No. (%)
Calcium pyrophosphate dehydrate	14 (58%)
Ankylosing spondylitis	3 (12.5%)
Rheumatoid arthritis	2 (8.3%)
Behcet's disease	1 (4%)
Familial Mediterranean Fever	1 (4%)
Elevated CRP/ESR, (mean)	19 (60 mg/l)
Patient underwent temporal artery biopsy	4 (16.6%)