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Crystal diseases, metabolic bone diseases and bone diseases other than osteoporosis

FRI0220

ULTRASOUND IN ASSESSMENT OF DISEASE COURSE IN GOUT: THE 24 MONTH SINGLE-CENTRE PROSPECTIVE OBSERVATIONAL STUDY

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Background: Today, despite the great potential of ultrasound (US) in gout, there is lack of longer duration US follow-up studies in this disease.

Objectives: The aim was to evaluate the 24 month's treatment effect of urate-lowering therapy on gout-specific US lesions and to determine the most representative target for US follow-up in gout.

Methods: A 24 month prospective observational single-centre study was carried out. Patients with gout diagnosis, confirmed by identification of monosodium urate crystals, with at least one tophus in the joint or tendon or one double contour sign (DC) on US, were selected for the study. The serum uric acid (SUA) level was assessed every three months. US evaluations of 36 joints and four tendons (m. triiceps and patellar) were performed every six months starting from the baseline, by one rheumatologist, blinded to the SUA levels and clinical data. Outcomes were: change in US features (tophus, DC count and tophus size) in joints and tendons according median of SUA level during the follow up period from M3 to M24. Two stages of SUA levels were defined: high, $\geq 360 \mu\text{mol/l}$; and low, $< 360 \mu\text{mol/l}$ (considered as within the treatment target). Correlations between US findings modifications in different locations, and between US findings modifications and SUA levels, were estimated by the Pearson correlation coefficient.

Results: We included 40 gouty patients (mean $\pm$ SD age 54.1 $\pm$ 9.7 years, 90.0% males, disease duration 8.5 $\pm$ 8.8 years). Mean $\pm$ SD baseline SUA level was 504.8 $\pm$ 32.9 $\mu\text{mol/l}$.

Among the 31 completers at M24, 21 (71%) achieved median SUA $< 360 \mu\text{mol/l}$. On month 24 the global number of patients with DC and tophus was reduced from 91% to 32% and from 100% to 64%, respectively. A total of sixty-four percent of patients in the study had not reached the US cure (DC or T being still found in at least one joint or tendon) after two years of treatment in the group with the median of SUA less than 360 $\mu\text{mol/l}$. The comparison of crystal clearing process in joints and tendons showed an excellent correlation of mean percentage change in total tophus number ($r=0.900$) and size ($r=1.0$) in joints and tendons, investigating 21 gout patients who participated in all five US study visits during the 24 months of follow-up. A strong positive correlation was observed between the changes of tophus size in left and right first MTP joints ($r=0.718$ [95% confidence interval: 0.370; 0.875], $p<0.001$) also between the changes of tophus size in toe and total intra-articular tophus size, measured by US ($r=0.726$ [95% confidence interval: 0.347; 0.925], $p<0.001$) on month 24 (compared to month 0). It was found a negative correlation between the mean SUA during 24 months follow up and the reduction in tophus size on month 24 ($r=0.602$)

Conclusions: Only one third of patients with median SUA $< 360 \mu\text{mol/l}$ were free of US gout signs after 2 years of treatment. Due to positive link between the change in tophus size in the first MTP joint and changes in the whole intraarticular urate pool, also tendons, the tophaceous deposition in the first MTP joint could be the most representative target for follow-up morphological analysis in gout clinical trials or monitoring the disease's activity in clinical practice with US.

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FRI0221

GOUT IS ASSOCIATED WITH AN INCREASED RISK OF CANCER – A NATIONWIDE COHORT STUDY INCLUDING OVER 70,000 GOUT PATIENTS

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Background: In addition to the possible carcinogenic effect of chronic inflammation, gout patients may experience increased risk of cancer due to additional risk factors such as obesity, diabetes, sedentary lifestyle, smoking and increased alcohol consumption. There is limited data on the association between gout and different cancer types. We investigated the incidence of cancer among Danish gout patients compared to national cancer rates.

Methods: All patients diagnosed with gout in the period 1978–2015 according to the Danish National Patient Registry (including in- and outpatient hospital contacts) were linked with The Danish Cancer Registry to identify incident cancers. Follow-up for cancer started at date of first gout diagnosis and ended at date of cancer, death, emigration or end of 2015, whichever came first. Standardised incidence ratios (SIR) were calculated using sex and 5 year age and calendar-specific incidence rates for first primary cancers in the general population in Denmark.

Results: We observed 6205 first primary cancers among 70 591 gout patients. Compared to an expected number of 5308 in the general population, this corresponded to a SIR for any-cancer of 1.17 (95% confidence interval (CI): 1.14–1.20). SIRs were highest for cancer sites associated with smoking, obesity and excess alcohol consumption: mouth/tongue, pharynx, oesophagus, liver, pancreas, lung, pleura and kidney (table 1). Excess risks were also observed for colorectal cancer, breast cancer, endometrial cancer, multiple myeloma and other types of leukaemia but not for Hodgkin and Non-Hodgkin lymphomas.

Conclusions: Gout patients are at risk of cancer, especially cancer types associated with smoking, obesity and excess alcohol consumption, but also multiple myeloma and leukaemia. It is unknown if uric-acid lowering therapy and/or lifestyle changes reduce this risk.

Observed number (Obs) of incident cancers and standardised incidence ratios (SIRs) among 70 591 patients with gout.

Cancer site	Obs	SIR (95% CI)	Cancer site	Obs	SIR (95% CI)	Cancer site	Obs	SIR (95% CI)
<i>Buccal cavity and pharynx</i>			<i>Respiratory system</i>			<i>Male genital organs</i>		
Lip	14	0.74 (0.40–1.24)	Nasal, ear, sinus	11	0.89 (0.44–1.59)	Prostate	973	1.01 (0.95–1.08)
Tongue/mouth	88	1.57 (1.27–1.93)	Larynx	66	1.18 (0.91–1.50)	Testis	28	1.40 (0.93–2.02)
Pharynx	99	1.93 (1.57–2.35)	Lung	863	1.12 (1.05–1.20)	<i>Urinary tract</i>		
<i>Digestive organs</i>			Pleura	11	5.53 (2.76–9.89)	Kidney	214	1.80 (1.57–2.06)
Oesophagus	116	1.32 (1.09–1.59)	Melanoma	184	0.99 (0.85–1.15)	Renal pelvis and ureter	34	1.16 (0.80–1.62)
Stomach	149	1.04 (0.88–1.22)	Breast	385	1.17 (1.06–1.29)	Urinary bladder	462	1.07 (0.98–1.18)
Small intestine	20	1.28 (0.78–1.98)	<i>Female genital organs</i>			<i>Lymphatic and hematopoietic tissues</i>		
Colon	636	1.18 (1.09–1.28)	External	15	1.07 (0.60–1.76)	Hodgkin	10	0.84 (0.40–1.55)
Rectum	326	1.11 (1.00–1.24)	Cervix	29	1.21 (0.81–1.74)	Non-Hodgkin	124	0.77 (0.64–0.92)
Liver	158	2.24 (1.90–2.62)	Endometrial	114	1.75 (1.44–2.10)	Multiple myeloma	98	1.37 (1.11–1.67)
Gallbladder	50	1.26 (0.93–1.66)	Ovary	39	0.79 (0.56–1.08)	Lymphatic leukaemia	97	1.09 (0.88–1.33)
Pancreas	238	1.41 (1.23–1.60)				Other leukaemia	101	1.59 (1.31–1.94)

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FRI0222

ASSOCIATION BETWEEN BLOOD LEAD LEVELS AND GOUT: THE UNITED STATES NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 2007–2014

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Background: Lead is a heavy metal with no physiological role in humans. It is well known that excessive exposure to lead is associated with cardiovascular, gastrointestinal and neurological complications. However, recent studies have demonstrated that lead can increase the tubular reabsorption of urate, resulting in hyperuricaemia and the development of gout.

Although blood lead levels are dropping in the US general population, the association between low blood lead levels and gout remains inconclusive.

Objectives: To evaluate the relationship between serum blood lead levels and the development of gout in the US general population.

Methods: Adult participants with blood lead measurements and self reported gout in NHANES 2007–2014 were included in the analysis.

Results were analysed using SPSS complex sample module version 22. Logistic regression with sample weight adjustment was used to study the association between blood lead levels and gout. Odds ratio (OR) and 95% confidence interval (95% CI) were estimated. Sub-group analysis was conducted in participants with blood lead level <5 µg/dL.

Results: 18837 adult participants were included in the analysis. 18 270 participants had blood lead levels below 5 µg/dL (The current reference range for acceptable blood lead levels in healthy persons without excessive exposure to environment source of lead).

The prevalence of gout increased with blood lead levels. In the total population, the odd ratio of gout was 4.96 in subjects with blood lead levels above 2.21 µg/dL. After adjusting for body mass index, hypertension, renal function and use of diuretics, the odd ratio of gout was 2.65 which remained significant.

The subgroup analysis of subjects with blood lead levels below 5 µg/ml showed similar findings. The risk of gout is increased when blood lead levels are higher than 1.43 µg/dL.

Abstract FRI0222 – Figure 1. (A) Prevalence of gout according to quintiles of blood level. (B) Association between quintiles of blood lead level and gout at blood lead level <5µg/dL

Conclusions: Low blood lead levels are associated with gout. The risk of gout is increased when the blood lead level is higher than 1.43 µg/dL. Therefore, measures should be taken to minimise the environmental exposure to lead.

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FRI0223

IS PERFORMANCE OF THE 2015 ACR/EULAR GOUT CLASSIFICATION CRITERIA AFFECTED BY DISEASE DURATION AND GENDER? RESULTS FROM AN ITALIAN MULTICENTRE STUDY FOCUSED ON THE MANAGEMENT OF CRYSTAL-INDUCED ARTHRITIDES (ATTACK STUDY)

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Background: Gout is a common form of arthritis, but early disease and phenotypes related to gender¹ may favour diagnosis misclassification, unless monosodium urate (MSU) crystals are searched for in synovial fluid (SF). The 2015 ACR/EULAR gout classification criteria² were validated in Rheumatology and primary settings,³ and the impact of disease features on performance were observed,⁴ yet little studied.

Objectives: To assess the performance of the 2015 ACR/EULAR gout criteria in a cohort of crystal-induced arthritides stratified by disease duration and gender in a real-life setting in Italy.

Methods: In/outpatients referring to Rheumatology Units for acute arthritis were enrolled into an ongoing multicentre cohort study designed for achieving improvement in the management of crystal-induced arthritis (ATTACK) by the Italian Society for Rheumatology. Gout was defined as MSU +SF (gold standard), irrespective of the clinical diagnosis, and the ACR/EULAR criteria were applied as full (all domains) and clinical-only set excluding imaging and SF analysis. To classify a patient as having clinical gout, the sufficient criterion (MSU +SF) was ignored and cutoff score ≥8 was used. Overall sensitivity and specificity were calculated. Disease duration (early if <2 years) was considered and gender effect explored.

Results: Of 199 adult patients (65±12 years, 75% male, 96% Caucasian) recruited in 11 hospitals, complete SF analysis and ACR/EULAR score were obtained in 105 (53%). MSU+ were 62/105 (59%), 47/62 (76%) were non-tophaceous and 25 (40%) early diseases. Calcium pyrophosphate (CPP) was the most prevalent crystal in non-MSU+. Details on performance (95% confidence intervals) are shown in table and on a receiver operating characteristic plot (figure 1).

Abstract FRI0223 – Table 1

	Sensitivity%		Specificity%	
	Full	Clinical-only	Full	Clinical-only
Overall n=105	76 (63–86)	71 (58–82)	95 (86–99)	81 (67–92)
<2 years n=49	48 (28–69)	40 (21–61)	100 (86–100)	92 (73–99)
≥2 years n=56	95 (82–99)	92 (78–98)	89 (67–99)	68 (44–87)
Male n=74	77 (64–87)	74 (60–85)	94 (71–100)	65 (38–86)
Female n=31	60 (15–95)	40 (5–85)	96 (80–100)	92 (75–99)

Overall good performance and high specificity of full and clinical-only sets were observed. In early disease criteria had high specificity, but low sensitivity, while performance was stable in longstanding gout. Specificity (clinical-only) and sensitivity were low when criteria were applied to males and females, respectively.