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Osteoarthritis: a vascular disease

OP0354

RADIOGRAPHIC EROSIONS ARE ASSOCIATED WITH FLUORESCENCE OPTICAL IMAGING ENHANCEMENT IN HAND OSTEOARTHRITIS

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Background: Erosive hand osteoarthritis (OA) is a phenotype characterised by more inflammation and erosions of the subchondral bone. Fluorescence optical imaging (FOI) is a novel imaging technique demonstrating altered microcirculation in wrist and finger joints as a sign of inflammation. No previous hand OA study has explored the validity of FOI against radiography.

Objectives: The aim of the current study was to explore the association between radiographic findings and FOI enhancement in the distal (DIP) and proximal interphalangeal (PIP) joints.

Methods: The NOR-HAND study is an observational hand OA study, in which 251 patients (88% female, median age 61 (interquartile range 56–66) years, 35% erosive hand OA) underwent FOI and x-rays of both hands. The FOI-scan was performed after the administration of an intravenous fluorescence dye (indocyanine green, ICG) and 360 images (1/second) were produced in 6 min. Based on the inflow and washing out of the dye the pictures were divided into 3 phases. Finally, the prima vista mode (PVM) represented a composite picture of the first 240 images of the examination. For each phase, fluorescence enhancement in the joints was graded from 0–3 based on signal intensity. Radiographic severity of the joints was evaluated with the Verbruggen Veys (VV) anatomical phase scoring system, which is based on the assumption that OA in finger joints will progress through different phases. To study whether more advanced radiographic phases were associated with FOI enhancement in the same joint, we applied logistic regression analyses with generalised estimating equations adjusting for age, sex, BMI and absence/presence of erosive hand OA, defined at patient level as having at least one DIP and PIP joint(s) in the erosive or remodelled phase.

Results: FOI demonstrated no and uncommon enhancement of the metacarpophalangeal and thumb base joints, respectively, thus we analysed DIP and PIP joints only. FOI enhancement was most commonly seen in phase 2 and PVM, also in the non-affected joints (table 1). The frequency of enhancement was lower for phase 3 and in particular for phase 1. Joints in the erosive phase had statistically significantly higher odds of FOI enhancement in phase 1, 2 and PVM as compared to the non-affected joints (table 1). Having erosive hand OA in other DIP and PIP joints was also associated with FOI enhancement ($p < 0.05$ in all phases except in phase 1), and our stratified analyses confirmed that FOI enhancement in the non-erosive phases was more common in the erosive vs the non-erosive hand OA patients.

Abstract OP0354 – Table 1 Odds of FOI enhancement in joints with increasing radiographic severity according to the verbruggen veys anatomical phase scoring system

	FOI Phase 1, Grade 1-3			FOI phase 2, Grade 1-3			FOI phase 3, Grade 1-3			FOI PVM, Grade 1-3		
	N (%)	OR	CI 95%	N (%)	OR	CI 95%	N (%)	OR	CI 95%	N (%)	OR	CI 95%
All Hand OA Patients												
N phase*	15/1618 (1)	1		1125/1582 (71)	1		333/1575 (21)	1		978/1632 (60)	1	
S phase*	28/2269 (1)	1.16	0.58–2.33	1582/2212 (71)	0.80	0.64–1.00	134/2202 (24)	0.62	0.51–0.76	1311/2288 (57)	0.73	0.62–0.87
E phase*	3/211 (1)	1.71	0.53–5.48	159/206 (77)	1.05	0.7–1.59	40/205 (20)	0.41	0.28–0.61	128/212 (60)	0.79	0.57–1.10
R phase*	12/294 (4)	4.02	1.52–10.6	150/169 (89)	1.89	1.16–3.08	70/169 (41)	0.85	0.56–1.29	136/172 (79)	1.62	1.02–2.56
				96/116 (83)	1.33	0.65–2.72	35/116 (30)	0.50	0.33–0.76	74/124 (60)	0.66	0.42–1.05
Erosive Hand OA												
N phase*	2/191 (1)	1		154/188 (82)	1		70/188 (37)	1		138/196 (70)	1	
S phase*	15/838 (2)	2.63	0.62–11.2	613/818 (75)	0.79	0.50–1.27	247/818 (30)	0.69	0.46–1.02	529/849 (62)	0.76	0.51–1.13
E phase*	2/158 (1)	2.68	0.34–20.9	123/154 (80)	1.11	0.62–1.98	38/154 (25)	0.53	0.33–0.85	102/158 (65)	0.88	0.54–1.44
R phase*	12/294 (4)	7.91	1.32–47.4	150/169 (89)	1.91	1.04–3.52	70/169 (41)	0.94	0.60–1.51	136/172 (79)	1.70	0.98–2.95
				96/116 (83)	1.35	0.62–2.94	35/116 (30)	0.57	0.36–0.90	74/124 (60)	0.70	0.40–1.20
Non-erosive Hand OA												
N phase*	13/1427 (1)	1		971/1394 (70)	1		263/1387 (19)	1		840/1436 (58)	1	
S phase*	13/1431 (1)	0.85	0.36–2.01	969/1394 (70)	0.79	0.61–1.01	287/1384 (20)	0.60	0.47–0.76	782/1439 (54)	0.72	0.59–0.87
E phase*	1/53 (2)	2.95	0.66–13.1	36/52 (69)	0.88	0.44–1.76	2/51 (4)	0.14	0.04–0.54	26/54 (48)	0.62	0.36–1.04

*N phase = Normal phase, *S phase = Stationary phase (classical appearance of OA), *E phase = Joint space narrowing phase, *R phase = Erosive phase (erosion of the subchondral bone), *R phase = Remodelling phase (new irregular sclerotic subchondral plates, large osteophytes)

Conclusions: Joints in the erosive phase have more frequent FOI enhancement than non-affected joints. Furthermore, FOI enhancement in non-erosive phases is more common in patients with erosive vs non-erosive hand OA, suggesting that erosive hand OA is a more inflammatory phenotype. FOI enhancement in phase 2, 3 and PVM was common in joints without radiographic pathology, whereas enhancement in phase 1 was uncommon in joints with severe pathology. Thus,

there is a need to consider other FOI scoring methods for the assessment of FOI enhancement in hand OA.

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Emerging topics in the management of the antiphospholipid syndrome

OP0355

PULMONARY THROMBOENDARTERECTOMY IS A CURATIVE RESOLUTION FOR CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION ASSOCIATED WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME: A RETROSPECTIVE COHORT STUDY

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Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare and life-threatening condition with a poor prognosis in antiphospholipid syndrome (APS) patients. A specialised and multidisciplinary evaluation are needed for APS associated CTEPH. As a curative option for CTEPH, pulmonary thromboendarterectomy (PTE) requires careful risk and benefit assessment in APS patients.

Objectives: This retrospective cohort study aimed to investigate the clinical manifestations and prognosis of CTEPH in APS patients with or without PTE.

Methods: Consecutive patients with APS associated CTEPH diagnosed between January 2012 to September 2017 at Peking Union Medical College Hospital were retrospectively evaluated. Patients were divided into two groups by whether underwent PTE or not. Demographics, clinical manifestations, antiphospholipid antibodies profiles, target medications, treatment were collected as possible influencing factors. Chi-square test was used to analyse the short-term prognosis while Kaplan Meier curve and log rank test were used to analyse long-term prognosis (outcome events: deterioration of cardiac function or death).

Abstract OP0355 – Table 1 Baseline demographic and clinical characteristics of 20 APS associated CTEPH patients

Variables	Total (n=20)	With PTE (n=8)	Without PTE (n=12)	P-value
Female, n(%)	13 (65.0)	4 (50.0)	9 (75.0)	0.27
Median age, yrs	29 ^(19–51)	28 ^(22–32)	34 ^(19–51)	0.09
APS median duration, months	36 ^(1–252)	48 ^(1–76)	32 ^(1–152)	0.49
APL profiles	14 (70.0)	6 (75)	8 (66.7)	1.00
ACL, n(%)	17 (85.0)	7 (87.5)	10 (83.3)	1.00
Anti-β2GP1, n(%)	16 (80.0)	8 (100)	8 (66.7)	0.12
LA, n(%)				
Diagnosis	8 (40.0)	6 (75.0)	2 (16.7)	0.02
Primary APS, n(%)	12 (60.0)	2 (25.0)	10 (83.3)	
SLE-APS, n(%)				
CTEPH Median duration, n(months)	18 ^(1–144)	48 ^(1–76)	7 (1–144)	0.89
Manifestations	5 (25)	2 (25.0)	4 (33.3)	1.00
Chest pain, n(%)	20(100)	8 (100.0)	12(100)	-
DOE, n(%)	4 (20)	0	4 (33.3)	0.12
Cough, n(%)	7 (35)	2 (25.0)	5 (41.7)	0.64
Hemoptysis, n(%)				
Other Thrombotic Events, n(%)	17(85)	7 (87.5)	10 (83.3)	1.00
Target therapies	10 ⁽⁵⁰⁾	5 (62.5)	5 (41.7)	0.65
PDE5i	4 (20)	2 (25.0)	2 (16.7)	1.00
Bosentan				
Baseline WHO FC	7 (35.0)	3 (37.5)	4 (33.3)	0.33
II, n(%)	11 (55.0)	5 (63.5)	6 (50.0)	
III, n(%)	2 (10.0)	0	2 (16.7)	
IV, n(%)				
Posttreatment WHO FC	10 (50.0)	7 (87.5)	3 (25.0)	0.01
I, n(%)	7 (35.0)	1 (12.5)	6 (50.0)	
II, n(%)	3 (15.0)	0	3 (25.0)	
III, n(%)				

Results: A total of the 20 APS associated CTEPH patients were enrolled, 8 underwent PTE and 12 without PTE. Common CTEPH developed by these patients included chest pain, dyspnea on exertion, cough and hemoptysis. Chi-square test ($p=0.01$) and Kaplan Meier curves (Log rank test, $p=0.04$) showed that there was statistically significant difference in both short-term and long-term prognosis among patients with PTE and without PTE. On the other hand, Cox regression analysis showed diagnosis (PAPS or SLE-APS), aPL (antiphospholipid antibody) profiles, thrombocytopenia, other Thrombotic Events, target therapies,

baseline WHO FC have no effects on the prognosis of CTEPH in patients with APS.

Abstract OP0355 – Figure 1 Kaplan-Meier survival curves of APS patients associated CTEPH after treatment (anticoagulation and/or PTE).

Conclusions: After a full specialised and multidisciplinary risk-benefit evaluation to limit the risk of thrombosis or bleeding and to manage possible thrombocytopenia, for those CTEPH developed in APS patients, PTE is a curative resolution.

Disclosure of Interest: None declared

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OP0356 PLASMA BLAST PROLIFERATION IS ASSOCIATED WITH TOLL LIKE RECEPTOR 7 POLYMORPHISMS AND UPREGULATION OF TYPE I INTERFERON, CONTRIBUTING TO THE ANTIBODY PRODUCTION IN ANTIPHOSPHOLIPID SYNDROME

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Background: Antiphospholipid antibodies (aPL) as pathogenic autoantibodies in systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS) are supported by a number of clinical, *ex vivo* and animal studies. Nevertheless, aPL are not eliminated by corticosteroid administration or immunosuppression. Novel therapy targeting aPL production is currently unmet needs, in contrast, little is known on its pathological mechanism.

Objectives: This study aimed to clarify the mechanism of aPL production by lymphocyte subset analysis, genomic analysis and *ex vivo* experiments.

Methods: B cell and T cell subsets, a total of 21 subsets, were evaluated in peripheral blood mononuclear cells (PBMC) of 26 primary APS (PAPS), 18 SLE-associated APS (SLE/APS) patients and 10 healthy controls by flow cytometry. Twenty-one single nucleotide polymorphisms (SNP), which were shown to be associated with autoimmune or thrombotic diseases, were analysed in genomic DNA of those patients by TaqMan genotyping assay. Interferon (IFN) score was calculated based on the mRNA expression of Ly6e, Mx1, IFIT1 and IFIT3 in PBMC. To evaluate the aPL-producing capability of plasmablasts, PBMC obtained from APS patients were cultured following depletion of CD19 + CD20+ or CD19+CD20 cells and the culture supernatants were applied to aPL measurements by enzyme-linked immunosorbent assay and cell assay using β 2GPI/HLA-DR7 overexpressing HEK293T cells.¹

Results: In PAPS and SLE/APS patients, plasmablasts, Th2 cells and Th17 cells were increased while pre- and post-switched memory B cells, regulatory B cells and regulatory T cells were decreased compared to healthy controls. Genomic analysis revealed that the increase of plasmablasts ($p=0.032$) and the decrease of memory B cells ($p=0.013$) were more pronounced in patients with a risk allele of SNP in toll like receptor 7 (TLR7) gene (rs3853839). IFN score was significantly higher in the TLR7 SNP risk allele carriers, confirming the downstream signalling of TLR7 ($p=0.029$). *Ex vivo* experiments showed that aPL, including anti-cardiolipin/ β 2-glycoprotein I-HLA class II complexes -IgG and -IgM, were present in the culture supernatant of CD19 + CD20+depleted PBMC from APS patients, but not in that of CD19 + CD20 depleted cells.

Conclusions: Our data indicate an important role of plasmablasts in the production of aPL. Furthermore, plasmablast proliferation was associated with TLR 7 and type I IFN, suggesting a common pathophysiology in SLE and APS. Targeting plasmablasts might be a novel, immunological therapeutic approach in the treatment of APS.

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The links between gout and kidney function

OP0357 HYPERECHOIC DEPOSITS IN THE RENAL MEDULLA ARE ASSOCIATED WITH SEVERE GOUT AND DECREASED EGFR: A TRANSVERSAL STUDY IN 503 VIETNAMESE PATIENTS

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Background: Renal medulla crystal deposits have been demonstrated by pathology in severe gout but little studied by ultrasound (US) scan.

Objectives: To assess the frequency of hyperechoic renal medulla (HERM) in gouty patients and factors associated with their development.

Methods: Renal US scan using a Ecube 9 echograph (Alpinion S. Korea), was performed in gout patients (ACR/EULAR criteria) consecutively seen at the Vien Gut general clinic, Ho Chi Minh City, Vietnam, and receiving no ULT at presentation. Age and sex of patients, gout features, associated diseases, serum (S) uric acid (UA), eGFR (MDRD), urinary lab stick parameters, urine UA/creatinine ratio, and fractional clearance of urate (FCU) were recorded. Patients with HERM were counted and compared with those who had no medullary deposits by the Wilcoxon rank sum test for continuous variables and the Fischer exact test for categorical variables. Multivariable logistic model was used to assess relation between variables at inclusion in the study and presence of medulla deposits.

Results: 503 consecutive patients (500 males) were included. They had a median age of 46 years, median BMI of 25 kg/m², median gout duration of 4 years. 280 (56%) had clinical tophi, 154 (31%) urate arthropathy, 28 (5.6%) urolithiasis, 112 (22%) hypertension, 58 (11.5%) type 2 diabetes, 5 (1%) coronary heart disease. Their median eGFR was 78 ml/min, SUA 423 micromol/L, FCU 0.063, urine UA/creatinine ratio 0.253, urinary pH 6.

Diffuse and bilateral HERM on the B mode with frequent twinkling artefacts on the Doppler mode was identified in 181 (36%) of the 503 patients. Univariate analysis showed that HERM associated with higher age, longer duration of gout, clinical tophi, urate arthropathy ($p<0.0001$ for each of the variables), higher uricemia ($p=0.001$), hypertension ($p=0.0008$), CHD ($p=0.0006$), lower eGFR ($p<0.0001$), leucocyturia ($p=0.02$), proteinuria ($p=0.02$). No association with US-diagnosed urolithiasis, hematuria, urine UA/creatinine ratio, FCU and urinary pH was found. In multivariate analysis, log of the duration of gout (OR: 2.22 (CI: 1.63–3.08), $p<0.001$), clinical tophi (OR: 8.21 (4.23–16.91) $p<0.001$), urate arthropathy (OR: 3.74 (2.18–6.52, $p<0.001$), and lower eGFR (OR: 0.86 (0.75–0.99) for each 10 ml/min decrease, $p=0.04$) were significantly associated with HERM.

Conclusions: In our gout population, HERM was observed in 36% of patients, correlated with decreased renal function, and clearly associated with severe gout, but not with features of uric acid lithiasis.

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OP0358 WHY DO NOT ALL CHRONIC KIDNEY DISEASE PATIENTS GET GOUT? IMPAIRED NEUTROPHIL CHEMOTAXIS IN HYPERURICEMIA-RELATED CKD

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Background: One characteristic feature of acute gout is the infiltration of neutrophils into the inflamed joints, where they recognise monosodium urate (MSU) crystals leading to an acute inflammatory response. The development of chronic kidney disease (CKD) is associated with increased serum uric acid (UA) levels also known as hyperuricemia, a major risk factor for gout. Despite hyperuricemia, acute gout is less frequent in CKD patients. However, the effects of hyperuricemia on leukocyte chemotaxis in CKD are not fully understood.