adhesion and trans-endothelial migration were measured using fluorescence-based assays. Reactive oxygen species (ROS) production was measured using an enzymatic assay to assess hydrogen peroxide (H_2O_2) generation. NETosis was measured using a novel capture ELISA. Bronchoalveolar lavage (BAL) were obtained from ILD or control patients and assessed for NETs.

Results FMISO-PET scans indicated localised hypoxia in fibrotic regions in ILD patients. Hypoxia was also determined in lung sections, which demonstrated positive HIF-1 α in ILD but not control lung sections. ILD-BAL had significantly greater levels of NETs compared to control ($p=0.0039$). Hypoxia did not affect b_1 integrin expression, however increased surface expression of the α_M and α_X subunits ($p=0.0001$ and 0.0179 respectively). Unstimulated, PMA- and LPS-stimulated neutrophil adhesion to both resting and activated endothelial monolayers were enhanced under hypoxia. Neutrophil trans-endothelial migration, across both resting and activated endothelial cells, was also greater in hypoxia ($p<0.05$). Interestingly, whilst ROS generation was not affected by hypoxia, both spontaneous and PMA-induced NETosis were increased under hypoxic conditions ($p<0.05$ and 0.001 respectively).

Conclusions We have demonstrated that localised hypoxia is a feature of the ILD lung. Moreover, elevated NETs were found in ILD-BAL, suggesting a role for aberrant neutrophil activation in ILD pathology. Hypoxia increased neutrophil b_2 integrin expression, adhesion to endothelial monolayers, trans-endothelial migration and NETosis. Further work is underway to investigate the signalling pathways underlying neutrophil activation in ILD.

Changes in pulmonary rehabilitation: new diseases, new approaches

S80

A FEASIBILITY STUDY OF A MULTI-CENTRE RANDOMISED CONTROLLED TRIAL OF ASTHMA-TAILORED PULMONARY REHABILITATION (AT-PR) VERSUS USUAL CARE (UC) IN INDIVIDUALS WITH SEVERE ASTHMA

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Introduction There is limited evidence regarding the acceptability and efficacy of pulmonary rehabilitation (PR) for patients with severe asthma. We investigated the feasibility of performing a randomised controlled trial of asthma-tailored pulmonary rehabilitation (AT-PR) versus usual care (UC).

Method Patients with severe asthma were recruited and randomised 2:1 to AT-PR or UC. The primary outcome was recruitment, retention and adverse event rates. Secondary outcome measures were assessed before and after a 12 week intervention period and included the incremental shuttle walk test (ISWT), two cardiopulmonary exercise tests on a treadmill (ITM) and cycle-ergometer (ICE), quadriceps muscle strength, the asthma control questionnaire (ACQ), chronic respiratory questionnaire (CRQ), asthma quality of life questionnaire (AQLQ), hospital anxiety and depression scale (HADS) and measures of airway inflammation (sputum eosinophil count

and fractional exhaled nitric oxide [FeNO]). Analysis of covariance adjusting for baseline differences was used to compare the effect of ATPR compared to UC. By recruiting 60 patients, a recruitment rate of 30% was estimated with a 95% CI of $\pm 7\%$.

Results 61 out of 235 eligible patients were recruited (26%); 38 females, mean (SD) age 54 (13) yr, BMI 32 (7) kg/m², FEV₁ 1.95 (0.74) L, FEV₁/FVC 69 (11)% and 51 were randomised to AT-PR ($n=34$) or UC ($n=17$). The retention rates for AT-PR and UC were 62% and 53%, respectively. There were 7 serious adverse events but none related to the AT-PR sessions. The Results for the secondary outcome measures are shown in Table 1.

Conclusion AT-PR may be effective for patients with severe asthma but any future trial design would need to be modified to improve retention rate. In this small study, changes in airway inflammation were similar between AT-PR and usual care.

Abstract S80 Table 1 Comparison of exercise performance, asthma control, health related quality of life, depression and anxiety and airway inflammation between AT-PR and UC.

	AT-PR Group (n=21)		UC Group (n=9)		Difference between AT-PR and UC
	Before	After	Before	After	
ISWT	418	450	443	403	74
(m)	(172)	(199)	(121)	(104)	(25 to 124)
ITM VO _{2pk} (ml/kg/ min)	22.5	23.2	22.9	22.3	1.4
	(6.2)	(7.6)	(3.9)	(2.4)	(-1.1 to 3.8)
ICE VO _{2pk} (ml/kg/ kg)	17.5	18.8	16.9	16.1	2.0
	(6.0)	(6.9)	(4.3)	(2.8)	(-0.3 to 4.2)
QMVC	103	116	113	110	22
(Newton)	(53)	(64)	(35)	(28)	(4 to 41)
ACQ	2.1	1.9	1.5	1.9	-0.4
	(0.8)	(0.8)	(0.9)	(1.0)	(-0.9 to 0.1)
CRQ-D	3.1	4.1	3.7	3.6	0.9
	(1.2)	(1.3)	(1.5)	(1.1)	(0.1 to 1.8)
CRQ-F	3.7	4.7	4.7	4.4	0.9
	(1.1)	(1.2)	(1.7)	(1.6)	(-0.1 to 1.8)
CRQ-EF*	5.1	5.4	6.1	6.1	-0.1
	(1.4)	(1.1)	(0.7)	(0.8)	(-0.6 to 0.5)
CRQ-M*	4.7	5.4	6.1	6.0	0.2
	(1.3)	(1.1)	(1.0)	(0.8)	(-0.5 to 0.9)
AQLQ*	19.0	19.7	22.2	21.7	-0.2
	(4.5)	(4.0)	(3.0)	(2.6)	(-2.7 to 2.3)
HADS-A*	6.3	5.1	3.2	2.4	0.4
	(4.4)	(3.7)	(2.5)	(2.8)	(-1.3 to 2.1)
HADS-D*	4.8	3.5	2.8	2.4	-0.3
	(2.7)	(2.8)	(1.6)	(1.0)	(-1.9 to 1.3)
Sputum	-0.1	0.1	0.6	-0.4	0.3
Eos #	(1.0)	(0.8)	(1.0)	(0.6)	(-0.6 to 1.2)
FeNO	33	30	36	37	-4
(ppb)	(23)	(22)	(16)	(16)	(-14 to 5)

Data presented as mean (SD) for before and after intervention results and mean (95% CI) for changes between group.

*significant difference at baseline between groups, # data presented as geometric mean (log SD).

AT-PR; asthma-tailored pulmonary rehabilitation, UC; usual care, ISWT; incremental shuttle walk test, ITM; maximal incremental treadmill test, VO_{2pk}; peak oxygen uptake, ICE; maximal incremental cycle-ergometer test, QMVC; quadriceps maximal voluntary contraction, ACQ; asthma control questionnaire, CRQ; chronic respiratory questionnaire, CRQ-D; CRQ Dyspnoea, CRQ-F; CRQ Fatigue, CRQ-EF; CRQ Emotional Function, CRQ-M; CRQ Mastery, AQLQ; Asthma Quality of Life Questionnaire, HADS; Hospital Anxiety and Depression Score, HADS-A; HADS Anxiety, HADS-D; HADS Depression, EOS; eosinophil count, FeNO; fractional exhaled nitric oxide, ppb; parts per billion.