Abstract M141 Table 1 Change in peak CPET variables and inspiratory capacity at isotime with and without beta-blockade in 46 subjects with and without COPD

	COPD (n = 25)		No COPD (n = 21)	
β-blocker	ON	OFF	ON	OFF
	17.4	17.8	19	18.9
Peak VO2	(3.5)	(3.5)	(6.1)	(6.3)
	1.43	1.46	1.58	1.56
Peak VO2/kg	(0.31)	(0.32)	(0.51)	(0.47)
	102#	106	113	110
Peak Work	(27)	(27)	(30)	(31)
	37.2 #	38.7	39.2	39.3
Peak VE/VO2	(4.9)	(5.7)	(5.3)	(5.1)
	33.9	34.6	34.6	35.3
Peak VE/VCO2	(3.3)	(3.9)	(3.9)	(3.8)
	12.6 ##	10.9	14 ##	11.9
Peak O2 Pulse	(2.6)	(2.4)	(3.7)	(3.1)
	114 ##	134	114 ##	132
Peak HR	(15)	(17)	(25)	(19)
Δ IC isotime (ml)	-142 ~	-188 ~	-15	-16

~ $p < 0.05$ COPD vs. no COPD, # $p < 0.05$ on vs. off beta-blockers and ## $p < 0.01$ on vs. off beta-blockers

the impact of beta-blockade in people under abdominal aortic aneurysm surveillance we examined the impact of beta-blockade on CPET variables and dynamic hyperinflation at peak exercise

55 subjects were recruited though only 46 completed incremental CPET off and on beta-blockers. Mean age was 70 (6) years and 42 (91%) were male. IHD or heart failure was diagnosed in 13 people and COPD diagnosed in 7. However, 24/46 (52%) had post-bronchodilator airflow obstruction consistent with COPD (10 mild, 10 moderate and 4 severe). 18 were routinely prescribed beta-blockers (mainly bisoprolol). Those taking beta-blockers stopped treatment for the second CPET and other subjects commenced weight-adjusted bisoprolol before the second CPET.

The 25 COPD subjects had a mean FEV_1 of 2.14 (0.62) L, FEV_1 predicted 76 (20)% and FEV_1/FVC 0.54 (0.11). The main results are shown in the table. Compared with the subjects without COPD at peak exercise the COPD subjects had slightly lower VO2, work and ventilatory equivalents but these did not differ significantly. When beta-blocked both COPD and non-COPD subjects had a lower heart rate ($p < 0.001$) and consequently oxygen pulse ($p < 0.001$) but there was a minimal effect on other variables. The COPD patients showed a greater fall in IC ($p = 0.02$) but the addition of a beta-blocker did not have any additional effect. The 7 subjects already diagnosed with COPD did not differ from the whole COPD group.

In an unselected clinic population with arterial vascular disease a majority of people had, mostly undiagnosed, COPD albeit predominantly mild to moderate. Continuation or commencement of beta-blockers had little effect on level of peak exercise or degree of dynamic hyperinflation. This supports the use of beta-blockers in this COPD population, both in a peri-operative setting and for a cardiac indication.

M142 THE ASSOCIATION BETWEEN EXACERBATION FREQUENCY AND STROKE RISK, IN PATIENTS WITH COPD: A MATCHED CASE-CONTROL STUDY

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Introduction and objectives COPD patients have been shown to have a higher incidence of MI and stroke, than the general.[1] There is also evidence that the risk of MI and stroke, in COPD patients, increases following an exacerbation.[2] However, the association appears stronger between COPD exacerbations and MI, than it does between COPD exacerbations and stroke.[1,2] We hypothesise that COPD patients, who are frequent exacerbators, have a higher stroke risk, than those who are infrequent exacerbators, even when stable.

Methods COPD patients, with a first stroke between 2004 and 2013, were identified in the UK CPRD database, as cases. Controls, were COPD patients, registered in the CPRD database, matched 3:1, to cases on age, sex and GP practice. We defined "frequent exacerbators" as COPD patients, with ≥ 2 exacerbations, resulting in treatment, per year and "infrequent exacerbators" as ≤1 exacerbation, per year. We also grouped exposure into four levels; 0, 1, 2 or ≥3 exacerbations, per year, to allow an analysis for trend between exacerbation number and stroke. A subgroup analysis of the association between exacerbation frequency and stroke type (ischaemic/ haemorrhagic or TIA) was also carried out. Conditional logistic regression was used for the analyses.

Results There were 6,441 cases and 19,323 controls. No difference was found in odds of stroke, comparing frequent and infrequent exacerbators (adjusted‡ OR 0.95, 95% CI 0.89–1.01, p = 0.09), or in the odds for stroke of any type. However, there was a reduction in odds of stroke associated with increased number of exacerbations, per year, with evidence for a linear trend (p = 0.002) (see Table 1.)

Conclusion These findings do not support the hypothesis that exacerbations in COPD are associated with increased stroke risk and warrant further investigation.

‡Adjusted for age, sex, general practice, smoking status, family history, hypertension, heart failure, CABG, angina, B-blocker and Calcium channel blocker.

REFERENCES

1 Feary, JR, *et al*. Prevalence of major comorbidities in subjects with COPD and incidence of myocardial infarction and stroke: a comprehensive analysis using data from primary care. *Thorax*, 2010;65(11):p. 956-62
2 Donaldson, GC, *et al*. Increased risk of myocardial infarction and stroke following exacerbation of COPD. *Chest*, 2010:137(5): p. 1091-7

M143 PROGRESSION OF CENTRAL ARTERIAL STIFFNESS IN COPD AFTER 2 YEARS OF OBSERVATION

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Background COPD is a systemic disease with associated comorbidities including cardiovascular disease which have significant impact on morbidity and mortality. The heterogeneity of COPD has led to the concept of phenotypes; one of which may describe patients at greater cardiovascular risk. Aortic pulse wave velocity (aPWV) is a validated measure of arterial stiffness and an independent predictor of cardiovascular outcomes, and has been shown to be elevated in patients with COPD.[1] We hypothesised that a subgroup of patients (progressors) would demonstrate increased aPWV over 2 years.

Methods The ARCADE study is a longitudinal study of cardiovascular risk and other comorbidities. Assessments include spirometry, BMI, aPWV and blood pressure, (BP), mean arterial

Abstract M143 Table 1 Baseline characteristics of patients (expressed as mean ± SD)

	Progressors n = 97	Non-progressors n = 103	p=
Gender (male:female)	48:49	46:57	0.294
Age (years)	66.5 ± 7.5	66.9 ± 6.5	0.669
FEV_1 (L)	1.30 ± 0.59	1.33 ± 0.53	0.776
FVC (L)	2.53 ± 0.89	2.47 ± 0.75	0.614
FEV_1/FVC (L)	**0.49 ± 0.11**	**0.53 ± 0.12**	**0.044**
FEV% predicted	52 ± 17	57 ± 21	0.071
BMI (kg/m^2)	28 ± 6	28 ± 5	0.281
Systolic BP (mmHg)	144 ± 17	149 ± 18	0.091
Diastolic BP (mmHg)	81 ± 12	83 ± 9	0.168
Mean arterial pressure (mmHg)	**102 ± 12**	**106 ± 11**	**0.036**
aPWV (m/s)	**9.5 ± 2.2**	**10.4 ± 2.4**	**0.004**
Heart rate (bpm)	74 ± 11	76 ± 11	0.350
6MWT (m)	300 ± 98	309 ± 110	0.563

pressure (MAP), heart rate and 6 min walk distance (6MWT). Based on the change in PWV in hypertensive patients, progressors were defined as individuals with >0.5 m/s PWV increase, over 2 years.[2]

Results Thus far 200 patients with COPD have completed the 2 year follow-up assessment. At baseline the progressor and non-progressor were similar in age, gender, BMI, heart rate and 6 MWT. However the progressors had greater airways obstruction, and lower mean arterial pressure and aPWV (Table 1). After 2 years the mean [95% CI] PWV change in progressors was +1.7 [2.0–1.5]m/s while FEV_1 declined by 140 [76–206]ml ($p < 0.05$). In contrast the non-progressors had no change in lung function, while there was a decrease in aPWV 0.7 [0.5–0.9] m/s and MAP 5 [3–7] mmHg ($p < 0.05$).

Conclusions Almost half of the ARCADE subjects with COPD had a significant increase of PWV, the clinical relevance requires investigation using longer-term outcome data. The identification of CV risk phenotypes in COPD and the underlying pathophysiology may help identify novel therapeutic targets and improve CV outcomes for patients.

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REFERENCES

1 Sabit, R., *et al*., AJRCCM, 2007. 175(12): p. 1259-1265
2 Benetos, A., *et al*., Circulation, 2002. 105(10): p. 1202-1207

M144 ACUTE DIETARY NITRATE SUPPLEMENTATION REDUCES THE OXYGEN COST OF SUBMAXIMAL EXERCISE IN COPD

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Introduction The recognised link between plasma nitrite levels and exercise performance suggests a role for the nitrate-nitrite-nitric oxide pathway in facilitating exercise. Research in healthy individuals has demonstrated a reduction in the oxygen cost of exercise at submaximal workloads following nitrate supplementation. Dietary nitrate administration has been associated with reductions in blood pressure and augmented exercise performance. The effect of acute nitrate dosing on performance and metabolic parameters during cardiopulmonary exercise testing in COPD has not previously been investigated.

Objectives To investigate the hypotheses that acute nitrate dosing would improve exercise performance, reduce the oxygen cost of submaximal exercise performance and lower arterial blood pressure in COPD patients (GOLD stage II-IV).

Methods We performed a randomised, double-blind, placebo-controlled cross-over study comparing the effect of 140 ml of beetroot juice (containing 12.9 mmol nitrate) with a matched placebo of nitrate-depleted beetroot juice in COPD patients not receiving oral nitrates. Subjects were randomised to consume beetroot juice (BR) or placebo (PL) 3 h prior to endurance cycle ergometry, performed at 70% maximal workload assessed by a baseline incremental maximal, symptom-limited test. Blood pressure measurements were taken at baseline and immediately prior to the exercise test. After a washout period of a minimum of 7 days the protocol was repeated with the crossover beverage.

Results 25 COPD patients were recruited of whom 21 successfully completed the study (age 68 ± 7 years; BMI 25.2 ± 5.5 kg/m^2; FEV_1 percentage predicted 50.1 ± 21.6%; peak VO_2 during incremental cycle ergometry 18.0 ± 5.9 ml/min/kg). Diastolic blood pressure was significantly lowered by nitrate supplementation (-6.9 ± 7.8 BR vs. –1.4 ± 8.4 mmHg PL, p = 0.008). Nitrate supplementation significantly reduced oxygen consumption during equivalent isotime exercise (60–70% isotime 16.6 ± 5.6 BR vs. 17.1 ± 5.9 ml/min/kg PL, p = 0.017; 70–80% isotime 16.7 ± 5.7 BR vs. 17.2 ± 5.5 ml/min/kg PL, p = 0.010; 80–90% isotime 16.8 ± 5.7 BR, vs. 17.5 ± 5.75 ml/min/kg PL, p = 0.004). The endurance time was not significantly different between the groups (5.65 (3.90–10.40) BR vs. 6.40 (4.01–9.67) minutes PL, p = 0.50).

Conclusion The acute administration of nitrate reduces oxygen consumption and diastolic blood pressure during equivalent exercise in COPD patients.

M145 PREVALENCE AND DETERMINANTS OF VITAMIN D DEFICIENCY IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background Vitamin D deficiency may be a risk factor for exacerbations of chronic obstructive pulmonary disease (COPD). Studies investigating the prevalence and determinants of vitamin D deficiency among COPD patients in the UK are lacking.

Methods We conducted a cross-sectional study in 278 COPD patients aged 40–85 years screened for eligibility to participate in a clinical trial of vitamin D supplementation. Lifestyle and demographic data were collected by questionnaire and a blood sample was collected for analysis of serum 25-hydroxyvitamin D (25[OH]D) concentration and DNA extraction. Serum 25(OH)D concentration was determined by liquid chromatography – tandem mass spectrometry. Thirty-seven single nucleotide polymorphisms (SNP) in 13 vitamin D-related genes (DBP, DHCR7, CUBN, LRP2, CRTAM, LTA4 H, CYP2R1, CYP3A4, CYP27A1, CYP27B1, CYP24A1, VDR, RXRA) were typed using Taqman allelic discrimination assays. Logistic regression was used to