Introduction In many chronic diseases vitamin D has been proposed as an adjunctive anti-inflammatory therapy. Vitamin D upregulates MKP1, thereby downregulating p38 phosphorylation and the NFKB inflammatory cascade (Zhang *et al*, J Immunol. 2012;188(5):2127–35). Steroids exert anti-inflammatory effects via this cascade, and exhibit synergy with vitamin D for some effects (Yu *et al*, Journal of the National Cancer Institute. 1998;90(2):134–41). Patients with COPD have chronic pulmonary inflammation, with upregulation of NFKB, yet do not exhibit a good response to steroids. Vitamin D therapy has been trialled in COPD patients, albeit with disappointing results (Lehouck *et al*, Annals of internal medicine. 2012;156(2):105–14). We hypothesised that COPD patients' inflammatory response would differ from health, and that vitamin D would exhibit synergy with steroids *in vitro* to improve this.

Methods PBMCs isolated from 10 COPD patients and 10 healthy control subjects were incubated with LPS, vitamin D, dexamethasone, a p38 MAPK inhibitor or combinations of these agents. Supernatants were harvested for TNF and IL6 measurements (ELISA).

Results LPS caused a marked rise in IL6 in both healthy controls ($p = 0.044$) and COPD patients ($p = 0.008$). IL6 reduction with vitamin D was only seen in health. IL6 reduction with addition of dexamethasone was not statistically significant ($p = 0.636$) in COPD. Combinations of agents failed to produce any additional benefit in both health and COPD.

The response to vitamin D was heterogeneous; half of healthy subjects showed an anti-inflammatory response but in COPD only 12.5% of patients exhibited this. The difference in response rate was not significant ($p = 0.120$, Fishers exact test), though this may be due to low power. Similarly reduced response rate to dexamethasone was seen in COPD.

Conclusion Vitamin D does not enhance the anti-inflammatory effect of steroids. The anti-inflammatory effects of vitamin D are no different between COPD and health; variability of response may be one reason for lack of effect of vitamin D in clinical trials to date in COPD patients.

M138 DO STANDARD CARDIOVASCULAR RISK SCORES IDENTIFY RISK IN PATIENTS WITH COPD?

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Introduction Patients with COPD have increased risk of cardiovascular (CV) disease compared to smokers without COPD,[1] with over 25% of deaths CV related.[2] Several CV risk calculators for the general population exist but it is unclear whether they are applicable for COPD.

Hypothesis

Standard CV risk calculators do not identify the increased risk in patients with COPD.

Methods Subjects with a smoking history >10 pack years, with and without COPD, were assessed at clinical stability, COPD n = 191 and controls n = 106. Post-bronchodilator spirometry and blood pressure were performed, blood taken for lipids and self-reported medical and smoking history recorded. In those without documented established CV disease or diabetes (COPD n = 135 and controls n = 88), 10 year CV risk was calculated using ACC/AHA[3] and NHLBI[4] calculators.

Results Both groups were well matched for gender and mean arterial blood pressure (MAP), with the COPD group slightly older, Table 1. Mean CV risk scores were similar between patients with COPD and controls, Table 1, ACC/AHA $p = 0.16$ and NHLBI $p = 0.59$. When using an established cut-off point of 20% for high 10 year CV risk, similar proportions were identified as high risk: the ACC/AHA calculator - 37% of the patients with COPD and 33% of controls; and with the NHLBI calculator 15% of the patients with COPD and 10% of controls were identified as high-risk.

Abstract M138 Table 1

Mean (SD) unless stated otherwise	COPD	Controls
n	135	88
Age (years)	67 (8)	65 (10)
Gender male n (%)	79 (59)	56 (64)
FEV_1% predicted	56 (19)	100 (14)
Smoking pack years	45 (26)	29 (19)
Smoking status current: ex n (%)	40 (30): 95 (70)	18 (20): 70 (80)
MAP (mmHg)	105 (13)	105 (12)
ACC/ AHA risk score	19 (12)	16 (12)
NHLBI risk score	11 (8)	10 (8)

Discussion Although nearly double the proportion of patients with COPD compared to controls with a smoking history have current CV disease or diabetes in this cross-sectional study, the increased risk of future incident CV disease in patients with COPD was not identified using standard calculators.

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4 NHLBI Available from: http://cvdrisk.nhlbi.nih.gov/

M139 FRAILTY AND PREMATURE CARDIOVASCULAR AGEING IN COPD

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Background Presence of comorbidities in chronic obstructive pulmonary disease (COPD) parallels the accumulation of multiple system deficits associated with ageing and assessed as frailty. An important association of frailty in the elderly is increased cardiovascular disease, which is also a major cause of mortality in COPD.[1] However, frailty has not been extensively studied in COPD. We hypothesised that frailty in COPD would be associated with biomarkers of greater systemic involvement including cardiovascular and indicating premature cardiovascular ageing.

Methods Frailty was determined as a Frailty Index (FI) using the 61-element comprehensive geriatric assessment questionnaire in 500 patients with stable COPD, confirmed with spirometry, and 150 non-COPD comparators. This cross-sectional study was taken from within the ARCADE study. Other assessments included body composition; handgrip strength (HGS); aortic pulse wave velocity (PWV); cardiac haemodynamics; 6 min walk distance (6MWD); Timed Up and Go (TUG) test; St George's Respiratory Questionnaire (SGRQ) and C-reactive protein (CRP). The FI was calculated by dividing the number of deficits that the patient had by the maximum, 61

Results Patients and comparators were similar for age, BMI and gender proportion. The FI was greater in the COPD group;

Abstract M139 Table 1 Comparison between frail and non-frail patients with COPD

	Frail (n = 446)	Non-Frail (n = 54)	p value
Age (years)	66 (7)	65 (7)	0.380
FEV_1% predicted	58 (20)	66 (21)	**0.011**
BMI (kg/m^2)	28.2 (5.6)	26.4 (3.2)	**0.049**
Waist circumference (cm)	100 (15)	94 (10)	**0.025**
Fat Mass (kg)	27.1 (11)	23.1 (7.2)	**0.027**
HGS (kg)	26.6 (9.7)	32.5 (10.1)	**0.001**
Aortic PWV (m/s)	10.0 (2.4)	9.0 (1.9)	**0.012**
Stroke Volume (ml)	85 (20)	92 (23)	**0.042**
Central systolic blood pressure	146 (19)	143 (16)	0.377
Central diastolic blood pressure	84 (11)	82 (9)	0.643
Central mean blood pressure	104 (12)	103 (11)	0.605
6MWD (m)	313 (121)	450 (72)	**0.001**
TUG (s)	11.3 (3.8)	8.7 (1.4)	**0.001**
Smoking (packs/year)	41 (25)	36 (23)	0.229
No. Exacerbations/ year	2.3 (1)	1.0 (1)	**0.001**
CRP (mg/L)#	3.6 (2.9)	2.80 (2.2)	0.174
SGRQ	53.1 (19.1)	21.6 (13.6)	**0.001**

mean (95% CI), 0.15 (0.14–0.16) than in comparators, 0.05 (0.03–0.05), independent of age, p

Conclusion Patients with COPD were frail compared with the comparator group of current or ex-smokers, independent of age. Frailty status in the patients was associated with a greater severity of the extra-pulmonary involvement including cardiovascular risk based on greater aortic PWV. Increased aortic PWV in frail patients was independent of blood pressure. These findings are consistent with premature cardiovascular ageing in COPD.

REFERENCE

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M140 EFFECT OF BETA-BLOCKADE ON LUNG FUNCTION IN A POPULATION WITH ARTERIAL VASCULAR DISEASE WITH AND WITHOUT COPD

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Introduction Patients are frequently prescribed β-blockers for heart failure, ischaemic heart disease and peri-operatively, especially for vascular surgery. However, β-blockers remain under prescribed in patients with COPD despite epidemiological evidence indicating little negative impact. This reluctance to use β-blockers is due to concerns about increased airway hyper-responsiveness and bronchoconstriction. As part of a study of peri-operative β-blockade in patients with abdominal aortic aneurysm (AAA) we examined the effect of β-blockers on lung function.

Methods We prospectively recruited 55 AAA patients with no selection bias for COPD or β-blocker use. Thirty eight patients successfully completed detailed lung function testing (PFT) measured by body plethysmography both on and off β-blockers. Subjects already taking β-blockers continued usual treatment while others were prescribed weight adjusted bisoprolol for 48 h.

Results Mean age was 70 (5) years and 33 (77%) subjects were male. 16/38 (42%) were already taking beta-blockers and 5 people (15%) were diagnosed with COPD although 15 (39%) had COPD based on spirometry. Ten (26%) were current smokers and 19 (50%) ex-smokers. The lung function results are shown in the table. Beta-blockade had no significant impact on most lung function measures in both COPD and non-COPD subjects. Specific airways resistance (sRaw) was significantly higher when subjects were taking β-blockers but this effect did not differ between COPD and non-COPD subjects (Δ sRaw: whole group p = 0.004, COPD p = 0.025, non-COPD p = 0.031).

Abstract M140 Table 1 Change in lung function variables with and without beta-blockade in 38 subjects with and without COPD. # $p < 0.05$ on vs. off beta-blockers

	COPD (n = 15)		No COPD (n = 23)	
β-blockers	On	Off	On	Off
	2.00	2.12	2.83	2.89
FEV1 (L)	(0.48)	(0.55)	(0.59)	(0.61)
	73.7	77.9	104.4	106.3
FEV1 %	(14.6)	(17.2)	(17.5)	(17.9)
	3.59	3.67	3.75	3.69
FVC (L)	(0.65)	(0.72)	(0.83)	(0.8)
	101.7	103.9	109.9	109.6
FVC (%)	(15.8)	(16.4)	(17.92)	(20.2)
	55.4	57.4	75.18	76.3
FEV/FVC	(7.6)	(9.0)	(6.4)	(4.6)
	2.84	2.90	2.92	2.84
IC (L)	(0.55)	(0.36)	(1.57)	(0.6)
	4.08	3.82	2.83	2.75
RV (L)	(0.6)	(1.07)	(1.26)	(1.3)
	7.51	7.51	6.66	6.58
TLC (L)	(1.28)	(1.49)	(1.46)	(1.7)
	5.92	6.04	6.41	6.44
DLco	(2.24)	(2.28)	(1.45)	(1.5)
	73.1	74.8	78.9	80.4
DLco (%)	(24.4)	(25.0)	(15.9)	(16.5)
	1.06	1.06	1.25	1.24
Kco	(0.34)	(0.33)	(0.2)	(0.22)
	2.48	2.61	1.95	2.11
Raw	(0.47)	(1.02)	(0.7)	(0.74)
	12.89 #	11.71	8.35 #	7.61
sRaw	(3.25)	(2.76)	(3.3)	(3.2)
	0.09	0.09	0.14	0.14
sGaw	(0.02)	(0.03)	(0.06)	(0.05)

Discussion β-blockers had little effect on static lung function including FEV1 and specific conductance. The small change in resistance was seen in subjects with and without COPD. In this population there appears to be no reason for not using a cardio-selective β-blocker both in this peri-operative setting and for cardiac indications.

M141 IMPACT OF BETA-BLOCKADE ON EXERCISE CAPACITY AND DYNAMIC HYPERINFLATION IN PEOPLE WITH AND WITHOUT COPD AWAITING VASCULAR SURGERY

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Beta-blockers have a key role in the management of heart failure but have been under-utilised in people with COPD due to fear of bronchoconstriction and its impact on symptoms and function. Beta-blockers are also used peri-operatively in people undergoing vascular surgery due to improved cardiac function though this practice is contentious due to a risk of post-operative complications, particularly stroke. As part of a study looking at