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Nutritional status and intake in patients with non-cystic fibrosis bronchiectasis (NCFB) -a cross sectional study.

Abstract

Background & Aims

Bronchiectasis is a heterogeneous, chronic respiratory condition, in which the role of nutrition remains unclear and nutritional guidance is lacking. Few studies have explored the role of nutrition in disease management, and little is known about nutritional requirements during periods of stability or metabolic stress. The aim of this study was to characterise nutritional status and intakes in a cohort of patients and identify potential associations with body composition and functional capacity

Methods

A prospective observational cohort study was undertaken in an adult population (>17 years). Bronchiectasis was confirmed by high-resolution computerised tomography (HRCT). Anthropometric (weight, height, Body Mass Index (BMI), triceps skinfold thickness (TSF), mid upper-arm circumference (MUAC) and mid arm muscle circumference (MAMC)] lung function and nutritional intakes were measured. Results were analysed as a whole and by disease aetiology [primary ciliary dyskinesia (PCD), Idiopathic cause (IC), bronchiectasis in association with asthma and other] and associations tested

Results

In total, 128 participants (65.5% female) completed the study. Median handgrip strength (HGS) in the total sample was only 66.5 (IQR 60.5-89.8) of reference population norms and was low for those with PCD [58.0 (IQR 43.5-70.0))]. Univariate regression indicated that BMI was a statistically significant predictor of lung function in the whole population with HGS and weight identified as statistically significant predictors of lung function in PCD. The total population and each sub-group

failed to meet estimated average requirements for energy but exceeded the Reference nutrient intake (RNI) for protein. Vitamin D was consistently <35% of the RNI.

Conclusion

BMI lay within normal to overweight ranges within the whole population and sub-groups, but masked important functional, body composition and nutritional deficits exist. This was particularly so within a younger sub-group with PCD, who had impaired muscle function, when compared to other causal and associative diseases

Key words: Nutrition, bronchiectasis, body composition

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Introduction

Bronchiectasis is a chronic debilitating respiratory condition which may be either congenital or acquired [1,2]. It is associated with many underlying diseases, including pneumonia, tuberculosis, cystic fibrosis (CF), primary ciliary dyskinesia (PCD), immunodeficiency, rheumatoid arthritis, [3,4] and environmental exposure. Bronchiectasis is characterised by thickening and dilatation of the bronchial walls, abnormal muco-ciliary clearance, airway inflammation and a predisposition to infection. Neutrophil infiltration and raised pro-inflammatory cytokines driven by a cycle of repeated bacterial and viral infections can result in a milieu of infection and inflammation which further impairs lung function, health status and recovery from infective episodes [5,6]. Its increasing prevalence [7,8] and heterogeneous nature highlights the importance of characterising disease sub-populations as treatment may well differ between the various phenotypes.

While studies support the concept that nutrition is important in determining outcomes in bronchiectasis [9-11], evidence is still emerging. Unlike other respiratory diseases such as CF and chronic obstructive pulmonary disease (COPD) where nutritional intervention has a distinct role in disease stabilisation or functional status [12,13], the wide spectrum of clinical phenotype associated with bronchiectasis has created challenge in assessing new therapies and interventions such as nutrition. As a result, few studies have explored its role in disease management, and little is known about nutritional requirements during periods of either stability or metabolic stress [6]. Nutritional guidance is lacking and instead treatments have focused on antibiotic therapy [14] and physiotherapy [15] to enable clearance and management of infection.

Most nutritional studies have focused on micronutrient status, in particular Vitamin D. In a study by Ferri et al, [16], 64% of subjects were found to be deficient in Vitamin D and reduced levels were associated with an increase in bacterial lung colonisation [17]. Vitamin D supplementation may also

contribute towards reduced frequency of exacerbations and suppression of the inflammatory response [18].

Less is known about macronutrient intakes, the nutritional status of this population, and whether there is any correlation with body composition and functional capacity. Emerging evidence suggests that the measurement and understanding of body composition is important to support effective medical and nutritional management of chronic conditions, recognising the impact of reduced lean tissue mass (LTM) and fat mass and its proinflammatory impact on chronic lung disease. Whilst initial case control studies in small populations have identified reductions in peripheral muscle endurance [19] and fat free mass [20] compared to healthy individuals, an understanding of the relationship between nutritional status, dietary intake and body composition is lacking. Within current guidance for the management of Non-Cystic Fibrosis bronchiectasis (NCFB), the need for further research into nutritional supplementation has been acknowledged [21].

The aim of this study was therefore to characterise nutritional status and dietary intakes in a cohort of patients with NCFB and identify potential associations with body composition and functional capacity.

Methodology

Study design: This was a prospective observational study. Patients attending a Regional NCFB clinic from July 2017 to July 2018 were consecutively recruited at their routine clinic appointments as part of annual review during a period of clinical stability. All participants had confirmed bronchiectasis, diagnosed by high-resolution computerised tomography (HRCT) and were ≥ 17 yrs. Patients who were pregnant, had a cancer diagnosis or were aged less than 17 yrs. were excluded. The frequency of chest physiotherapy was recorded for each participant.

Measures

Baseline data recorded as part of routine care were retrieved for each participant. The recording of each parameter was undertaken following a standardised operating procedure at each clinic visit.

Anthropometry Weight (kg) and height (m) were collected using calibrated SECA weighing scales (SECA 956 Class III, SECA, Birmingham. UK) and Leicester Height measure (MK II, SECA, Birmingham, UK). Body mass index (BMI) was calculated for each participant (Weight/Height^2). Participants were classified according to the following BMI ranges; <18.5 kg/m^2 (Underweight), 18.6-24.9 kg/m^2 (normal range), 25-29.9 kg/m^2 (overweight), 30-39.9 kg/m^2 (obese), 40-49.9 kg/m^2 (morbidly obese). [22]

Pulmonary function was assessed by means of standard spirometry using a Vitalograph Compact II Spirometer (Vitalograph Ltd, UK). FEV_1 and FVC were compared with reference values and reported as the percentage of the predicted normal value. The number of infective episodes over the previous year was recorded.

Peripheral muscle strength was evaluated by Hand Grip Strength (HGS), using a Takei 5401 Handgrip dynamometer (Takei Scientific Instruments Co., Ltd, Tokyo, Japan). This was performed with the participants in standing position, arm by their side with full elbow extension. Measurements were repeated 3 times for the non-dominant side. Values were expressed as a mean of all three measures. Measures were then compared to consolidated grip strength values adjusted for age and sex with values less than 85% of standard mean considered as impaired muscle function [23].

Triceps skinfold thickness (TSF) was measured using Harpenden skinfold calipers (Baty International, Burgess Hill, West Sussex, UK). The midpoint was determined from the acromium to the olecronan process and a skinfold measure was taken at the midpoint, with a mean determined from three repeated measures. Mid Upper Arm Circumference (MUAC) was recorded at this midpoint using a tape measure. Mid arm muscle circumference (MAMC), an established measure of muscle protein mass, was calculated from MAC and TSF using a

standard formula: MAMC = MAC - (3.1415 × TSF). The MAMC and TSF results were expressed as a percentage of the expected reference values, adjusted for sex and age [24]. Values were then dichotomised into those >50th centile and those <50th centile according to reference norms.

Nutritional Intake A 24-hour dietary recall (using a multiple pass technique) was undertaken for each participant at 3 time points (baseline recruitment and each subsequent week for 2 weeks, until a total of 3 were retrieved) by a registered dietitian. Dietary recall interviews were undertaken face to face at the clinic appointment and then by telephone interview. Each dietary recall was coded, and energy, protein, carbohydrate, fat, vitamin D, iron and Calcium intakes were calculated. A mean of all seven nutrients for each individual patient was then recorded. Food records were analysed by the same dietitian using MyFood 24© [25] and intakes compared to the EAR (energy) and RNI (protein, calcium, vitamin D) [26,27]. Macronutrient values were also presented as a proportion of total energy intake.

Disease aetiology: All participants were characterised by disease aetiology defined as primary ciliary dyskinesia (PCD), Idiopathic cause, bronchiectasis in association with asthma and other (inclusive of Immunoglobulin, Post Infective, Auto –immune, other genetic cause)

Microbiology: All participants were also characterised by their predominant microbiological status throughout the study period

Comorbidity: Presence of diabetes was also recorded for all participants

Statistical Analysis: Data was analysed using IBM SPSS statistics version 24 (IBM Corp, Armonk, N.Y. USA) by whole population and then grouped by aetiology. Data was checked for normality using the Shapiro Wilk test. Data variables were varied in their distribution. Data was therefore presented in a standard way as median and interquartile range (IQR) . Pearson´s (r) or Spearman´s (rho) correlations were used to explore associations of lung function (FEV $_1$%) with anthropometric measures (MAMC, HGS, TSF, BMI, Weight) and nutrient intake (energy, protein, carbohydrate, fat,

vitamin D, iron and calcium). Kruskal- Wallis was used to determine differences between the medians of values within aetiological groups. Linear regression analysis was used to identify predictors of lung function outcome. Statistical significance was set at a p-value less than 0.05 ($p<0.05$).

Ethics

Health Research Authority granted ethical approval, by proportionate review at South Central Hampshire B Research Ethics Committee (IRAS 216351).

Results

Participants

In total, 129 participants were recruited to the study. Of this number, one was lost to incorrect diagnosis of NCFB (n=128) and 125 completed nutritional recall interviews. The total population was predominantly female (65.6%), with the majority of participants lying just within the overweight range [mean BMI 25.1(± 5.4) kg/m^2]. Participant characteristics are presented in Table 1.

Analysis by disease aetiology indicated that idiopathic disease was the most predominant (38.5%). Significant difference was noted in median age between aetiological groups; those with PCD [23.0 years (IQR 19.0-27.0)] more than 4 decades younger than those presenting with idiopathic disease [70.0 years (IQR 59.0-75.0)], bronchiectasis in association with asthma [67.0 years (IQR 59.0-71.0)]or 'other' aetiologies [70.0 years ([IQR 54.0-75.0)], $p<0.001$.

Anthropometry

Mean handgrip strength in the total sample was only 66.5% (IQR 60.5-89.8) of reference population norms. Significant differences were noted between aetiological sub-groups. Participants with PCD had a lower percentage of normative values than all other aetiologies, [58.0% (IQR 43.5-70.0)]. In contrast there were no differences noted in MAMC (an estimate of somatic protein reserve**)** or triceps

skinfold thickness between groups (Table 1). Mean MAMC adjusted for age and gender reflected 46% of the total population having adequate measurements based on calculations of <90% of 50th centile being inadequate and >90% of 50th centile being adequate compared to normative values with similar results in all other aetiologies. TSF, a measure of predicted fat mass, did reflect higher numbers less than 50th centile cut offs.

Table 1 Baseline characteristics of patients with bronchiectasis [in total and by disease aetiology]

			Aetiology				
	Total participants Proportion (%) or median (Interquartile range)		Primary ciliary dyskinesia (PCD) Proportion (%) or median (Interquartile range)	Idiopathic Proportion (%) or median (Interquartile range)	Bronchiectasis + asthma Proportion (%) or median (Interquartile range)	Other (Immunoglobulin Post Infective, Autoimmune, other genetic) Proportion (%) or median (Interquartile range)	P value
Number (%)	128		25 (19.5%)	49 (38.5%)	24 (18.6%)	30 (23.4%)	
Sex (M/F) %	44/84 (34.4% M).		8/17 (32.0% M)	17/32 (35.0% M)	7/17 (29.0% M)	12/18 (40.0% M)	p=0.85
Age (Yrs)	65.5 (37.5-73)		23.0 (19.0-27.0)	70.0 (59.0-75.0)	67.0 (59.0-71.0)	70.0 (54.0-75.0)	p<0.001
Weight (kg)	63.1 (55.0-77.6)		60.9 (51.7-68.3)	66.0 (56.1-83.5)	63.4 (57.9-75.6)	66.9 (51.8-83.8)	p=0.48
BMI (Kg/m^2)	23.8 (21.4-28.1)		22.1 (20.6-25.4)	25.6 (21.6-30.1)	23.5 (22.1-30.1)	23.0 (20.5-26.6)	p=0.15
FEV_1 (L)	1.5 (1.1-1.2)		1.6 (1.4-2.8)	1.6 (1.1-1.2)	1.4 (1.0-1.2)	1.6 (1.1-2.1)	p=0.70
FEV_1 (%)	67.0 (52.3-80.8)		64.0 (50.5-75.5)	70.0 (55.0-83.0)	63.0 (53.0-80.0)	68.0 (50.0-84.0)	p=0.20
FVC (L)	2.4 (1.9-3.1)		2.7 1.9-3.2)	2.5 (1.8-3.2)	2.3 (1.8-3.0)	2.5 (2.0-2.9)	p=0.70
FVC (%)	80.5 (65.0-94.0)		73.0 64.0-86.5)	86.0 (68.0-86.5)	79.0 (71.5-100.5)	75.0 (63.0-100.0)	p=0.10
Handgrip (Kgf)	15.4 (10.5-22.8)		15.6 (12.7-19.9)	16.8 (10.6-28.1)	13.4 (8.9-17.4)	15.8 (10.5-23.8)	p=0.23
Handgrip (% norm)	66.5 (60.5-89.8)		58.0 (43.5-70.0)	78.0 (56.0-97)	56.0 (37.5-74.5)	77.0 (50.0-95.0)	p=0.02
MUAC	29.3 (26.5-32.3)		29.0 (26.6-31.0)	29.5 (26.5-32.8)	29.5 (26.5-32.9)	29.4 (25.8 -32.0)	p=0.72
TSF (mm)	15.7 (12.2-18.5)		15.7 (12.4-18.1)	16.9 12.1-13.7)	16.1 (13.0-17.7)	14.3 (11.2-17.9)	p=0.52
○ TSF >50th percentile	31/128 (24%)		7/25 (28%)	14/49 (29%)	11/24 (46%)	7/30 (23%)	p=0.47
MAMC (cm)	24.1 (22.1-26.9)		23.6 (21.5-26.2)	25.1 (21.8-26.9)	25.0 (22.6-27.9)	24.1 (21.8-± 4.1)	p=0.66
○ % MAMC >50th percentile	59/128 (46%)		12/25 (48%)	22/49 (44%)	12/24 (50%)	13/30 (43%)	p=0.95
Infections (number previous year)	2.0 (1.0-4.0)		3.0 (0.5-5.5)	2.0 (1.0-3.0)	2.0 (1.0-5.0)	3.0 (1.0-5.0)	p=0.49
Diabetes	4/128 (3.1%)		0/25 (0%)	1/49 (2%)	1/24 (4%)	2/30 (6.7%)	p=0.99
Microbiology n (%) ○ None isolated ○ Haemophilus ○ Pseudomonas ○ Staph Aureus ○ Aspergillus ○ Other	 31 (24.2%) 42 32.8%) 33 (25.8%) 7 (5.5%) 6 (4.7%) 9 (7.0)		 2 (8.0%) 12 (48%) 9 (36%) 2 (8.0%) 0 0	 21 (42.9%) 10 (20.4%) 10 (20.4%) 1 (2.0%) 3 (6.1%) 4 (8.2%)	 4 (16%) 10 (40%) 7 (28%) 0 (0%) 1 (4%) 3 (12%)	 4 (13.8%) 10 (34.5%) 7 (24.1%) 4 (13.8%) 2 (6.9% 2 (6.9%)	p=1.00

FEV_1 forced expiratory volume in 1 second; FEV_1 (%) forced expiratory volume in 1 second (% predicted value); FVC, forced vital capacity; FVC (%) forced vital capacity (% predicted value);BMI, Body Mass Index, MAMC, midarm muscle circumference; TSF, triceps skinfold thickness.

When the total population was stratified by lung function (FEV_1 (%) quartile) no differences were observed between participants (Table 2). In contrast, significant differences were observed across all strength parameters in the total population when classified by BMI into categories of underweight, normal weight, overweight and obese. Those classified as underweight had lower handgrip strength, handgrip as a percentage of the norm, mid upper arm circumference, triceps skinfold thickness and mid arm muscle circumference (Table 2)

Table 2 Nutritional and strength parameters [stratified by lung function and BMI category]

	Predicted FEV_1(%) quartiles				
	1st Quartile (<52%) Median (IQR)	2d Quartile (53% -67%) Median (IQR)	3rd Quartile (68%-80%) Median (IQR)	4th Quartile (>81%) Median (IQR)	P-value
Number (n)	32	33	33	30	
Weight (kg)	62.3 (50.9-70.4)	60.0 (52.2-71.5)	72.9 (58.5-83.6)	65.3 (53.4-86.8)	p=0.10
BMI (Kg/m^2)	22.2 (20.6-26.9)	23.5 (21.2-27.5)	25.4 (21.8-30.4)	24.0 (21.5-29.3)	p=0.16
Handgrip (Kgf)	15.7 (10.7-27.1)	14.0 (9.9-18.7)	17.8 (11.5-23.8)	15.4 (11.1-28.5)	p=0.41
Handgrip (% norm)	65.5 (48.0-86.8)	65.0 (50.5-88.5)	68.0 (52.5-91.5)	70.0 (45.8-90.5)	p=0.89
MUAC (cm)	28.8 (25.7-31.4)	28.4 (25.6-31.5)	31.0 (28.3-32.6)	29.7 (27.4-33.3)	p=0.08
TSF (mm)	14.1 (10.8-17.4)	15.6 (13.5-20.5)	16.0 (11.5-18.2)	16.8 (13.2-19.2)	p=0.09
MAMC (cm)	24.3 (21.2-26.5)	23.4 (20.5-26.7)	25.7 (24.0-27.8)	24.1 (22.5-28.3)	p=0.08
	BMI Categories				
	Underweight (BMI<18.5) Median (IQR)	Normal weight (BMI 18.5-24.9) Median (IQR)	Overweight (BMI 25.0-29.9) Median (IQR)	Obese (BMI >30) Median (IQR)	P-value
Number (n)	5	71	28	24	
Handgrip (Kgf)	11.7 (9.1-14.5)	14.1 (9.9-18.2)	22.4 (16.3-29.8)	15.7 (13.2-27.2)	p=0.003
Handgrip (% norm)	56.0 (33.6-69.0)	61.0 (47.0-79.0)	75.0 (66.0-99.5)	83.0 (54.5-95.5)	p=0.01
MUAC (cm)	21.0 (20.8-22.6)	27.0 (25.7-29.0)	32.0 (31.0-34.0)	33.3 (31.7-38.8)	p<0.001
TSF (mm)	13.6 (7.4-16.0)	14.9 (11.4-17.5)	16.2 (12.1-18.9)	19.3 (17.2-24.2)	p=0.001
MAMC (cm)	17.9 (16.8-18.7)	22.9 (20.8-24.5)	26.8 (25.4-28.7)	28.3 (25.5-31.1)	p<0.001

There was a significant association between weight and lung function (FEV_1%) within the total population *[r* (126) =0.18, p =0.036 and BMI and FEV_1%) [*r* (126) =0.18, p =0.043

In those with PCD there was a significant association between handgrip strength and lung function *r* (23) =0.41 p=0.042, which was not seen in other aetiologies.

Nutritional intake

Mean total energy intakes for the whole population (n=125) were below estimated requirements [27] as were energy intakes for each sub-group (Table 2). Protein intakes exceeded the RNI for protein for the whole population and all sub-groups with Vitamin D consistently <20 % of the RNI (Table 3). Whilst none reached statistical significance between groups, those with PCD had the lowest mean intakes of protein, iron, calcium and vitamin D.

Table 3 Comparison of nutritional intake by whole population and according to aetiology

	Whole population (125)	PCD	Idiopathic	Bronchiectasis + asthma	Other (Immunoglobulin Post Infective Auto – immune, other genetic)	p value
Energy intake (kcal)	1645 (1262-2019)	1615 (1161-2352)	1768 (1322- 2003)	1496 (1236.- 2019)	1680 (1340-1843)	0.14
Energy intake (%EAR)	77.0 (62.3-94.8)	79.0 (66.0-95.5)	81.1 (± 28.8)	71.0 (59.0-98.0)	79.0 (65.0-93.0)	0.5
Protein intake (g)	66.0 (52.0-81.0)	70.0 (52.0-84.0)	70.18 (± 24.7)	62.0 (50.0-78.5)	62.0 (53.5-84.5)	0.34
Protein (% total energy)	16 13.0-18.5)	15.0 (13.0-19.0)	15.5 (13.8-18.0)	15.0 (13.0-17.5)	17.0 (13.3-18.8)	0.27
Protein (% RNI)	131.3 (93.9-168.8)	116.0 (88.2-170.4)	139.2 (98.8-173.2)	120.6 (95.9-169.1)	133.1 (110.9-160.8)	0.54
Protein (% 1 g/kg)	99.9 73.7-127.8)	90.6 (67.8- 128.1)	104.7 (74.6-130.4))	90.5 (71.9 -126.8)	100.0 (83.4-120.8)	0.65
Carbohydrate intake (g)	181.1 (141.3-216.0)	183.3 (153.3-227.3)	181.1 (134.9-218.8)	191.3 (140.7-240.2)	175.5 (134.5-194.0)	0.81
Carbohydrate (% total energy)	41.0 (36.4-46.7)	44.5 (37.0-49.1)	40.1 (± 7.0)	45.5 (37.8-48.9)	40.4 (36.1-45.9)	0.12
Fat (g)	66.3 (48.4-82.9)	61.3 (44.2-82.8)	74.1 (54.6-90.3)	65.3 (48.5-89.3)	64.3 (46.6-75.2)	0.23
Fat (% total energy)	37.2 (31.9-41.0)	34 (30.2-38)	40.3 (35.3-43.1)	37.0 (30.9-39.8)	36.0 (30.4-38.7)	0.004
Fe (mg)	9.2 (7.0-11.9)	8.0 (6.2-9.5)	9.2 (7.3-11.1)	10.0 (8.0-13.5)	9.0 (7.0-11.9)	0.68
Fe (% RNI)	100.7 (68.9-126.4)	80.4 (57.4-113.2)	103.4 (80.4-126.4)	114.9 (78.7-155.1)	86.2 (68.9-136.7)	0.40
Ca (mg)	721 (570.5-954.5)	702.0 (468.5-916.5)	786.0 (593.0-1065.0)	705.0 (532.5-928.0)	713.5 (587.8-995.8)	0.72
Ca (% RNI)	103.0 79.8-134.3)	100.2 (66.9-124.0)	112.3 (82.7-112.1)	100.7 (76.1-132.6)	101.9 (84.0-142.3)	0.72
Vitamin D (µg)	2.0 (1.0-3.0)	1.0 (0.0-3.0)	2.0 (1.0-3.0)	2.0 (1.0-3.0)	2.0 (1.0-2.0)	0.81
Vitamin D (% RNI)	20.0 (10.0-30.0)	10.0 (0.0-30.0)	20.0 (10.0-30.0)	20.0 (10.0-30.0)	20.0 (10.0-20.0)	0.81

Table 2 legend: EAR, Estimated average requirement; RNI, Reference Nutrient intake

Predictors of lung function

Univariate regression indicated that weight (β = .185, p = 0.036), and BMI (β = .179 p < 0.043) were statistically significant predictors of lung function in the whole population with HGS and weight identified as statistically significant predictors of lung function in PCD (β = .431, p = 0.03, β = .409 p = 0.04) (Table 3) Vitamin D intake was a significant predictor of lung function for 'other' aetiologies, but not for any other category.

Table 4. Univariate predictors of lung function by whole population and aetiology

Predictors	All participants		PCD		Idiopathic		NCFB + Asthma		Other	
	P value	Confidence Intervals	P value	Confidence Intervals	P value	Confidence Intervals	P value	Confidence Intervals	P value	Confidence Intervals
Aetiology	0.082	- 4.84 - 0.29								
Sex	0.388	- 4.27, – 10.94	0.11	-26.03 – 2.85	0.25	- 0.46 – 17.61	0.19	- 6.32 – 30.89	0.61	- 15.43 – 25.60
Weight	0.036*	0.02 - 0.44	0.04*	0.02 - 1.15	0.90	- 0.31 – 0.27	0.51	- 0.38 – 0.75	0.05	- 0.09 – 1.07
BMI	0.043*	0.02 - 1.34	0.40	- 1.20 – 2.90	0.78	- 0.82 – 1.09	0.49	- 1.10 – 2.21	0.07	- 0.16 – 3.00
HGS	0.983	- 3.93 - 0.38	0.03*	0.12 - 2.32	0.06	- 0.10- 0.02	0.76	- 0.97 - 1.31	0.68	- 0.77 – 116
TSF	0.061	- 0.030 -1.36	0.38	-0.73 – 1.83	0.59	-0.77 – 1.34	0.82	- 1.95 – 2.43	0.09	-0.28 – 3.16
MAMC	0.141	- 0.23 – 1.61	0.88	- 2.08 – 2.42	0.49	-0.92 – 1.90	0.28	- 0.89 – 2.95	0.42	- 1.49 – 3.47
Energy	0.481	- 0.00 – 0.01	0.77	- 0.01 – 0.12	0.46	-0.01– 0.01	0.15	-0.00 – 0.01	0.96	- 0.025 – 0.02
Protein	0.548	- 0.07 – 0.13	0.69	- 0.28 – 0.19	0.32	-0.33 -0.11	0.10	- 0.02 – 0.24	0.78	-0.56 – 0.42
Vitamin D	0.246	- 0.24 – 0.61	0.40	- 2.32 – 5.58	0.26	- 2.78 – 0.77	0.35	- 1.82 – 4.87	0.01*	- 12.52 - -1.55

**Statistically significant results*

Discussion

This is the first study to report dietary intake, body composition and functional capacity (as measured by handgrip strength), in a population with bronchiectasis. Our results show that whilst BMI lay within normal to overweight ranges within the whole population and sub-groups, important functional, body composition and nutritional deficits exist. This is particularly so within a younger sub-group with PCD, who had impaired muscle function, when compared to other causal and associative diseases.

Anthropometry

Anthropometric measures of body composition including tricep skinfold thickness (TSF), mid upper arm circumference (MUAC) and mid arm muscle circumference (MAMC) (a measure of somatic protein reserves) were comparable to normative values with no statistically significant differences between groups. This was reflected in BMI which remained in the normal or overweight range for the whole population and aetiological sub-groups. In contrast peripheral muscle strength, measured by handgrip strength, was impaired within the total population suggesting functional deficits are

present. Previous studies have also shown a significant reduction in peripheral muscle strength [19, 28] and exercise capacity [19] in bronchiectasis. It suggests peripheral muscle strength, measured by simple handgrip measures may have potential as an outcome measure for use in routine monitoring, pulmonary rehabilitation and risk stratification in clinical practice

Similar findings have been reported in other respiratory diseases. In COPD, HGS is associated with CT-based markers of body composition, but not BMI [29] and more recently in those with interstitial lung disease, severity is associated with upper limb muscle dysfunction and worse physical performance, independent of muscle mass[30]. The presence of impaired muscle functionality, independent of muscle mass and BMI, aligns with the revised European consensus on definition and diagnosis of sarcopaenia [31]. Here the definition of sarcopaenia was extended, adding muscle function to previous classifications that relied on low muscle mass alone, recognising that strength is better than mass in predicting adverse outcomes. Our own findings support this, with approximately half (46%) of the total population having functional muscle impairment in the presence of adequate somatic protein reserve.

Although a reduction in peripheral muscle strength (functionality) was reflected across all aetiologies, it was significant in those with PCD where 96% of individuals failed to achieve normative values (>85%) and only 8% remained free of respiratory pathogens during the study period The autosomal recessive nature of PCD, distinguishes it from other forms of bronchiectasis and in line with European registry data [32] PCD was characterised by earlier decline in lung function. These findings are supported by an earlier study in younger children with PCD who displayed deficits in exercise capacity and respiratory muscle strength as early as age 10 years [33]. Impaired muscle strength and function may predate adulthood by many years in PCD indicating a need for closer group monitoring.

A positive association between HGS and lung function in the PCD population was also observed, not shown in other aetiologies but has been noted in both healthy [34] and respiratory populations [35]. In respiratory conditions such as COPD and Cystic fibrosis, the loss of muscle mass in patients with poorer nutritional status has been hypothesized to contribute to worsening of lung function as a result of increased metabolic demand from poor respiratory function [36,37]. Potentially, these mechanisms may also be present in underweight patients with PCDWithin our own population, the lower strength parameters noted for those with low BMI (<18.5kg/m^2) would suggest that interventions to improve BMI might have a positive impact on lung function. Further research to understand longitudinal trends of weight, muscle functionality and its association with lung function and repeated infections is warranted.

Nutritional Intake

Muscle mass and function are both influenced by protein intake. All aetiologies met dietary protein reference values and the proportional intakes of energy by protein (15% of energy intake) recommended within national guidelines [26]. This was sufficient to maintain muscle mass within normal range but could not maintain optimal muscle function, which relies on both protein intake and resistance exercise [38]. This study did not assess physical activity levels which may have provided further insight into specific contributions of both factors. However, it suggests that adequate protein intakes were achieved when compared to reference nutrient intakes. Comparison of protein with adjusted requirements recommended by the PROTAGE study [39] of 1g/kg/day show that targets of 1g/kg were almost met in the total population but not for those with bronchiectasis and asthma and PCD compounding the limited muscle function, especially in this younger PCD group. Further work to assess and monitor nutritional intakes is needed to inform whether recommendations for other respiratory diseases such as COPD and Cystic Fibrosis [6,40] might also be required for PCD.

Vitamin D intakes were only 20% of dietary reference values for the whole population and similarly low for all aetiologies. The immunomodulatory role of Vitamin D within lung disease is well established [41]. From a mechanistic perspective Vitamin D is involved in the regulation of pathogen recognition receptors (PRRs) on the respiratory epithelial cells, which limit viral or bacterial spread and activation of the immune system, through the production of cytokines and anti-microbial peptides (AMPs). It is implicated in the enhancement of AMPs, reduction of antigen presenting capacity, suppression of T cell inflammation and reduction in B cell immunoglobulin production [41]. Our own findings align with previous studies in bronchiectasis showing high levels of deficiency (defined as <25nmol/l) ranging from 50-64% [16,42] with a recent systematic review in COPD concluding, those with lowest levels of <25nmol/l demonstrate the greatest benefits of supplementation in reducing chest exacerbations. Dietary intake therefore appears suboptimal and would suggest strategies to improve intake through supplementation are required. Of note our PCD subgroup had similar or greater infection rates (3 exacerbations per year) compared to all other aetiological groups, despite being 30 years younger in age. In bronchiectasis, three or more exacerbations per year at baseline have been shown to be associated with worse quality of life, greater likelihood of future hospitalisation, increasing exacerbation frequency and mortality over a 5 year follow up period [43]. Together these are powerful drivers to investigate potential strategies such as Vitamin D supplementation and establish target levels that might address the greater risks associated with PCD. It would also suggest that routine annual monitoring is required which would align with guidance from other respiratory conditions [40]

The lowest intakes for iron and calcium were also within this PCD group, although only iron intakes were suboptimal in terms of meeting recommendations. Together it illustrates that those with PCD have greater nutritional vulnerability, apparent at a significantly younger age. Further exploration of nutritional intakes over time with appropriate nutritional needs and intervention is

required to begin to address some of these identified deficiencies in nutritional status and their impact on health and quality of life.

The prospective nature of this study and large sample, reflected a true clinic population. The use of a single researcher, standard operating procedures for anthropometry and dietary recall helped to minimise error when measuring body composition and dietary intake. The high completion rate (98%) indicates strong adherence to the protocol adding rigour. Reliance on anthropometric data rather than DEXA measures might be considered limiting but enabled high completion rates.

Conclusion

In conclusion NCFB is a condition requiring repeated medical intervention to enable clinical stability. Patients have limitations within normal daily living, which can be influenced by their nutritional status. Whilst seventy percent of the whole participant group had impaired handgrip measures when compared to normative values for sex and age this was statistically significant in those with PCD, identifying a younger but more nutritionally vulnerable group. Further research to understand nutritional needs and associated improvement in functionality and its influence on clinical outcomes and quality of life is warranted.

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Conflict of interest

The author declares they have no conflicts of interest

Statement of Authorship

Linsey King: Conceptualization, Methodology, data curation, project administration, formal analysis, writing- Original draft preparation

Daniel Peckham.: Conceptualisation, resources, reviewing and editing

Helen White: Visualization, reviewing and editing

Ian Clifton*:* Conceptualisation, Reviewing

Giulia Spoletini: Visualisation

Theocharis Ispoglou: Reviewing

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