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ORIGINAL ARTICLE

Correlation of spirometry indices to chest radiology in the diagnosis of chronic airway disease among regional and rural Indigenous Australians

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Key words
airway disease, Indigenous, lung function test, radiology, respiratory, spirometry.

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Abstract

Background: The majority of Indigenous Australians reside in non-urban locations, with reduced access to chest radiology such as computed tomography (CT). Spirometry and chest X-ray (CXR) may be used in the absence of CT; however, the correlation of spirometry indices to CT-defined chronic airway diseases (i.e. chronic obstructive pulmonary disease (COPD) and bronchiectasis) compared with CXR among Indigenous people is sparsely reported.

Aim: To evaluate spirometry indices against CXR and CT findings among adult Indigenous Australians.

Methods: Indigenous patients who had undergone a spirometry test between 2012 and 2020 and had a CXR or chest CT scan assessed for the presence ($^{+}$)/absence ($^{-}$) of airway diseases were included in this study.

Results: Of 643 patients (57% female, 31% remote/very remote), 364 (57%) had CT and CXR available. Patients who were 'CT^{-} and CXR^{-}' for airway diseases (48%) recorded a mean FVC, FEV_1 and FEV_1/FVC of 61%, 59% and 0.76 compared to 57%, 49% and 0.66 in the 'CT^{+} and CXR^{-}' group and 53%, 39% and 0.58 in the 'CT^{+} and CXR^{+}' group. CXR showed sensitivity (44%) and specificity (88%), while spirometry showed 62% and 77% compared to CT. Spirometry demonstrated predominately restrictive impairment among 'CT^{-} and CXR^{-}' and mixed/obstructive impairment among 'CT^{+} and CXR^{-}' and 'CT^{+} and CXR^{+}' groups.

Conclusion: Indigenous Australians tend to demonstrate restrictive impairment in the absence of radiological evidence of airway disease. However, in the presence of airway disease, combinations of mixed and obstructive impairments were common. Obstructive impairment shows greater sensitivity for identifying COPD than that shown by CXR; however, CXR shows greater specificity. Hence, spirometry in conjunction with chest radiology should be utilised to aid in the assessment of airway diseases in this population.

Abbreviations: AO, airway obstruction; ASGS, Australian Statistical Geographical Standard; BD, bronchodilator; BDR, bronchodilator responsiveness; BDR^{T}, traditional; BDR^{U}, updated; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CT, computed tomography; CXR, chest X-ray; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; LLN, lower limit of normal; NPV, negative predictive value; NT, Northern Territory; Post-BD, post-bronchodilator; PPV, positive predictive value; Pre-BD, pre-bronchodilator; R^2, McFaddens R squared measure; TEHS, Top End Health Service; $^{-}$, negative; $^{+}$, positive

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Introduction

Chronic respiratory diseases are one of the leading causes of morbidity and mortality worldwide.[1] Chronic airway diseases (i.e. chronic obstructive pulmonary disease (COPD) and bronchiectasis) are being increasingly recognised as contributing to the major health burden among adult Indigenous populations.[2,3] In Australia, the Northern Territory (NT) Indigenous Australian population are recognised to have rates of chronic airway diseases significantly higher

than their non-Indigenous counterparts, contributing significantly to hospitalisations and early mortality.[4–8]

The vast majority of Indigenous Australians in the NT (81%) reside in remote or very remote communities, anywhere from 100 to 1000 km by road from the capital city of Darwin, where the only tertiary care referral hospital in the Top End, NT is located.[9] In this context, impaired access to advanced specialist healthcare, including radiological investigations such as computed tomography (CT), limit the potential for early diagnosis and management of respiratory disorders, similar to what is seen among other Indigenous populations around the world.[10] Hence, remote health practitioners are reliant on limited resources that are available at the primary healthcare level, such as spirometry and chest X-ray (CXR), for the diagnosis and management of respiratory conditions.[11–13]

However, among Indigenous people, there are little published data on the typical patterns seen or the accuracy of spirometry in the diagnosis and assessment of the severity of airway diseases compared with chest radiology, although the correlation of spirometry indices to chest radiology has been reported for various other ethnic populations.[14–16] Therefore, the aim of this study was to evaluate spirometry indices according to CXR and CT findings demonstrating the presence or absence of chronic respiratory conditions, in particular COPD and bronchiectasis, among adult Indigenous Australians residing in the Top End Health Service (TEHS) region of the NT of Australia.[17]

Methods

Setting and ethical approval

This study was conducted at the respiratory and sleep service at the Royal Darwin Hospital and Darwin Respiratory and Sleep Health/Darwin Private Hospital based in the TEHS region. This study is a part of a larger project assessing factors influencing and implications of lung function parameters and radiology in Indigenous Australians, inclusive of study participants from our previous reports,[18,19] and was approved by the Human Research Ethics Committee of the NT, TEHS and Menzies School of Health Research (Reference No.: Human Research Ethics Committee 2019-3445).[20]

Study patient inclusion and data collection

Indigenous Australian adult patients who underwent spirometry testing between 2012 and 2020 and had a CXR or chest CT scan assessed for the presence/absence of radiological evidence of airway diseases, more specifically, COPD and bronchiectasis, were included in the analysis. Patients' age, sex, height, body mass, smoking status and residence locations were recorded at the time of spirometry testing. Residence was reported by suburb or postcode and applied to Australian Statistical Geographical Standard (ASGS) to define patients as outer regional (ASGS level 3 – the capital city of the region, Darwin, is within this category), remote (ASGS 4) or very remote (ASGS 5).[21]

Radiological data

For the purpose of this study, radiology data were assessed specifically for the presence or absence of radiological evidence of underlying COPD or bronchiectasis and were determined as per the reporting radiologist reports. The presence of COPD was determined if the radiology demonstrated evidence of COPD, in particular the presence of chronic airway inflammation (chronic bronchitis-small airway disease), emphysema or bullous disease.[22] Presence of bronchiectasis was determined if the radiology showed evidence of bronchiectasis.[23] CT and CXR results were classified as negative ($^-$) or positive ($^+$). Positive was defined if the radiology showed evidence of COPD, bronchiectasis or both comorbid. Three groups were defined for analysis: (i) 'CT^- and CXR^-', (ii) 'CT^+ and CXR^-' and (iii) 'CT^+ and CXR^+'. Although some patients were identified with 'CT^- and CXR^+', this grouping was not utilised in the further analysis due to low numbers ($n = 24$) and the higher validity of CT in identifying respiratory conditions.

Spirometry tests

Spirometry tests were performed through a portable single-breath carbon monoxide diffusing capacity device, EasyOne Pro®, ndd Medical Technologies (Medizintechnik).[24] Only spirometry results that were graded as acceptable and repeatable were included in the analysis. The spirometry tests were performed according to the 2005 American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines.[25] In our centre and in the absence of specific spirometric norms for Indigenous Australians, the predicted values were calculated using the Third National Health and Nutrition Examination Survey reference sets (no ethnic correction was used).[26]

Forced expiratory volume in 1 s (FEV_1, L, %), forced vital capacity (FVC, L, %) and FEV_1/FVC (absolute value) were determined before bronchodilator (BD) and after BD. Multiple definitions were applied to define and classify spirometric impairments[27–29] and clinically significant BD responsiveness (BDR)[13] including:

- Restrictive impairment: post-BD FVC < lower limit of normal (LLN) and post-BD $FEV_1/FVC \geq 0.7$
- Mixed impairment: post-BD FVC < LLN and post-BD $FEV_1/FVC < 0.7$
- BDR traditional (BDR^T) (pre- to post-BD change in either FEV_1 or FVC of ≥200 mL and ≥12% initial value) *OR* BDR updated (BDR^U) (pre- to post-BD change in either FEV_1 or FVC of ≥10% predicted value)
- Airway obstruction (AO): pre- or post-BD FEV_1/FVC < LLN (AO^{preLLN}, $AO^{postLLN}$ respectively) or 0.07 (see Table A1)
- Global initiative for chronic obstructive lung disease staging[29]
- Abnormal spirometry was defined as the presence of any spirometric impairment

Two risk parameters were created by combining CXR and AO: (i) defining a case as positive if either CXR or AO were positive (R^{eith}) and (ii) defining a case as positive if both CXR and AO were positive (R^{both}).

Statistical methods

Clinical and spirometry parameters distributions were assessed visually with weight, body mass index and smoking pack-years deviating significantly from a normal distribution and thus presented as medians (interquartile ranges) (IQR), while age, height and spirometry parameters approximated a normal distribution and were presented as means (95% confidence intervals (CI)), with categorical parameters presented as numbers (%). Demographic and clinical parameters were compared between patients who had only a CT scan, only a CXR or both a CT and CXR through chi-squared two-tailed test for categorical parameters, two-tailed analysis of variance for normally distributed parameters and Kruskal-Wallis test for non-parametric parameters. Among patients with both CT and CXR available spirometric parameters were tested between 'CT and CXR' results ('CT^- and CXR^-', 'CT^+ and CXR^-', 'CT^+ and CXR^+') through univariate regression utilising 'CT^- and CXR^-' patients as baseline. Among patients with only CXR available, spirometric parameters were tested between CXR results (CXR^- or CXR^+) through univariate regression utilising negative patients as baseline. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for CXR result, and each definition of AO on spirometry against CT-defined abnormalities were calculated using standard methods. Among patients with both CT and CXR scans available, univariate logistic regression models were developed to define the effect of clinical and spirometric parameters on the odds of CT scans identifying an airway disease for patients with or without CXR evidence of COPD or bronchiectasis, reporting odds ratios (95% CI), factor *P*-values and McFadden's *R*-squared measure (R^2). Alpha was set to $P = 0.05$ throughout, and all analyses were conducted in STATA IC 15 (StataCorp LLC, College Station, Texas, USA).

Results

Clinical and demographics

Of the 1350 spirometry tests performed during the study period, 742 patients had acceptable spirometry and 643 had a radiology report available. Of these, 12 (2%) had only a chest CT scan, 267 (41%) had only CXR available and 364 (57%) had both CT and CXR (Fig. 1). One-third (36%) of patients had at least one chronic abnormality identified, of which COPD was most prevalent (30%). A significantly higher proportion of patients who had both CT and CXR available were identified to have either COPD or bronchiectasis (52% vs 33% CT alone, and 15% CXR alone) with COPD alone (27%), or concurrent COPD with bronchiectasis (16%) more prevalent than bronchiectasis alone (11%). Bronchiectasis was identified on CT in 25% of patients, but only identified in 4% on CXR (Table 1).

Spirometry and radiology correlation

Among patients who had both CT and CXR available, percent predicted values were consistently well below

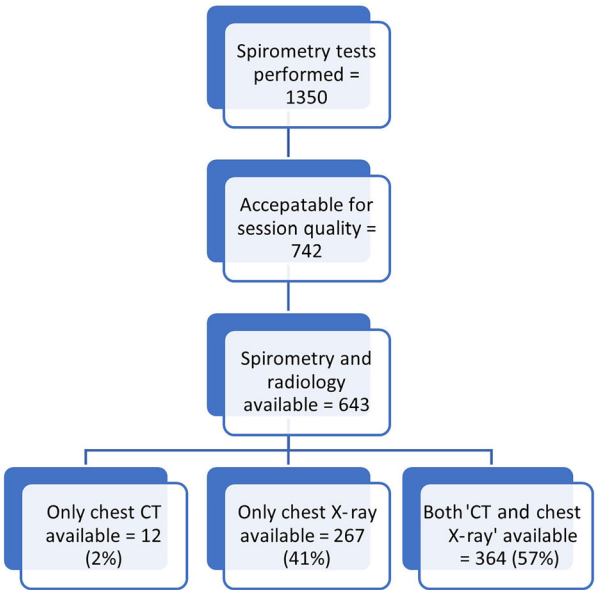


Figure 1 Flow chart showing number of patients who had spirometry and chest radiology included in the study. CT, computed tomography.

Table 1 Demographic and clinical variables for patients with CT scan, and those with only CXR

Clinical variables	Unit/category	Total ($n = 643$)	CT and CXR ($n = 364$)	CT group ($n = 12$)	CXR group ($n = 267$)	*P*-value
Sex, *n* (%)	Female	366 (57)	214 (59)	6 (50)	146 (55)	0.522
Residence, *n* (%)	Outer regional	432 (69)	251 (70)	10 (83)	171 (67)	0.110
	Remote	41 (7)	16 (5)	0 (0)	25 (10)	
	Very remote	153 (24)	90 (25)	2 (17)	61 (24)	
Age, mean (95% CI)	years	51.12 (50.14, 52.09)	53.72 (45.89, 61.79)	48.32 (38.23, 58.59)	49 (40.17, 57.48)	<0.001*
Height, mean (95% CI)	m	1.66 (1.65, 1.66)	1.65 (1.6, 1.72)	1.62 (1.58, 1.66)	1.66 (1.6, 1.73)	0.057
Weight, median (IQR)	kg	74 (60, 90)	70 (58, 86)	83 (66.5, 94)	76 (62, 97)	<0.001*
Body mass index, median (IQR)	kg/m^2	26.85 (21.97, 32.06)	25.71 (21.22, 31.21)	30.54 (26.5, 35.21)	27.83 (22.91, 34.61)	<0.001*
Corpulence status, *n* (%)	Underweight	70 (11)	50 (14)	0 (0)	20 (7)	0.012*
	Normal weight	191 (39)	117 (32)	2 (17)	72 (27)	
	Overweight	150 (23)	83 (23)	3 (25)	64 (24)	
	Obese	229 (36)	111 (31)	7 (58)	111 (42)	
Smoking status/data	Current smoker, *n* (%)	314 (49)	176 (49)	7 (58)	131 (49)	0.270
	Former smoker, *n* (%)	224 (35)	137 (38)	3 (25)	84 (32)	
	Never smoker, *n* (%)	101 (16)	49 (14)	2 (17)	50 (19)	
	Pack-years, median (IQR)	18 (5, 37.5)	18.75 (5, 37.8)	22 (14, 33.75)	16.5 (4.5, 31.5)	0.385
No chronic airway disease, *n* (%)		409 (64)	175 (48)	8 (67)	226 (85)	<0.001*
Chronic obstructive pulmonary disease (COPD), *n* (%)		194 (30)†	157 (43)†	3 (25)	34 (13)	<0.001*
Bronchiectasis, *n* (%)		111 (17)†	100 (28)†	3 (25)	8 (3)	<0.001*
COPD and bronchiectasis, *n* (%)		62 (10)†	59 (16)†	2 (17)	1 (0)	<0.001*
Any chronic airway disease, *n* (%)		234 (36)	189 (52)	4 (33)	41 (15)	<0.001*

*Statistically significant association ($P < 0.05$).

P-values derived from analysis of variance (normally distributed parameters), Kruskal-Wallis test (non-parametric parameters), chi-squared test (categorical parameters) or Fisher's exact test (for cells with values <10) for difference between CT and CXR, CT-only or CXR-only groups.

†Nine patients had either COPD on CT and bronchiectasis on CXR or bronchiectasis on CT and COPD on CXR but did not have both present within the same scan, so the total count of findings sums to 241 and 198.

CI, confidence interval; IQR, interquartile range.

the available reference norms regardless of whether any abnormal radiology findings were present or not (Table 2). The predicted values of FVC and FEV_1 were highest in the 'CT^- and CXR^-' group (each 61% predicted after BD) followed by the 'CT^+ and CXR^-' group (57% and 51%, respectively, after BD) and then the 'CT^+ and CXR^+' group (54% and 40%, respectively, after BD). Although radiology did not identify any chronic abnormalities in the first group, normal spirometry was identified in only 7%, with a restrictive impairment identified in 71% and a mixed impairment in 19%. Mixed impairment was significantly more prevalent among patients with either only CT^+ or both CT^+ and CXR^+ for abnormality (44% and 66% respectively). A significantly greater prevalence of clinically significant FEV_1 BDR was identified among patients with 'CT^+ and CXR^-' (17%) compared to any other group, while a greater prevalence of clinically significant FVC BDR was identified among patients with 'CT^+ and CXR^+' (21%). Although there was significant overlap between CT^+, CXR^+ and AO^{preLLN}, 12% of patients with CT^+ did not display AO or any signs of CXR abnormality (Fig. 2).

Within the 'CT and CXR' group, using CT as the gold standard for the presence of either COPD or bronchiectasis, CXR showed a sensitivity of 44% and specificity of 88% in identifying any airway disease versus no airway disease (Fig. 3). The use of AO^{preLLN} reported the greatest sensitivity and specificity of all AO variables, or spirometry impairments (Table A1), and was therefore used for the rest of this analysis including within the R^{eith} and R^{both} variables. AO^{preLLN} showed greater sensitivity (62%) yet lesser specificity compared to CXR (77%). R^{eith} showed the greatest sensitivity and specificity of any (combined score of 146), and the NPV was 77% in this model. For R^{both} the specificity was the highest achieved (93%), and in this model, the PPV was 79%. When CXR results were refined to include

Table 2 Spirometry results for patients with both CT and CXR screenings by presence or absence of chronic abnormality (COPD or bronchiectasis)

Data	Unit/category	CT^- and CXR^- ($n = 175$)	CT^+ and CXR^- ($n = 92$)	*P*-value	CT^+ and CXR^+ ($n = 73$)	*P*-value
FVC	LLN (L), mean (95% CI)	2.99 (2.89, 3.09)	3.06 (2.92, 3.19)	0.459	2.96 (2.82, 3.09)	0.663
	BD (L), mean (95% CI)	2.26 (2.15, 2.37)	2.14 (1.98, 2.3)	0.219	1.95 (1.79, 2.1)	0.003*
	Before BD (%), mean (95% CI)	59.51 (57.31, 61.71)	54.67 (51.62, 57.73)	0.012*	50.43 (46.82, 54.04)	<0.001*
	BD (L), mean (95% CI)	2.32 (2.21, 2.43)	2.24 (2.09, 2.4)	0.440	2.06 (1.9, 2.21)	0.012*
	BD (%), mean (95% CI)	61.12 (58.96, 63.28)	57.36 (54.45, 60.27)	0.045*	53.45 (49.93, 56.97)	<0.001*
	BDR (% change), mean (95% CI)	3.29 (2.04, 4.54)	6.75 (2.84, 10.67)	0.032*	7.38 (4.99, 9.78)	0.019*
	BDR^T, *n* (%)	15 (9)	13 (14)	0.159	15 (21)	0.008*
	BDR^U, *n* (%)	28 (16)	21 (23)	0.171	24 (33)	0.003*
FEV_1	LLN (L), mean (95% CI)	2.28 (2.19, 2.37)	2.32 (2.2, 2.43)	0.622	2.24 (2.12, 2.35)	0.572
	BBD (L), mean (95% CI)	1.73 (1.64, 1.83)	1.44 (1.3, 1.57)	<0.001*	1.14 (1.01, 1.26)	<0.001*
	BBD (%), mean (95% CI)	58.03 (55.52, 60.54)	47.21 (43.44, 50.99)	<0.001*	38.11 (34.14, 42.07)	<0.001*
	AftBD (L), mean (95% CI)	1.81 (1.71, 1.91)	1.54 (1.4, 1.68)	0.001*	1.19 (1.06, 1.32)	<0.001*
	After BD (%)	60.58 (58.08, 63.08)	50.53 (46.69, 54.36)	<0.001*	40.06 (36.03, 44.08)	<0.001*
	BDR (% change), mean (95% CI)	5.24 (3.83, 6.64)	8.77 (5.96, 11.59)	0.011*	6.48 (4.18, 8.77)	0.409
	BDR^T, *n* (%)	16 (9)	16 (17)	0.049*	6 (8)	0.816
	BDR^U, *n* (%)	39 (22)	38 (41)	0.001*	23 (32)	0.126
FEV_1/FVC, mean (95% CI)	LLN	0.69 (0.68, 0.7)	0.69 (0.69, 0.7)	0.897	0.68 (0.68, 0.69)	0.220
	Before BD (Abs)	0.76 (0.75, 0.78)	0.66 (0.63, 0.69)	<0.001*	0.58 (0.54, 0.61)	<0.001*
	ABD (Abs)	0.78 (0.76, 0.79)	0.67 (0.64, 0.7)	<0.001*	0.58 (0.54, 0.61)	<0.001*
GOLD, *n* (%)	Mild	0 (0)	0 (0)	—	0 (0)	—
	Moderate	15 (39)	9 (20)	0.022*	7 (13)	<0.001*
	Severe	19 (50)	20 (45)		22 (42)	
	Very severe	4 (11)	15 (34)		24 (45)	
Spirometry profile, *n* (%)	Normal	13 (7)	4 (4)	0.327	2 (3)	0.158
	Restrictive impairment	124 (71)	44 (48)	<0.001*	18 (25)	<0.001*
	Mixed impairment	33 (19)	40 (43)	<0.001*	48 (66)	<0.001*
	AO^{preLLN}	31 (18)	49 (53)	<0.001*	53 (73)	<0.001*
	AO^{preAbs}	37 (21)	50 (54)	<0.001*	53 (73)	<0.001*
	$AO^{postLLN}$	30 (17)	43 (47)	<0.001*	51 (70)	<0.001*
	$AO^{postAbs}$	38 (22)	44 (48)	<0.001*	53 (73)	<0.001*
	BDR^T	23 (13)	24 (26)	0.008*	16 (22)	0.084
	BDR^U	46 (27)	42 (46)	0.002*	31 (42)	0.016*

*Statistically significant association ($P < 0.05$).

P-values derived from univariate linear regression utilising 'CT^- and CXR^-' as reference (continuous data) or chi-squared test (categorical data). Data of 24 patients who were negative on CT but positive on CXR were excluded from this analysis. Abs, absolute; AO, airway obstruction; BD, bronchodilator; BDR, bronchodilator responsiveness; BDR^T, traditional BDR; BDR^U, updated BDR; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; GOLD, global initiative for chronic obstructive lung disease; LLN, lower limit of normal; post, post-BD; pre, pre-BD; −, no chronic airway disease findings; +, chronic airway disease finding.

only studies taken within 2 years of the CT scan ($n = 102$, 28%) sensitivity of CXR alone rose to 50% and specificity 94% (PPV 82%, NPV 78%).

In further analysis testing for COPD specifically, CXR showed a sensitivity of 45% and specificity of 88% (Fig. 4). AO^{preLLN} showed greater sensitivity (66%) and lesser specificity (74%). R^{eith} showed the greatest validity (combined sensitivity and specificity of 148) and the highest NPV. For R^{both}, the specificity was the highest achieved (92%), though the NPV and PPV did not differ so significantly from the CXR-alone model.

Logistic regression analysis

Univariate logistic regression models reported differing outcomes for CT-identified COPD or bronchiectasis between patients with or without CXR evidence (Table 3). Higher percent-predicted values of FVC and FEV_1 and absolute values of FEV_1/FVC were associated with significantly reduced odds of CT^+ in both CXR^+ and CXR^- groups. In the CXR^- group, FEV_1/FVC ratio was the strongest predictor with an R^2 of 0.11–0.12, while in the CXR^+ group the R^2 dropped to 0.056–0.069. Conversely, the R^2 of FVC and FEV_1 percent predicted values

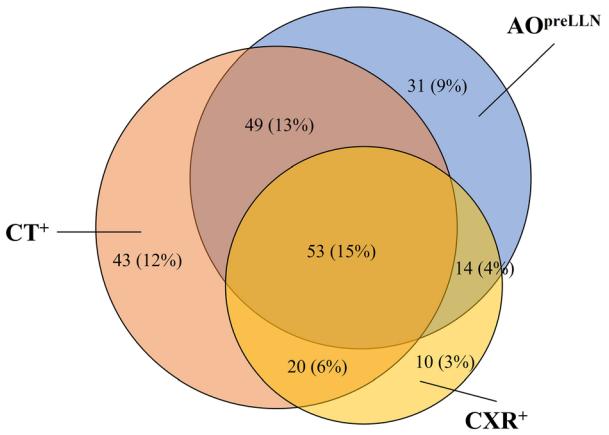


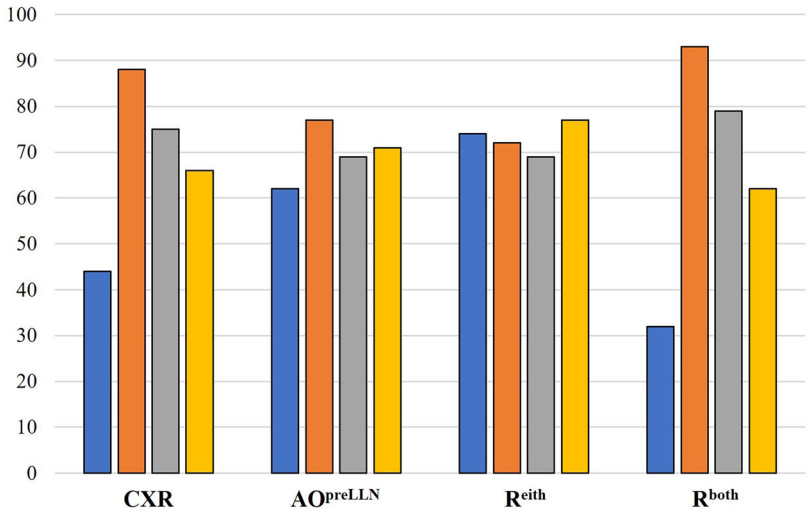
Figure 2 Venn diagram showing overlap between patients with positive CT, CXR and AO^{preLLN} among those with both CT and CXR available ($n = 364$). A total of 144 patients (40%) were negative on all signs. Data presented as number (%). AO, airway obstruction; CT, computed tomography; CXR, chest X-ray; LLN, lower limit of normal; Pre, pre-bronchodilator; +, positive.

was increased in CXR^+ patients compared to CXR^-. In the CXR^- group, male sex significantly increased the odds of CT^+ while either overweight or obese significantly decreased the odds. In the CXR^+ group, overweight or obese had no significant effect, while underweight and any smoking history were associated with significantly increased odds of CT^+.

Discussion

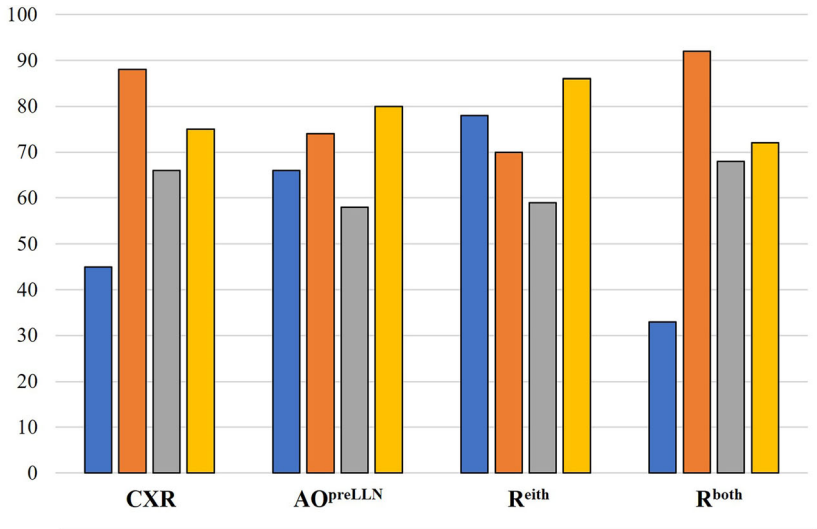
This is one of the few studies to demonstrate the association of spirometric parameters to radiology findings among Indigenous Australian adult patients. Several key findings were observed:

1 Differing spirometric impairments were observed between patients based on whether CT, CXR or both identified COPD or bronchiectasis.
2 Restrictive spirometric impairment was the predominant pattern among patients demonstrating no radiological evidence of airway diseases.
3 Among patients with both CT and CXR available, percent predicted values of FVC and FEV_1 and absolute FEV_1/FVC were more severely reduced when both CT and CXR were positive for the presence of airway disease.
4 Against the gold standard of CT, CXR showed low sensitivity (44%) but higher specificity (88%) in either identifying airway disease in general or COPD specifically, while an AO on spirometry showed improved (yet still moderate) sensitivity (62%) and lower specificity (77%).
5 AO on spirometry in conjunction with CXR appears to be superior in the accurate diagnosis of airway disease compared to either in isolation.
6 Patients with bronchiectasis had lower FVC values and a restrictive impairment, whereas patients with COPD showed a significantly lower FEV_1/FVC ratio.



	CXR	AO^{preLLN}	R^{eith}	R^{both}
Sensitivity	44	62	74	32
Specificity	88	77	72	93
PPV	75	69	69	79
NPV	66	71	77	62

Figure 3 Accuracy of chest X-ray (CXR), spirometry and combination of these on identifying computed tomography defined cases of chronic airway disease. AO, airway obstruction; LLN, lower limit of normal; NPV, negative predictive value; PPV, positive predictive value; Pre, pre-bronchodilator; R^{eith}, either CXR or AO were positive; R^{both}, both CXR and AO were positive. (■), Sensitivity; (■), specificity; (■), PPV, (■), NPV.



	CXR	AO^{preLLN}	R^{eith}	R^{both}
Sensitivity	45	66	78	33
Specificity	88	74	70	92
PPV	66	58	59	68
NPV	75	80	86	72

Figure 4 Accuracy of chest X-ray (CXR), spirometry and combination of these on identifying computed tomography defined cases of chronic obstructive pulmonary disease. AO, airway obstruction; LLN, lower limit of normal; NPV, negative predictive value; PPV, positive predictive value; Pre, pre-bronchodilator; R^{eith}, either CXR or AO were positive; R^{both}, both CXR and AO were positive. (■), Sensitivity; (■), specificity; (■), PPV, (■), NPV.

In the Indigenous Australian context, it is crucial to acknowledge that spirometric norms specific to the adult Indigenous population are still lacking.[30] The limited data published in the literature among adult Indigenous Australians suggest that the FVC and FEV_1 predicted values could be lower by up to 20% in comparison to Australian Caucasian counterparts.[18,31,32] We observed in this study that the FVC and FEV_1 values were around 60% predicted, though typically with a preserved FEV_1/FVC ratio among patients with no evidence of airway disease on either CT or CXR. Due to the high prevalence of abnormalities identified on spirometry even among the 'no airway disease' group (restrictive impairment in 71%, AO in 17–22%, mixed impairment in 19%, BDR^T in 13%, and BDR^U in 27%), it is challenging to use standard spirometric threshold values as predictors of radiologically defined COPD or bronchiectasis. Having appropriate reference norms is vital in a multi-ethnic population, especially during the clinical decision-making process at the primary healthcare level for physicians caring for patients in rural and remote communities.[33–35] 35 Nevertheless, restrictive impairment was the most common spirometry impairment observed among our Indigenous Australian sample, particularly when either CT or CXR is negative for airway diseases.

Defining COPD on spirometry as an FEV_1/FVC ratio < LLN was found to have superior sensitivity and specificity in identifying COPD specifically, compared to using a value of <0.70 (either pre-BD or post-BD) (Table A1). Utilising both CXR and spirometry together showed greater accuracy compared to either alone in identifying true negative or true positive cases. When patients were negative for both AO^{preLLN} and CXR, 77% of true negative patients were identified, compared to 71% using spirometry alone, or 66% using CXR alone. On the other hand, when patients were positive for both AO^{preLLN} and CXR, 79% of true positive patients were correctly identified, compared to 75% using CXR alone and 69% using spirometry alone. For COPD specifically, negative on spirometry and CXR identified 86% of true negative cases compared to 80 and 75% on spirometry and CXR alone, respectively, while positive for both AO^{preLLN} and CXR identified 68% compared to 58 and 66% respectively.

Our study has demonstrated that spirometry parameters are significantly lower in the presence of either CXR or CT evidence of airway diseases compared to patients with no evidence of COPD or bronchiectasis. The reduction in spirometry values was slightly greater for patients with CXR evidence compared to CT evidence (Table A2) (mean difference in pre-BD predicted values for FVC, FEV_1 and absolute value of FEV_1/FVC for CT^+ patients against CT^-: 7%, 15% and 0.13 compared to CXR^+ against CXR^-: 8%, 16% and 0.14). However, patients with 'CT^+ and CXR^+' evidence showed the greatest reductions (9%, 20% and 0.19 for FVC, FEV_1 and FEV_1/FVC pre-BD respectively). Among CT^+ patients, those showing bronchiectasis had significantly lower FVC values and appeared to have a reduced FVC BDR

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Table 3 Univariate logistic regression for predicting abnormal findings on CT scan reporting odds ratios (OR) (95% confidence interval (CI)), factor *P*-values and pseudo R^2 by presence of chronic airway disease on CXR

Parameters	Data/unit/category	CXR^- ($n = 267$)			CXR^+ ($n = 97$)		
		OR (95% CI)	*P*-value	R^2	OR (95% CI)	*P*-value	R^2
Spirometry	FVC pre-BD (%)	0.98 (0.96, 1)	0.012*	0.019	0.96 (0.93, 0.99)	0.006*	0.080
	FVC post-BD (%)	0.98 (0.96, 1)	0.044*	0.012	0.96 (0.93, 0.99)	0.008*	0.070
	FVC BDR (% change)	1.03 (1, 1.05)	0.076	0.013	1.03 (0.98, 1.09)	0.224	0.015
	FVC BDR^T	1.78 (0.8, 3.87)	0.163	0.006	2.84 (0.6, 13.47)	0.188	0.020
	FVC BDR^U	1.55 (0.83, 2.29)	0.173	0.005	3.43 (0.93, 12.64)	0.064	0.039
	FEV_1 pre-BD (%)	0.97 (0.95, 0.98)	<0.001*	0.066	0.96 (0.93, 0.98)	0.001*	0.119
	FEV_1 post-BD (%)	0.97 (0.95, 0.98)	<0.001*	0.056	0.96 (0.93, 0.98)	0.001*	0.124
	FEV_1 BDR (% change)	1.03 (1.01, 1.05)	0.016*	0.018	1 (0.96, 1.05)	0.904	0.001
	FEV_1 BDR^T	2.09 (0.99, 4.41)	0.052	0.011	0.99 (0.19, 5.24)	0.986	0.001
	FEV_1 BDR^U	2.45 (1.42, 4.24)	0.001*	0.030	1.38 (0.48, 3.93)	0.547	0.003
	FEV_1/FVC pre-BD (Abs)	0.001 (0, 0.01)	<0.001*	0.120	0.03 (0, 0.52)	0.017*	0.056
	FEV_1/FVC post-BD (Abs)	0.001 (0, 0.01)	<0.001*	0.112	0.01 (0, 0.35)	0.009*	0.069
Spirometry profile	Restrictive impairment	0.38 (0.22, 0.64)	<0.001*	0.039	0.66 (0.24, 1.78)	0.407	0.006
	Mixed impairment	3.31 (1.89, 5.79)	<0.001*	0.052	1.92 (0.75, 4.89)	0.171	0.017
	AO^{preLLN}	5.29 (3.01, 9.31)	<0.001*	0.103	1.89 (0.72, 4.95)	0.193	0.015
	AO^{preAbs}	4.44 (2.57, 7.68)	<0.001*	0.086	2.24 (0.86, 5.82)	0.097	0.025
	$AO^{postLLN}$	4.24 (2.4, 7.48)	<0.001*	0.075	1.96 (0.76, 5.05)	0.163	0.018
	$AO^{postAbs}$	3.3 (1.92, 5.7)	<0.001*	0.055	1.59 (0.6, 4.21)	0.350	0.008
Age	(Years)	1.01 (0.99, 1.03)	0.351	0.003	0.99 (0.95, 1.03)	0.645	0.002
Sex	(Female reference)	1.77 (1.06, 2.97)	0.030*	0.014	1.61 (0.63, 4.08)	0.320	0.009
Corpulence status	Underweight	2.04 (0.75, 5.53)	0.162	0.113	6.24 (1.27, 30.74)	0.024*	0.080
	Overweight	0.48 (0.24, 0.94)	0.033*		1.44 (0.42, 4.9)	0.559	
	Obese	0.17 (0.08, 0.34)	<0.001*		0.67 (0.18, 2.56)	0.560	
Smoking status (non-smoker reference)	Current	2.18 (0.94, 5.06)	0.070	0.011	8.61 (1.61, 46.07)	0.012*	0.062
	Former	2.03 (0.89, 4.62)	0.094		5 (1.05, 23.86)	0.044*	

*Denotes statistically significant association ($P < 0.05$).

P-values derived from univariate logistic regression. Abs, absolute; AO, airway obstruction; BD, bronchodilator; BDR, bronchodilator responsiveness; BDR^T, traditional BDR; BDR^U, updated BDR; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; LLN, lower limit of normal; post, post-BD; pre, pre-BD; Pseudo R^2, McFaddens *R*-squared measure; −, negative; +, positive.

compared to patients showing COPD (Table A3). There were no significant differences in FEV_1 parameters; however, COPD patients showed a significantly lower FEV_1/FVC ratio compared to bronchiectasis patients and a higher prevalence of AO. As bronchiectasis patients recorded a reduced FVC (which was reduced even further among patients with combined COPD and bronchiectasis), they also recorded a higher prevalence of restrictive impairment (54% vs 29% in COPD alone and 38% in combined COPD and bronchiectasis). In contrast, a previous study among Indigenous patients with bronchiectasis from Central Australia reported all patients demonstrated a mixed spirometry impairment.[36] However, patients from this Central Australian study were those who presented to hospital, which may have potentially resulted in reduced spirometry parameters, compared to patients in the current study, who were seen in the community setting. What underlies the high prevalence of restrictive impairment here is unknown; however, it is plausible that multiple overlapping intrinsic and extrinsic factors are influential, such as comorbid cardiometabolic diseases,[37] low birth weight in this population,[38] recurrent childhood infections,[39] multiparity[40,41] or genetic predisposition and anthropometrics.[42] Whether a restrictive impairment may be useful as a spirometric marker for bronchiectasis is difficult to ascertain due to the high prevalence (70%) of restrictive impairment even among those patients with no radiological evidence of any airway diseases. Both AO and mixed impairment were seen more commonly in the COPD group compared to the bronchiectasis group (70 and 58% vs 46 and 43% respectively). However, an AO or mixed impairment was also prevalent among patients with combined COPD and bronchiectasis (62 and 55% respectively), and given the relatively high comorbid presence (30% of COPD cases showing bronchiectasis),[4–8] spirometric impairments may not be an ideal marker alone.

In regression models, the strength of correlation between spirometry values and CT findings differed based on whether the patient also had CXR evidence of COPD or bronchiectasis or not. In the case of patients with no CXR evidence of airway diseases, FEV_1/FVC

scores showed the greatest correlation to CT outcomes, while for patients with CXR evidence of airway disease, FEV_1 percent predicted values showed the greatest association. Overall, however, the strength of the correlations was relatively low ($R^2 < 0.20$). Regardless, the findings of this study indicate that appropriately performed spirometry[13] and CXR,[11] when available and especially when performed in conjunction, are valuable and complementary tools in assessing for the early diagnosis and potentially in the management of respiratory disorders in resource-poor settings.[43,44] However, as identified in this study, the prevalence of bronchiectasis and comorbid 'COPD and bronchiectasis' is high (25% and 15% on CT respectively), with few identifying features on spirometry. Thus, if patients are clinically judged to have significant respiratory conditions, investigations such as a chest CT should be considered when appropriate.

Indigenous populations have a higher burden of chronic medical comorbidities, including cardiorespiratory disorders, obstructive sleep apnoea, arterial hypertension, diabetes mellitus and chronic renal disease, alongside lower lung function values contributing to higher overall morbidity and mortality that are quite different to their Caucasian counterparts.[4–8,45–47] Impaired access to healthcare reduces the potential for accurate and early diagnoses and the resultant management of several respiratory conditions. Hence, making the best use of the available resources, as demonstrated in this study, will help in the early diagnosis and management of chronic health conditions in order to close the health gap among Indigenous population. Further studies are, however, warranted to understand the utility of culturally and clinically relevant diagnostic and management strategies specific to Indigenous populations.

Study limitations

The results of this study are restricted to Indigenous respiratory patients from the TEHS region of the NT of Australia. In this study, we did not investigate the presence or absence of respiratory symptoms or the severity scores for patients demonstrating abnormal radiology as we used available retrospective data. Furthermore, while we utilised radiology evidence to define our study participant with COPD, we acknowledge that relying entirely on chest radiology may not exclude all patients with underlying COPD. Moreover, spirometry and radiology, including CXR and CT scans, were performed at different time points, and it is plausible that either lifestyle or health changes occurred in the interim. All patients in the current study were also referred to the respiratory health service, so they are likely to have a higher burden of respiratory disease and impairment than the wider population.

Conclusion

This study has demonstrated a high prevalence of spirometric abnormalities even in the absence of radiological evidence of COPD or bronchiectasis, with a restrictive impairment being common. Spirometry or CXR alone shows relatively low sensitivity in identifying patients with underlying airway disease. However, when spirometry and CXR are used in combination, their predictive value for identifying the presence or absence of airway diseases significantly increases. In resource-poor or remote settings where access to chest CT is limited, spirometry and chest CXR can be utilised as a useful and cost-effective tool for the diagnosis and management of respiratory disorders in Indigenous populations.

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Appendix A

Table A1 Sensitivity and Specificity of different potential spirometric definitions of obstructive impairment tested against CT with any airway disease, and CT COPD within the group of patients with both 'CT and CXR' available

	AO^{preAbs}	AO^{preLLN}	$AO^{postAbs}$	$AO^{postLLN}$	Restrictive impairment	Mixed impairment
Any airway disease						
Sensitivity	62.42	61.82	58.79	56.97	37.58	53.33
Specificity	74.87	77.39	73.37	78.39	33.67	77.39
Sensitivity + specificity	137.3	139.21	132.16	135.36	71.24	130.72
PPV	67.32	69.39	64.67	68.61	31.96	66.17
NPV	70.62	70.97	68.22	68.72	39.41	66.67
COPD						
Sensitivity	67.19	66.41	63.28	60.94	32.81	56.25
Specificity	71.61	73.73	70.76	75	35.59	74.15
Sensitivity + specificity	138.8	140.14	134.04	135.94	68.41	130.40
PPV	56.21	57.82	54	56.93	21.65	54.14
NPV	80.1	80.18	78.04	77.97	49.41	75.76

Airway obstruction thresholds tested were: FEV_1/FVC <0.7 either pre (AO^{preAbs}) or post-BD ($AO^{postAbs}$), or FEV_1/FVC < LLN either pre (AO^{preLLN}) or post-BD ($AO^{postLLN}$). Abs, absolute; AO, airway obstruction; COPD, chronic obstructive pulmonary disease; CT, computed tomography; CXR, chest X-ray; LLN, lower limit of normal; post, post-bronchodilator; pre, pre-bronchodilator; NPV, negative predictive value; PPV, positive predictive value.

Table A2 Spirometry parameters for patients who had only chest X-ray (CXR) available

Data	Spirometry results	CXR^- ($n = 226$)	CXR^+ ($n = 41$)	*P*-value
FVC	LLN (L), mean (95% CI)	3.19 (3.1, 3.27)	3.12 (2.94, 3.29)	0.522
	Pre-BD (L), mean (95% CI)	2.64 (2.52, 2.77)	2.17 (1.94, 2.39)	0.002*
	Pre-BD (%), mean (95% CI)	65 (62.77, 67.24)	53.56 (49.09, 58.04)	<0.001*
	Post-BD (L), mean (95% CI)	2.7 (2.58, 2.82)	2.32 (2.1, 2.55)	0.013*
	Post-BD (%), mean (95% CI)	66.43 (64.29, 68.57)	57.37 (52.88, 61.86)	0.001*
	BDR (% change), mean (95% CI)	3.19 (1.85, 4.54)	6.89 (4.12, 9.66)	0.033*
	BDR^T, *n* (%)	25 (11)	8 (20)	0.193
	BDR^U, *n* (%)	31 (14)	12 (30)	0.018*
FEV_1	LLN (L), mean (95% CI)	2.47 (2.39, 2.55)	2.34 (2.19, 2.5)	0.199
	Pre-BD (L), mean (95% CI)	2.05 (1.94, 2.16)	1.38 (1.19, 1.58)	<0.001*
	Pre-BD (%), mean (95% CI)	63.17 (60.63, 65.71)	44.1 (38.26, 49.94)	<0.001*
	Post-BD (L), mean (95% CI)	2.13 (2.02, 2.24)	1.55 (1.34, 1.76)	<0.001*
	Post-BD (%), mean (95% CI)	65.72 (63.2, 68.25)	49.15 (42.98, 55.32)	<0.001*
	BDR (% change), mean (95% CI)	5.11 (3.74, 6.48)	11.74 (7.33, 16.15)	0.001*
	BDR^T, *n* (%)	22 (10)	9 (22)	0.034*
	BDR^U, *n* (%)	46 (20)	20 (50)	<0.001*
FEV_1/FVC, mean (95% CI)	LLN	0.7 (0.69, 0.71)	0.68 (0.64, 0.71)	0.032*
	Pre-BD (Abs)	0.77 (0.75, 0.78)	0.62 (0.58, 0.67)	<0.001*
	Post-BD (Abs)	0.78 (0.76, 0.79)	0.65 (0.6, 0.7)	<0.001*
GOLD, *n* (%)	Mild	2 (4)	0 (0)	0.175
	Moderate	20 (42)	7 (29)	
	Severe	20 (42)	9 (38)	
	Very severe	6 (13)	8 (33)	
Spirometry profile, *n* (%)	Normal	36 (16)	1 (3)	0.024*
	Restrictive impairment	142 (63)	15 (38)	0.005*
	Mixed impairment	42 (19)	21 (53)	<0.001*
	AO^{preLLN}	50 (22)	25 (61)	<0.001*
	AO^{preAbs}	43 (19)	29 (71)	<0.001*
	$AO^{postLLN}$	47 (21)	24 (60)	<0.001*
	$AO^{postAbs}$	48 (21)	24 (60)	<0.001*
	BDR^T	34 (15)	12 (30)	0.038*
	BDR^U	52 (23)	20 (50)	0.001*

*Denotes statistically significant association ($P < 0.05$).

P-values derived from univariate linear regression utilising CXR^- as reference (continuous data) or chi-squared test (categorical data). Abs, absolute; AO, airway obstruction; BD, bronchodilator; BDR, bronchodilator responsiveness; BDR^T, traditional BDR; BDR^U, updated BDR; CI, confidence interval; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; GOLD, global initiative for chronic obstructive lung disease; LLN, lower limit of normal.; pre, pre-BD; post, post-BD; −, negative; +, positive.

Table A3 Spirometry parameters for patients with computed tomography (CT) and chest X-ray (CXR) by their CT diagnosis

Data	Unit/category	CT: COPD ($n = 73$)	CT: bronchiectasis ($n = 37$)	CT: 'COPD and bronchiectasis' ($n = 55$)	*P*-value
FVC	LLN (L), mean (95% CI)	2.92 (2.78, 3.07)	3.02 (2.81, 3.23)	3.12 (2.96, 3.29)	0.199
	Pre-BD (L), mean (95% CI)	2.17 (1.99, 2.35)	2.03 (1.8, 2.26)	1.92 (1.73, 2.1)	0.159
	Pre-BD (%), mean (95% CI)	56.68 (53.08, 60.27)	52.06 (47.87, 56.26)	48.13 (43.99, 52.27)	0.006*
	Post-BD (L), mean (95% CI)	2.3 (2.12, 2.48)	2.11 (1.89, 2.33)	2.02 (1.83, 2.21)	0.089
	Post-BD (%), mean (95% CI)	60.14 (56.77, 63.52)	54.21 (50.2, 58.23)	50.59 (46.6, 54.57)	0.001*
	BDR (% change), mean (95% CI)	8.52 (3.63, 13.41)	4.9 (2.28, 7.53)	6.49 (3.65, 9.33)	0.497
	BDR^{T}, *n* (%)	15 (21)	5 (14)	8 (15)	0.619
	BDR^{U}, *n* (%)	23 (32)	8 (22)	14 (25)	0.531
FEV_1	LLN (L), mean (95% CI)	2.18 (2.06, 2.3)	2.34 (2.15, 2.53)	2.37 (2.23, 2.51)	0.100
	Pre-BD (L), mean (95% CI)	1.33 (1.18, 1.49)	1.4 (1.19, 1.61)	1.2 (1.05, 1.36)	0.305
	Pre-BD (%), mean (95% CI)	44.97 (40.65, 49.29)	45.95 (40.09, 51.8)	38.96 (34.14, 43.77)	0.104
	Post-BD (L), mean (95% CI)	1.41 (1.25, 1.57)	1.48 (1.26, 1.7)	1.28 (1.13, 1.44)	0.328
	Post-BD (%), mean (95% CI)	47.94 (43.46, 52.42)	48.5 (42.57, 54.43)	41.43 (36.56, 46.29)	0.092
	BDR (% change), mean (95% CI)	8.08 (4.84, 11.32)	6.92 (3.65, 10.19)	7.9 (4.92, 10.88)	0.889
	BDR^{T}, *n* (%)	11 (15)	5 (14)	6 (11)	0.800
	BDR^{U}, *n* (%)	25 (34)	13 (35)	23 (42)	0.682
FEV_1/FVC, mean (95% CI)	LLN	0.68 (0.68, 0.69)	0.7 (0.69, 0.71)	0.69 (0.68, 0.7)	0.005*
	Pre-BD (Abs)	0.6 (0.56, 0.63)	0.68 (0.63, 0.73)	0.62 (0.58, 0.66)	0.035*
	Post-BD (Abs)	0.6 (0.57, 0.64)	0.69 (0.64, 0.75)	0.63 (0.59, 0.67)	0.022*
GOLD, *n* (%)	Mild	0 (0)	0 (0)	0 (0)	—
	Moderate	11 (22)	3 (19)	2 (6)	0.045*
	Severe	25 (51)	5 (31)	12 (38)	
	Very severe	13 (27)	8 (50)	18 (56)	
Spirometry profile, *n* (%)	Normal	3 (4)	1 (3)	2 (4)	0.999
	Restrictive impairment	21 (29)	20 (54)	21 (38)	0.036*
	Mixed impairment	42 (58)	16 (43)	30 (55)	0.363
	AO^{preLLN}	51 (70)	17 (46)	34 (62)	0.050*
	AO^{preAbs}	53 (73)	17 (46)	33 (60)	0.023*
	$AO^{postLLN}$	47 (64)	16 (43)	31 (56)	0.107
	$AO^{postAbs}$	49 (67)	16 (43)	32 (58)	0.060
	BDR^{T}	21 (29)	9 (24)	10 (18)	0.415
	BDR^{U}	32 (44)	15 (41)	26 (47)	0.809
CXR result, *n* (%)	Negative	35 (48)	26 (70)	31 (56)	0.047*
	COPD	36 (49)	8 (22)	19 (35)	
	Bronchiectasis	1 (1)	2 (5)	4 (7)	
	'COPD and bronchiectasis'	1 (1)	1 (3)	1 (2)	
	Any chronic airway disease	38 (52)	11 (30)	24 (44)	0.080

*Statistically significant association ($P < 0.05$).

P-values derived from univariate linear regression utilising 'CT^{-} and CXR^{-}' as reference (continuous data) or chi-squared test (categorical data). Data of 24 patients who were CT^{-} but CXR^{+} were excluded from this analysis. Abs, absolute; AO, airway obstruction; BD, bronchodilator; BDR, bronchodilator responsiveness; BDR^{T}, traditional BDR; BDR^{U}, updated BDR; CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; GOLD, global initiative for chronic obstructive lung disease; LLN, lower limit of normal; pre, pre-BD; post, post-BD; −, negative; +, positive.