Bronchiectasis is characterized by aberrant bronchial dilatation (1). The structural changes have been associated with ventilatory dysfunction, exercise intolerance and ventilatory inhomogeneity (2,3) that may aggravate during exercise. A decreased ventilatory efficiency, reflected by the high carbon dioxide ventilatory equivalent (\(\frac{V_E}{VCO_2}\)), has been identified during incremental exercise in patients with COPD, especially when complicated with heart failure (4). At earlier stages of bronchiectasis, exercise intolerance might have become evident before cardiovascular complications developed (5). The mechanisms underlying exercise intolerance in patients with bronchiectasis without heart failure are, however, not entirely clear. By using incremental cycle ergometer, we determined the ventilation-gas exchange abnormalities in patients with bronchiectasis not complicated with physician-diagnosed heart failure.

Participants were enrolled between March 2017 and December 2018. The diagnosis of bronchiectasis was confirmed according to clinical symptoms (including chronic cough and sputum production) and chest high-resolution computed tomography within 12 months. For eligibility of study entry, patients with bronchiectasis were aged 18 years or greater, remained clinically stable, had no antibiotics use for >4 weeks, and had no physician-diagnosed heart failure. Patients with malignancy, heart attack within 6 months, or acute upper respiratory tract infections within 4 weeks were excluded. We also screened for possible right heart failure based on the radiologic signs on chest high-resolution computed tomography and echocardiography (among 23 out of 53 patients who have undergone the measurement). Healthy subjects were aged 18 years or greater, had no significant diseases influencing on exercise testing. Our study was approved by the Ethics Committee of The First Affiliated Hospital of Guangzhou Medical University. All participants gave written informed consent.

Patients underwent severity assessment with bronchiectasis severity index, impulse oscillometry, multiple-breath nitrogen washout test (which also measured the lung clearance index), spirometry, and cardiopulmonary exercise testing (CPET). All measurements were made with the commercial lung function testing instrument (Jaeger MasterScreen™. Carefusion Co., Ltd.). The methods for determining the etiology of bronchiectasis have been described previously (2). Healthy subjects underwent spirometry and CPET only. A cycle ergometer equipped with real-time gas-analyzer (COSMED Inc., Italy) was applied for CPET, including steady-state rest, 20-W increase in work rate at 1-min intervals until symptom limitation, and recovery. Main parameters comprised breath-by-breath ventilatory volume (\(V_{el}\)), tidal volume (\(V_t\)), oxygen consumption (\(VO_2\)), carbon dioxide production
(VCO₂), oxygen pulse (HR/VO₂), oxygen ventilatory equivalent (VE/VO₂), VE/VCO₂, and end-tidal carbon dioxide partial pressure (PetCO₂). Fatigue and dyspnea were graded using a 10-point scale (Borg’s scale) at rest and after maximal exercise. We took reference on a published study to define the cut-off value of hypocapnia based on the partial pressure of end-tidal carbon dioxide (PetCO₂) at different time points of exercise [4].

Statistical analysis was performed using Graphpad Prism 5.0 (Graphpad Inc., USA). Kolmogorov-Smirnov test was used to assess normality of the continuous variables. Independent t-test or Mann-Whitney test was conducted for two-group comparisons, and multiple-group comparisons (among patients with or without exercise-induced hypocapnia and healthy controls, see the definition in the results section below) were conducted with one-way analysis-of-variance or Kruskal-Wallis test, followed by Bonferroni correction. Correlation analysis was done using Spearman’s test.

Seventy-nine participants underwent screening, of whom 53 patients with bronchiectasis and 16 controls were analyzed. Reasons for the exclusion of bronchiectasis patients included joint deformity (n=2), FEV₁ <30% predicted (n=5), recent trauma (n=2) and heart failure (n=1). Fifty-eight point five percent of participants were middle-aged females who never smoked. The baseline characteristics are displayed in Table 1. Bronchiectasis severity was mostly graded as mild-to-moderate. Idiopathic (45.2%) and post-infection (35.8%) constituted the most common etiologies. None of the eligible participants had documented cardiovascular disorders except for grade II hypertension in one bronchiectasis patient. Sixty-seven point nine percent of the bronchiectasis patients had joint deformity (n=2), FEV₁ <30% predicted (n=5), recent trauma (n=2) and heart failure (n=1). Fifty-eight point five percent of participants were middle-aged females who never smoked. The baseline characteristics are displayed in Table 1. Bronchiectasis severity was mostly graded as mild-to-moderate. Idiopathic (45.2%) and post-infection (35.8%) constituted the most common etiologies. None of the eligible participants had documented cardiovascular disorders except for grade II hypertension in one bronchiectasis patient. Sixty-seven point nine percent of the bronchiectasis patients had joint deformity (n=2), FEV₁ <30% predicted (n=5), recent trauma (n=2) and heart failure (n=1).

Twenty-one (40%) patients with bronchiectasis had an increased ratio of residual volume to total lung capacity. Forty-five point two percent of bronchiectasis patients had restrictive/obstructive/mixed ventilatory dysfunction, and the mean FEV₁ was 72% predicted among 53 patients. Twenty-one (40%) patients with bronchiectasis had an increased ratio of residual volume to total lung capacity. Forty-five point two percent of bronchiectasis patients had restrictive/obstructive/mixed ventilatory dysfunction, and the mean FEV₁ was 72% predicted among 53 patients.

VE/VCO₂ was significantly higher in patients with bronchiectasis than in healthy controls throughout exercise (all P<0.01). However, there was no remarkable difference in VE/VCO₂ between healthy controls and bronchiectasis patients without hypocapnia at anaerobic threshold or maximal intensity exercise. VE/VCO₂ correlated strongly with PetCO₂ at maximal exercise (Figure 1), but not resting residual volumes or bronchiectasis severity. VE/VCO₂ nadir correlated significantly with the simultaneously measured PetCO₂ (P<0.01). We next stratified bronchiectasis patients based on PetCO₂ because it explained substantially for exertional ventilatory responses. Patients with consistently low PetCO₂ throughout exercise (<35 mmHg, hypocapnia group) did not differ from their counterparts regarding resting ventilatory function, diffusing capacity, lung volumes and airway resistance (all P>0.05, Table S2) (Table 1).

Patients with hypocapnia yielded markedly lower peak work rate and shorter inspiratory time, but higher VE/VO₂ and VE/VCO₂, at anaerobic threshold than patients without (all P<0.05). At submaximal exercise, patients with hypocapnia yielded systematically higher VE, VE/VO₂ and VE/VCO₂ but lower PetCO₂ than those without (all P<0.05, Table 2). Higher VE was associated with consistently higher respiratory rate and shorter expiratory time at different time points of exercise in patients with hypocapnia as compared with those without hypocapnia. The higher VE was, however, not associated with significant differences in Vt, the ratio of respiratory rate to inspiratory time, and the ratio of inspiratory to total respiratory time between patients with and without hypocapnia (Figure 1). Moreover, the disease severity (i.e., bronchiectasis severity index) did not correlate with most of the lung function parameters at different time points during exercise (data not shown).

There was no substantial difference in dyspnea or fatigue ratings at baseline between patients with and without hypocapnia. At maximal exercise, the increase was similar for dyspnea ratings although appearing greater for fatigue ratings in patients with hypocapnia.

Efficient ventilation is crucial to the exercise tolerability. In adults with cystic fibrosis, the ventilatory efficiency correlated significantly with the imaging severity of bronchiectasis that affects ventilatory inhomogeneity (6). First, our study has reaffirmed the ventilatory inefficiency (high VE/VCO₂ levels) throughout incremental exercise in bronchiectasis. The high VE/VCO₂ has previously been attributed to excessive ventilation in COPD-heart failure overlap (4), but the mechanisms in patients without clinically overt heart failure are less clear. The VE/VCO₂ was recorded at fixed work rate but might get close to the VE/VCO₂ nadir at anaerobic threshold or maximal exercise. By stratification based on PetCO₂ (which mirrored arterial
Table 1  Baseline characteristics of study participants

| Parameters                              | Bronchiectasis patients | Healthy subjects | P value* | P value** | P value# |
|-----------------------------------------|-------------------------|------------------|----------|----------|----------|
|                                         | Hypocapnia (n=34)       | No hypocapnia (n=19) |          |          |          |
| Anthropometry                           |                         |                  |          |          |          |
| Age (years)                             | 45.0±15.2               | 54.0 (18.0)      | 36.6±15.1 | 0.022    | 0.197    | 0.008    |
| Height (cm)                             | 160.6±8.2               | 162.2±5.9        | 162.2±8.1 | 0.700    | 0.458    | 0.895    |
| Body-mass index (kg/m²)                 | 19.4±2.4                | 21.9±3.8         | 22.7±2.5 | <0.001   | 0.035    | 0.354    |
| Females, n (%)                          | 22 (64.7)               | 9 (47.4)         | 9 (56.3)  | 0.467    | 0.219    | 0.601    |
| Never-smokers, n (%)                    | 33 (97.1)               | 19 (100.0)       | 14 (87.5) | 0.167    | 0.450    | 0.113    |
| Disease characteristics                 |                         |                  |          |          |          |
| No. of exacerbations in 2 years         | 1.0 (4.0)               | 1.0 (3.0)        | NA       | ND       | 0.541    | ND       |
| No. of bronchiectatic lobes             | 3.2±1.3                 | 4.0 (2.0)        | NA       | ND       | 0.092    | ND       |
| HRCT total score                        | 8.1±3.5                 | 5.0 (5.0)        | NA       | ND       | 0.044    | ND       |
| Bronchiectasis severity index category, n (%) |                |                  |          |          |          |
| Mild                                    | 13 (38.2)               | 11 (57.9)        | NA       | ND       | 0.168    | ND       |
| Moderate                                | 12 (35.3)               | 5 (26.3)         | NA       | ND       | 0.502    | ND       |
| Severe                                  | 9 (26.5)                | 2 (10.5)         | NA       | ND       | 0.170    | ND       |
| Bronchiectasis etiology, n (%)          |                         |                  |          |          |          |
| Idiopathic                              | 15 (44.1)               | 7 (36.8)         | NA       | ND       | 0.606    | ND       |
| Post-infectious                         | 10 (29.4)               | 9 (47.4)         | NA       | ND       | 0.191    | ND       |
| Other known etiologies                  | 9 (26.5)                | 3 (15.8)         | NA       | ND       | 0.373    | ND       |
| Sputum bacteriology, n (%)              |                         |                  |          |          |          |
| *Pseudomonas aeruginosa                 | 13 (38.2)               | 6 (31.6)         | NA       | ND       | 0.628    | ND       |
| Other PPMs                              | 13 (38.2)               | 5 (26.3)         | NA       | ND       | 0.380    | ND       |
| Commensals                              | 8 (23.5)                | 8 (42.1)         | NA       | ND       | 0.158    | ND       |
| Medications used within 6 months, n (%) |                         |                  |          |          |          |
| Mucolytics                              | 21 (61.8)               | 10 (52.6)        | NA       | ND       | 0.518    | ND       |
| Macrolides                              | 3 (8.8)                 | 0                 | NA       | ND       | 0.545    | ND       |
| Muscarinic receptor antagonist           | 7 (20.6)                | 0                 | NA       | ND       | 0.041    | ND       |

Mean ± standard deviation or otherwise median (interquartile range) were presented for numerical data depending on the normality, and categorical data were expressed as number (percentage) if appropriate. The threshold for statistical significance was 0.015 (after Bonferroni correction). Data in bold indicated the statistical analysis with significance. * P value denoted the comparison among the three groups; ** P value for the comparison between bronchiectasis patients with and without hypocapnia; # P value for the comparison between healthy controls and bronchiectasis patients without hypocapnia. PPMs, potentially pathogenic microorganisms, including *Pseudomonas aeruginosa, Haemophilus influenzae, Moraxella Catarrhalis, Haemophilus parainfluenzae, Staphylococcus aureus, Staphylococcus epidermis, Sphingomonas paucimobilis, Rothia mucilaginosa*. NA, not applicable; ND, not done.
Table 2 CPET parameters at anaerobic threshold and maximal exercise intensity in bronchiectasis patients and healthy subjects

| Parameters                  | Time point | Healthy subjects (n=16) | No hypocapnia (n=19) | Hypocapnia (n=34) | P value* | P value** | P value# |
|-----------------------------|------------|-------------------------|----------------------|-------------------|----------|----------|----------|
| Peak work rate              | AT         | 174.1±50.4              | 134.7±47.2           | 110.0 (48.8)      | <0.001   | <0.001   | 0.023    |
|                             | MI         | 58.0±19.2               | 48.7±15.2            | 48.2±8.2          | 0.220    | 0.718    | 0.185    |
| VE                          | AT         | 45.2±17.5               | 34.6±9.5             | 38.0±10.7         | 0.229    | 0.361    | 0.033    |
|                             | MI         | 1.6±0.6                 | 1.3±0.5              | 1.1 (0.3)         | 0.027    | 0.266    | 0.166    |
| VO₂ (L/min)                 | AT         | 1,707±717               | 1,258±399            | 1,231±406         | 0.040    | 0.795    | 0.029    |
|                             | MI         | 1,859±662               | 1,526±413            | 1,432±242         | 0.027    | 0.239    | 0.079    |
| VCO₂ (L/min)                | AT         | 1,713±731               | 1,265±403            | 1,242±412         | 0.051    | 0.825    | 0.032    |
|                             | MI         | 2,088±688               | 1,771±573            | 1,530±439         | 0.010    | 0.140    | 0.147    |
| HR (bpm)                    | AT         | 142.1±18.4              | 129.1±12.7           | 131.6±19.2        | 0.087    | 0.624    | 0.021    |
|                             | MI         | 166.5 (19.3)            | 151.3±12.0           | 146.3±16.3        | 0.005    | 0.164    | 0.020    |
| VO₂/HR                      | AT         | 11.8±4.0                | 9.7±2.4              | 8.5 (3.3)         | 0.078    | 0.483    | 0.066    |
|                             | MI         | 9.8 (5.2)               | 10.0±2.3             | 8.7 (3.8)         | 0.224    | 0.409    | 0.363    |
| RR                          | AT         | 29.4±6.1                | 27.2±6.9             | 32.8±5.9          | 0.009    | 0.006    | 0.346    |
|                             | MI         | 36.1±6.4                | 34.2±8.0             | 39.5±8.4          | 0.080    | 0.039    | 0.449    |
| VE/VO₂                      | AT         | 26.8±2.0                | 27.8±2.6             | 31.5±3.2          | <0.001   | <0.001   | 0.240    |
|                             | MI         | 31.9±6.6                | 31.5±5.1             | 34.0±5.1          | 0.151    | 0.140    | 0.835    |
| VE/VCO₂                     | AT         | 26.8±2.1                | 27.2±3.6             | 31.1±3.4          | <0.001   | <0.001   | 0.696    |
|                             | MI         | 27.9±3.1                | 27.4±3.2             | 31.7±3.0          | <0.001   | <0.001   | 0.662    |
| Ti                          | AT         | 1.0±0.2                 | 1.0 (0.4)            | 0.9±0.1           | 0.005    | 0.003    | 0.260    |
|                             | MI         | 0.8±0.1                 | 0.8±0.2              | 0.7±0.2           | 0.137    | 0.055    | 0.328    |
| Te                          | AT         | 1.2±0.3                 | 1.1 (0.3)            | 1.1 (0.3)         | 0.572    | 0.782    | 0.407    |
|                             | MI         | 1.0±0.2                 | 1.0±0.3              | 0.9±0.2           | 0.064    | 0.031    | 0.443    |

Mean ± standard deviation or otherwise median (interquartile range) were presented for numerical data, and categorical data were expressed as number (percentage) if appropriate. The threshold for statistical significance was 0.015 (after Bonferroni correction). Data in bold indicated the statistical analysis with significance. *, P value denoted the comparison among the three groups; **, P value for the comparison between bronchiectasis patients with and without hypocapnia; #, P value for the comparison between healthy controls and bronchiectasis patients without hypocapnia. CPET, cardiopulmonary exercise testing; AT, anaerobic threshold, MI, maximal intensity of exercise; VE, ventilatory volume; VT, tidal volume; RR, respiratory rate; SpO₂, pulse oximetry; VO₂, oxygen consumption; VCO₂, carbon dioxide production; VO₂/HR, oxygen pulse, which is the ratio of heart rate and oxygen consumption; VE/VO₂, oxygen ventilatory equivalent, which is the ratio of ventilatory volume and oxygen consumption; VE/VCO₂, carbon dioxide ventilatory equivalent, which is the ratio of ventilatory volume and carbon dioxide production; PetCO₂, end-tidal carbon dioxide pressure; Ti, inspiratory duration; Te, expiratory duration.
Figure 1 Ventilatory, gas exchange, and parameters reflecting on breathing and lung volume during incremental cycle exercise in bronchiectasis patients and healthy subjects. (A) The correlation between $V_{E}/V_{CO_{2}}$ and PetCO$_{2}$ at peak exercise; (B) the correlation between $V_{E}$ and VCO$_{2}$ at anaerobic threshold; (C) $V_{E}/VO_{2}$; (D) $V_{E}/VCO_{2}$; (E) PetCO$_{2}$; (F) RR; (G) Te; (H) RR/V$_{T}$; (I) Ti/Ttot; (J) changes in dyspnea scale at resting and maximal exercise; (K) changes in fatigue scale at resting and maximal exercise. Mean ± standard deviation were presented for all the values demonstrated in the figure. *, P<0.05 for the comparison among bronchiectasis patients with and without hypocapnia and healthy subjects at individual time points; **, P<0.01 for the comparison among bronchiectasis patients with and without hypocapnia and healthy subjects at individual time points. $V_{E}$, ventilatory volume; $V_{T}$, tidal volume; VO$_{2}$, oxygen consumption; VCO$_{2}$, carbon dioxide production; VO$_{2}$/HR, oxygen pulse, which is the ratio of heart rate and oxygen consumption; $V_{E}$/VO$_{2}$, oxygen ventilatory equivalent, which is the ratio of ventilatory volume and oxygen consumption; $V_{E}$/VCO$_{2}$, carbon dioxide ventilatory equivalent, which is the ratio of ventilatory volume and carbon dioxide production; PetCO$_{2}$, end-tidal carbon dioxide pressure; Te, expiratory time; Ti, inspiratory time; Ttot, total respiratory time per breath cycle; RR, respiratory rate; RR/V$_{T}$, the ratio of respiratory rate to tidal volume.
or capillary carbon dioxide partial pressure), we have identified patients with hypocapnia at different time points during exercise. Because PetCO$_2$ might not invariably be a reliable surrogate of PaCO$_2$, caution should be exercised in interpreting some of our findings. The reduced exercise tolerance might have also resulted from the dead space ventilation (7), because airflow limitation (47% among 53 patients) and increased residual volumes (~30.2%) were present at resting.

Second, patients with hypocapnia had more prominent airflow limitation, and consistently higher respiratory rate and a trend towards shorter expiratory time during exercise. Hence, the inspiratory constraint could also be due to the greater V$_E$. In COPD, although the high V$_E$/VCO$_2$ could be partially compensated by the inspiratory constraint and hypercapnia, V$_E$/VCO$_2$ may remain high because of the exaggerated dead space ventilation and greater respiratory drive, particularly when complicated with heart failure (4). We cannot preclude subclinical pulmonary hypertension or heart failure, particularly in those with bilateral bronchiectasis (8). This might help partially explain for the lack of significant difference in dyspnea scale between patients with and without hypocapnia.

Despite efforts to identify possible signs of right heart failure, echocardiography was not performed in every individual, and therefore we might have included some patients with early-stage right heart insufficiency. Catheterization was not performed before incremental exercise testing, thus pulmonary hypertension which is a crucial indicator of right heart failure could have been under-diagnosed. However, the invasiveness and requirement of medical expertise have limited the applicability of catheterization as a routine measurement in our clinical setting.

In summary, the greater ventilatory demand might have contributed to inspiratory constraint, partly explaining for the decreased ventilatory efficiency on exertion in patients with bronchiectasis without physician-diagnosed heart failure. Further studies are needed to determine whether interventions (i.e., pulmonary rehabilitation) could help improve the outcomes of bronchiectasis by increasing the ventilatory efficiency.

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**Footnote**

**Conflicts of Interest:** All authors have completed the ICMJE uniform disclosure form (available at 10.21037/jtd.2020.03.113). The authors have no conflicts of interest to declare.

**Ethical Statement:** The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Table S1: Radiologic signs among bronchiectasis patients

| Patient no. | Age (yrs) | Sex  | Signs of right heart failure on HRCT | Echocardiographic findings                  |
|-------------|-----------|------|-------------------------------------|--------------------------------------------|
| 1           | 35        | Female | Unremarkable                      | ND                                         |
| 2           | 62        | Female | Unremarkable                      | Mild tricuspid valve regurgitation         |
| 3           | 54        | Female | Unremarkable                      | ND                                         |
| 4           | 28        | Male   | Unremarkable                      | ND                                         |
| 5           | 51        | Male   | Unremarkable                      | ND                                         |
| 6           | 51        | Female | Unremarkable                      | Normal right heart function                |
| 7           | 56        | Male   | Unremarkable                      | Normal right heart function                |
| 8           | 41        | Male   | Unremarkable                      | ND                                         |
| 9           | 29        | Female | Unremarkable                      | Normal right heart function                |
| 10          | 52        | Female | Unremarkable                      | ND                                         |
| 11          | 63        | Male   | Unremarkable                      | Normal right heart function                |
| 12          | 65        | Male   | Unremarkable                      | ND                                         |
| 13          | 51        | Male   | Unremarkable                      | ND                                         |
| 14          | 39        | Male   | Unremarkable                      | ND                                         |
| 15          | 59        | Female | Unremarkable                      | ND                                         |
| 16          | 54        | Female | Unremarkable                      | ND                                         |
| 17          | 55        | Female | Unremarkable                      | ND                                         |
| 18          | 58        | Male   | Unremarkable                      | ND                                         |
| 19          | 69        | Male   | Unremarkable                      | ND                                         |
| 20          | 38        | Female | Unremarkable                      | ND                                         |
| 21          | 65        | Male   | Unremarkable                      | Mild pulmonary hypertension                |
| 22          | 56        | Female | Unremarkable                      | Mild tricuspid valve regurgitation         |
| 23          | 37        | Female | Unremarkable                      | Normal right heart function                |
| 24          | 55        | Male   | Unremarkable                      | ND                                         |
| 25          | 54        | Female | Unremarkable                      | Normal right heart function                |
| 26          | 23        | Female | Unremarkable                      | ND                                         |
| 27          | 70        | Female | Unremarkable                      | Mild tricuspid valve regurgitation         |
| 28          | 46        | Male   | Unremarkable                      | ND                                         |
| 29          | 59        | Male   | Unremarkable                      | ND                                         |
| 30          | 40        | Male   | Unremarkable                      | Mild tricuspid valve regurgitation         |
| 31          | 30        | Male   | Unremarkable                      | Normal right heart function                |
| 32          | 47        | Female | Unremarkable                      | ND                                         |
| 33          | 38        | Female | Unremarkable                      | ND                                         |
| 34          | 26        | Male   | Unremarkable                      | ND                                         |
| 35          | 51        | Female | Unremarkable                      | Normal right heart function                |
| 36          | 21        | Female | Unremarkable                      | Normal right heart function                |
| 37          | 66        | Female | Unremarkable                      | ND                                         |
| 38          | 25        | Male   | Unremarkable                      | ND                                         |
| 39          | 37        | Female | Unremarkable                      | Normal right heart function                |
| 40          | 57        | Male   | Unremarkable                      | Normal right heart function                |
| 41          | 24        | Female | Unremarkable                      | Mild pulmonary hypertension                |
| 42          | 27        | Female | Unremarkable                      | ND                                         |
| 43          | 61        | Male   | Unremarkable                      | ND                                         |
| 44          | 46        | Male   | Unremarkable                      | ND                                         |
| 45          | 56        | Female | Unremarkable                      | Mild tricuspid valve regurgitation         |
| 46          | 49        | Female | Unremarkable                      | ND                                         |
| 47          | 65        | Female | Unremarkable                      | Mild tricuspid valve regurgitation; mild pulmonary hypertension |
| 48          | 63        | Female | Unremarkable                      | ND                                         |
| 49          | 29        | Female | Unremarkable                      | Mild tricuspid valve regurgitation         |
| 50          | 51        | Male   | Unremarkable                      | ND                                         |
| 51          | 24        | Female | Unremarkable                      | Normal right heart function                |
| 52          | 31        | Female | Unremarkable                      | Normal right heart function                |
| 53          | 63        | Female | Unremarkable                      | Normal right heart function                |

ND, not done.
Table S2 Resting lung function parameters in bronchiectasis patients and healthy subjects

| Parameter | Healthy subjects (n=16) | No hypocapnia (n=19) | Hypocapnia (n=34) | P value* | P value** |
|-----------|------------------------|----------------------|-------------------|----------|----------|
| FVC (L)   | 3.30±0.94              | 2.71±0.82            | 2.57±0.85         | 0.057    | 0.578    |
| FVC pred% | 90.3±5.1               | 80.5±17.5            | 77.1±17.5         | 0.014    | 0.442    |
| FEV₁ (L)  | 2.78±0.83              | 2.03±0.77            | 1.77±0.68         | <0.001   | 0.282    |
| FEV₁ pred%| 90.1±6.1               | 76.1 (42.8)          | 63.2±19.2         | <0.001   | 0.109    |
| TLC (L)   | ND                     | 4.89±0.88            | 4.36±1.13         | NA       | 0.070    |
| TLC pred% | ND                     | 88.6±9.8             | 85.8±14.6         | NA       | 0.325    |
| RV (L)    | ND                     | 2.10±0.54            | 1.84±0.63         | NA       | 0.101    |
| RV pred%  | ND                     | 109.3±28.6           | 110.1±24.0        | NA       | 0.907    |
| RV/TLC    | ND                     | 43.2±9.9             | 42.2±9.4          | NA       | 0.944    |
| RV/TLC pred% | ND                 | 128.4±27.9          | 130.0±20.8        | NA       | 0.900    |
| D₂CO (mL/min/mmHg) | ND | 20.7 (7.0)          | 22.2±4.7         | NA       | 0.656    |
| D₂CO pred% | ND                | 86.4±11.2           | 85.7±15.6        | NA       | 0.836    |
| D₂CO/Vₐ (mL/min/mmHg/L) | ND | 5.09±0.62          | 5.20±0.74        | NA       | 0.686    |
| D₂CO/Vₐ pred% | ND           | 107.8±14.7         | 103.4±15.8       | NA       | 0.305    |
| Zₕ       | ND                     | 0.36 (0.19)          | 0.47±0.22         | NA       | 0.685    |
| Rₕ       | ND                     | 0.35 (0.16)          | 0.44±0.21         | NA       | 0.901    |
| R₂₀      | ND                     | 0.30 (0.06)          | 0.34±0.11         | NA       | 0.361    |
| Xₕ       | ND                     | –0.10 (0.08)         | –0.14 (0.13)      | NA       | 0.115    |
| Fres     | ND                     | 15.6±8.0             | 15.1±7.9          | NA       | 0.653    |
| AX       | ND                     | 0.25 (0.58)          | 0.47 (0.85)       | NA       | 0.521    |

Mean ± standard deviation or otherwise median (interquartile range) were presented for numerical data, and categorical data were expressed as number (percentage) if appropriate. *, P value denoted the comparison on individual clinical parameters among the three groups; **, P values for the comparison between bronchiectasis patients with and without hypocapnia. FVC, forced vital capacity; FEV₁, forced expiratory volume in one second; TLC, total lung capacity; RV, residual volume; D₂CO, diffusing capacity for carbon monoxide; D₂CO/Vₐ, diffusing capacity for carbon monoxide corrected with the alveolar volume; Zₕ, total respiratory impedance; Rₕ, airway resistance at 5 Hz; R₂₀, airway resistance at 20 Hz; Xₕ, elastance at 5Hz; Fres, resonant frequency; AX, the area of the resonance frequency.