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# Assessment of ventilation distribution in overweight and obese children with asthma using electric impedance tomography: a cross-sectional study

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## Abstract

**Background** Several studies have demonstrated an association between excessive body weight and asthma in children, underlining the link between obesity and resistance to treatments. The aim of this study is to investigate the pattern of ventilation distribution and to assess the response to bronchodilator (BD) in a cohort of overweight/obese children with asthma, using standard spirometry and Electric Impedance Tomography (EIT).

**Methods** Single-centre, cross-sectional study. Eligible children with asthma and excessive weight were enrolled during outpatient follow-up; EIT and spirometry were performed before and after the administration of 400 µg of inhaled salbutamol.

**Results** A $FEV_1 < -1.64$ z-score was found in 2/27 (7.4%) children (median age 12.4 yrs, 7 females); four children (14.8%) fulfilled the criteria for airway dysanapsis. Through EIT, a greater ventilation distribution was identified in the dorsal regions of the lungs. After BD, an increase in $FEV_1$ z-score was observed, however, only 8/27 (29.6%) children reported a significant bronchodilation at spirometry; the median total %GI index and total %RVD40 remained unchanged, while a significant reduction in the VL %ROI was observed. No significant correlations were observed between pre-post BD differences in $FEV_1$ z-score, %GI index, %RVD40 and anthropometric measures.

**Conclusion** Children with asthma and excessive weight had a peculiar pattern of regional ventilation distribution. BD administration generally resulted in a suboptimal spirometric response, with no significant changes in EIT measurements. The relatively limited response to BD could have several interpretations, and future studies are needed to better understand the mechanisms behind these findings.

**Keywords** Children, Obesity, Asthma, Electric impedance tomography, Ventilation

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## Introduction

Obesity has become one of the most significant pediatric chronic diseases worldwide, affecting one in three school-aged children in Europe [1]. Studies have linked excessive body weight to increased asthma in children, highligthing how obesity raises the likelihood of severe asthmatic exacerbations and steroid resistance [2]. Key mechanisms include local and systemic inflammation, metabolic dysregulation, and mechanical changes affecting lung function [3, 4]. Obese children may develop obstructive respiratory deficits due to altered airway growth (dysanapsis), even without asthma [5]. Fat deposition in the mediastinum and abdomen affects intra-cavity pressures, diaphragm movements, and chest wall dynamics [6], leading to gas trapping and ventilation inhomogeneity. This may explain why asthma symptoms are worse in obese patients [4, 7]. Moreover, several studies have reported inconsistent bronchodilator (BD) responses in obese asthmatic patients [8, 9].

Studies on regional ventilation distribution in obese patients have primarily focused on adults using routine pulmonary function tests and radiation techniques [10, 11]. Electrical impedance tomography (EIT) is a non-invasive, radiation-free method that offers real-time imaging of global and regional lung ventilation [12]. This technique is based on the measurement of bioimpedance variations within the thorax: small alternating electrical currents are delivered through a series of electrodes placed circumferentially around the chest, and the resulting voltage differences are recorded. Since air-filled lung tissue has high resistivity compared with blood and soft tissues, the changes in regional impedance during breathing can be reconstructed through dedicated algorithz ms into dynamic cross-sectional images of the lungs [12–14]. These functional images allow continuous evaluation of global and regional ventilation distribution, with the possibility of detecting heterogeneity in aeration and identifying areas of collapse or overdistention [12]. In clinical practice, EIT has been increasingly applied in pediatric intensive care, where it supports optimization of mechanical ventilation by guiding recruitment maneuvers, titration of positive end-expiratory pressure (PEEP), and early detection of atelectasis or overinflation [15]. Evidence suggests that EIT-guided PEEP titration in children with acute respiratory distress syndrome (ARDS) can improve lung recruitment without increasing overdistension, leading to better respiratory mechanics and gas exchange [16]. Beyond ARDS, EIT was applied in other conditions, including bronchiolitis, pneumonia, asthma, and cystic fibrosis, showing good correlation with spirometry and radiological findings [15, 17, 18]. Furthermore, recent research has explored its use in monitoring the effect of chest physiotherapy guiding a personalized approach [19].

Our study aims to assess global and regional ventilation patterns in obese asthmatic children using EIT, evalaute their BD response using standard spirometry, and test the feasibility of EIT in this population.

## Materials and methods

### Study design and participants

We conducted a single-centre, cross-sectional study on a convenient sample of pediatric patients aged 6–18 years with asthma and overweight/obesity, referred to the Pediatric Respiratory Disease outpatient clinics at Fondazione IRCSS Ca' Granda Ospedale Maggiore Policlinico in Milano, Italy, between March 2022 and August 2023. Eligible patients were selected based on their willingness to participate and were screened using an anamnestic questionnaire.

Asthma diagnosis was confirmed by a clinical history of typical respiratory symptoms and at least one previous spirometry showing expiratory airflow limitation (forced expiratory volume in the first second ($FEV_1$) and/or the ratio between $FEV_1$ and forced vital capacity (FVC) <−1.645 z-score) and/or positive BD responsiveness test (defined as an increase in $FEV_1$ from baseline of >10% predicted 15 minutes after 400 mcg of inhaled salbutamol) [20–22]. Overweight and obesity were defined using WHO 2007 growth references, with thresholds for Body Mass Index (BMI)-for-age set on standard deviation (sd) (overweight as BMI ≥ 1.0 sd and obesity as BMI ≥ 2.0 sd) [1, 23].

Children were excluded if they had a history of heart or kidney disorders, neurological disabilities, immunodeficiency, autoimmune or rheumatic diseases, cancer, spinal fracture, thoracic skin conditions, preterm birth (<32 weeks), chronic lung diseases (e.g. bronchopulmonary dysplasia), or recent asthma exacerbation (<1 month).

### Study procedures

#### *Anamnestic questionnaire*

Parents of eligible children completed a questionnaire covering gestational age at birth, neonatal issues, upper and lower tracts respiratory infections in the last year, hospitalizations for respiratory conditions, age of asthma onset, current maintenance therapy (i.e., inhaled corticosteroid, ICS or ICS/long-acting beta-agonist, LABA), episodic or persistent asthma (defined as uncontrolled symptoms or low lung function despite correct medication assumption and good adherence with Step 4 treatment [20]), allergic asthma (defined as reported above, in association with positive skin prick tests, SPTs, and/or elevated level of total Immunoglobulin E, IgE), exertional dyspnea, physical activity levels and exposure to parental tobacco smoking.

#### *Anthropometric measurements*

At enrollment, we measured height to the nearest 1 mm with a Harpenden stadiometer, weight to the nearest 0.1 kg with a portable, digital scale (Tanita, Tokyo, Japan), BMI, and body fat and free fat mass (FFM) using bioelectrical impedance analysis with a Tanita Body Composition Analyzer (BC-420 MA, Tanita, Tokyo, Japan). Triponderal mass index (TMI) was calculated as weight (kg) divided by height ($mt^3$) [24]. Neck and waist circumferences (WC) were measured to the nearest 1 mm with a tape measure, and a waist-to-height ratio (WHtR) above 0.5 indicated central obesity [25].

#### *Respiratory examinations*

Instrumental examinations were conducted after a one-week washout of maintenance therapy (ICS or ICS/LABA).

EIT was performed on spontaneously breathing children in a sitting position using a PulmoVista 500 EIT device (Dräger Medical AG, Lübeck, Germany). A thoracic belt with 16 electrodes was placed between the fourth and fifth intercostal space, and a reference electrode was positioned at the abdomen [12]. Alternating current was applied through a pair of electrodes, with voltages measured by the remaining 13 electrodes in a rotating sequence every 50 milliseconds [12]. Data were processed with the modified Newton-Raphson algorithm to produce a real-time 32 × 32 pixel map of lung electrical conductivity [26]. Each EIT measurement lasted about 2 minutes.

Five minutes after the first EIT analysis, spirometry was done using a Vyntus® BODY pneumotachograph (V3.10.9, Vyaire Medical, Inc.), with an airflow resistance of 0.036 $kPa{\cdot}L^{-1}{\cdot}s$ and dead volume of 160 ml, following ATS/ERS criteria [27]. Both EIT and spirometry were repeated 15 minutes after administering 400 mcg of inhaled salbutamol.

#### Respiratory data collection

EIT data were analyzed offline using the EITDiag software version 1.6 (Dräger Medical GmbH, Lübeck, Germany). We examined ten regular consecutive breaths in Tidal Volume (TV) for each child in spontaneous breathing, analysing data before and after BD. EIT images were manually segmented into four regions of interest (ROIs): ventral left (VL), ventral right (VR), dorsal left (DL), and dorsal right (DR). The software provided numerical values as percentages to assess local and global ventilation and its trends.

We assessed three EIT measures: tidal variation, spatial ventilation distribution, and temporal ventilation heterogeneity. Global tidal variation (TV) was calculated as the difference between end-expiratory global impedance and end-inspiratory global impedance, always expressed as 100%. This global tidal variation served as the reference for regional tidal variations (TV ROI), representing the percentage change in regional impedance [12, 28]. Spatial ventilation distribution was quantified using the global inhomogeneity (%GI) index, which measures the TV distribution within lung regions. A higher %GI index indicates greater impendence variation and heterogeneous ventilation [28, 29]. This index was calculated globally (Total %GI index) and for each of the four ROIs. Temporal ventilation heterogeneity, indicating the time required for air to reach the alveoli, was assessd using regional ventilation delay (RVD) [28]. We analyzed the percentage of time needed to reach 40% of RVD (%RVD40), calculated both globally (Total %RVD40) and for each ROI.

Data about airflows and lung volumes were obtained using spirometry from each patient, before and after BD. By using the SentrySuite™ Software, we analyzed FVC, $FEV_1$, $FEV_1/FVC_{ratio}$, and forced expiratory flow between 25 and 75% of the FVC ($FEF_{25-75}$). Spirometric data were expressed according to the Global Lung Function Initiative reference values [20]. Airway dysanapsis was defined as normal to high FVC z-score (≥0.674), normal $FEV_1$ z-score (≥−1.645), and low $FEV_1$/FVC (<80%) [5].

#### Statistical analysis

Data are summarized as mean (±1 sd) or median and interquartile ranges (IQR), and as counts and percentages (%). Differences between continuous variables are reported as mean differences with 95% confidence intervals (CI) and tested with the Wilcoxon signed rank test. Categorical variables were compared using Chi-square or Fisher exact statistic. For correlation analysis involving differences in $FEV_1$ z-score, $FEF_{25-75}$, Total %GI Index, %RVD40 and age, BMI z-score, TMI and WHtR, Spearman correlation (rho) was used, with Benjamin-Hochberg adjustment for multiplicity. All tests were two-sided with alpha set at 5%. Analyses were done using R software [30].

#### Ethics

The study was conducted in accordance with the Declaration of Helsinki [31], and all the participants' parents gave written informed consent. The study protocol was approved by the Ethics Committee of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico (Ethic Committee, Milan, Area 2, approval number 333_2016).

## Results

Over the twenty-nine subjects screened, we included twenty-seven children with asthma (7 females) with a median age of 12.4 years (IQR 11.0–13.3). None of them had relevant neonatal problems nor bronchopulmonary dysplasia. The 50% developed asthma between 4 and 9 years of age. Data about demographic characteristics

**Table 1** Patients' characteristics

| N | 27 |
|---|---|
| **Age** | 12.4 (10.4, 13.5) |
| *Range* | 7.4 - 13.4 |
| **Sex** | |
| Males | 20 (74.1%) |
| Females | 7 (25.9%) |
| **BMI z-score** | 2.4 (2.0, 2.7) |
| *Range* | 1.6 - 4.0 |
| **TMI** | 17.2 (16.1, 18.4) |
| *Range* | 14.5 - 23.7 |
| **WHtR** | 0.58 (0.52, 0.63) |
| *Range* | 0.47–0.67 |
| **Preterm birth** | 3 (11.1%) |
| **Hospitalizations for RDs** | 5 (18.5%) |
| **Age at asthma onset** | 6 (4, 9) |
| *Range* | 3–13 |
| **Maintenance therapy** | |
| ICS | 17 (63%) |
| ICS+LABA | 10 (27%) |
| **Frequency of asthma** | |
| Episodic | 19 (70.4%) |
| Persistent | 8 (29.6%) |
| **Allergic asthma** | 25 (92.6%) |
| **Exertional dyspnea** | 13 (48.1%) |

*Data are reported as median (I quartile, III quartile) or range (min-max) or counts with percentages (%)

RDs = respiratory diseases; ICS = inhaled corticosteroid; LABA = long-acting beta agonist; BMI = body mass index; TMI = triponderal mass index; WHtR = waist-to-height ratio

and anthropometric measurements are summarized in Table 1. Among the twenty-seven patients, eight (30%) were overweight and 19 (70%) obese. The WHtR was pathological and related to abdominal obesity in 21/27 children (78%).

### Data derived from spirometry and EIT

The results of spirometry and EIT are summarized in Table 2. In basal conditions, a z-score < −1.64 was found in 2/27 (7.4%) children for $FEV_1$ and in 5/27 (18.5%) participants for $MMEF_{75–25}$. The administration of BD determined globally a significant increase in $\%FEV_1$ (7.2, 95%CI: 4.7 to 9.4, $p < 0.001$), $FEV_1$ z-score (0.6, 95%CI: 0.4 to 0.8, $p < 0.001$), and $FEF_{25–75}$ z-score (0.9, 95%CI: 0.6 to 1.2. $p < 0.001$). However, only 8/27 (29.6%) children reported a positive BD responsiveness test, according to ERS/ATS guidelines. Four children (14.8%) fulfilled the criteria for airway dysanapsis.

Analysis of EIT data revealed considerable variability in ventilation distribution across different ROIs, as well as in the total and regional GI index and RVD40 percentages. The dorsal regions (DL and DR, Table 2) showed a higher percentage of ventilation distribution. After BD administration, there was a statistically significant reduction in the VL region (−2.3, 95%CI: −3.9 to −0.6, $p = 0.009$).

**Table 2** Data derived from spirometry and EIT* (*n* = *27*)

| Spirometry | Before BD | After BD | p-value° |
|---|---|---|---|
| **$FEV_1$%predicted** | 103.1 (96.1, 113.9) | 109.0 (105.8, 123.8) | <0.001 |
| *Range* | 76.8–161.1 | 80.3–163.1 | |
| **$FEV_1$z-score** | 0.3 (−0.3, 1.2) | 0.8 (0.5, 1.9) | <0.001 |
| *Range* | −2.0–4.7 | −1.7–4.9 | |
| Above LLN | 25 (92.6%) | 26 (96.3%) | >0.9 |
| **$FEV_1$/FVC z-score** | | | 0.617 |
| Above LLN | 22 (81.5%) | 24 (88.9%) | |
| **$MMEF_{75–25}$z-score** | −0.2 (−1.1, 0.2) | 0.7 (0.1, 0.9) | <0.001 |
| *Range* | −2.5–1.9 | −1.9–2.0 | |
| Above LLN | 22 (81.5%) | 26 (96.3%) | 0.134 |
| *EIT* | | | |
| **Respiratory rate** | 17.0 (15.0, 19.5) | 17.0 (14.0, 20.0) | 0.4 |
| *Range* | 12.0–26.0 | 11.0–28.0 | |
| **%ROI VL** | 21.0 (17.0, 24.0) | 18.0 (15.0, 21.5) | 0.009 |
| *Range* | 12.0–34.0 | 6.0–26.0 | |
| **%ROI VR** | 23.0 (21.0, 27.5) | 22.0 (21.0, 27.0) | 0.8 |
| *Range* | 8.0–34.0 | 10.0–34.0 | |
| **%ROI DL** | 27.0 (23.0, 28.0) | 27.0 (23.5, 30.0) | 0.11 |
| *Range* | 16.0–35.0 | 16.0–41.0 | |
| **%ROI DR** | 29.0 (27.0, 33.5) | 33.0 (26.5, 35.0) | 0.2 |
| *Range* | 19.0–44.0 | 24.0–41.0 | |
| **Total %GI index** | 40.0 (38.0, 42.0) | 39.0 (38.0, 43.0) | >0.9 |
| *Mean* | 39.8 (2.6) | 40.1 (4.3) | |
| *Range* | 35.0–44.0 | 32.0–48.0 | |
| **%GI index VL** | 8.0 (6.5, 9.0) | 8.0 (6.0, 9.0) | 0.4 |
| *Range* | 5.0–15.0 | 4.0–11.0 | |
| **%GI index VR** | 9.0 (7.0, 11.0) | 8.0 (7.0, 10.0) | 0.8 |
| *Range* | 3.0–15.0 | 5.0–18.0 | |
| **%GI index DL** | 10.0 (9.0, 11.0) | 11.0 (8.0, 11.5) | 0.6 |
| *Range* | 4.0–15.0 | 5.0–15.0 | |
| **%GI index DR** | 12.0 (11.0, 14.0) | 13.0 (10.0, 15.0) | 0.5 |
| *Range* | 6.0–19.0 | 9.0–20.0 | |
| **Total %RVD40** | 5.4 (4.8, 6.6) | 5.6 (4.0, 7.2) | 0.3 |
| *Range* | 3.4–9.3 | 3.4–8.4 | |
| **%RVD40 VL** | 6.6 (4.7, 8.4) | 7.1 (4.8, 9.3) | 0.6 |
| *Range* | 2.9–12.2 | 2.6–12.8 | |
| **%RVD40 VR** | 6.3 (5.3, 7.7) | 6.3 (4.3, 7.5) | 0.2 |
| *Range* | 2.8–10.2 | 2.5–9.5 | |
| **%RVD40 DL** | 4.0 (3.2, 4.6) | 3.8 (3.0, 5.1) | 0.4 |
| *Range* | 2.1–9.1 | 1.4–9.5 | |
| **%RVD40 DR** | 5.2 (4.4, 7.0) | 5.2 (3.9, 6.8) | 0.092 |
| *Range* | 3.1–10.3 | 2.4–7.8 | |

*Data are reported as median (I quartile, III quartile) or mean (with standard deviation) or counts with percentages (%), with range (min-max)

° Wilcoxon signed rank or Fisher's exact test

BD = bronchodilator; $FEV_1$ = forced expiratory volume in the first second; FVC = forced volume capacity; $MEF_{25–75}$ = mean flow between 25 and 75%; LLN = lower limit of normal; ROI = region of interest; VL = ventral left; VR = ventral right; DL = dorsal left; DR = dorsal right; GI = global inhomogeneity index; RDV = regional ventilation delay

Regarding the %GI index, the highest value was observed in the DR region, with no significant change following BD administration.

The median total %GI index remained stable before and after BD: 40.0 (IQR:38–42) vs 39.0 (IQR:38–43), respectively ($p > 0.9$). No evidence of difference was observed in the total and regional %RVD40 before and after BD administration: 5.4 (IQR:4.8–6.6) vs 5.6 (IQR:4–7.2), respectively ($p = 0.3$).

EIT measurements were well tolerated and all tests were of sufficient quality for analysis.

Analysis of anthropometric characteristics, spirometry and EIT data stratified by BD responders and non-responders (Table 3) revealed no discernible patterns between these groups.

### Correlation analysis

We observed moderate, statistically significant positive correlation between BMI z-score and WHtR (rho = 0.73, $p < 0.001$), BMI z-score and TMI (rho = 0.85, $p < 0.001$), WHtR and TMI (rho = 0.76, $p < 0.001$), and between $FEV_1$ z-score and $FEF_{25–75}$ z-score differences (rho = 0.63, $p < 0.001$). We did not find evidence of correlation between pre- and post-BD differences in respiratory parameters and selected covariates (Fig. 1). Specifically, the difference in $FEV_1$ z-score (–0.1, 95%CI: –0.46 to 0.31), total %GI Index (0.27, 95%CI: –0.20 to 0.59), and %RVD40 (–0.05, 95%CI: –0.45 to 0.32) did not correlate with age. Similarly, higher BMI z-score was poorly correlated with changes in BD response, including $FEV_1$ z-score (0.23, 95%CI: –0.21 to 0.54), total %GI Index (0.18, 95%CI: –0.28 to 0.58), and %RVD40 (0.06, 95%CI:-0.40 to 0.44). In contrast, TMI showed a fair correlation with the total %GI Index (0.30, 9%CI: –0.15 to 0.64) (Fig. 2). WHtR showed a poor correlation with $FEV_1$ z-score (0.26, 95%CI: –0.24 to 0.58) and $MMEF_{75–25}$ z-score (0.27, 95%CI: –0.21 to 0.64), and a nearly flat relationship with %GI tot.

## Discussion

Our study used EIT to assess children with asthma and predominant abdominal obesity. All had early-onset asthma, were on ICS or ICS+LABA maintenance therapy, and mostly exhibited an allergic phenotype. The sample

**Table 3** Participants' characteristics stratified by response to bronchodilator*

| Parameters | Non-responders (n = 19) | Responders (n = 8) | p-value° |
|---|---|---|---|
| **Age, years** | 12.4 (10.4, 13.5) | 12.2 (11.2, 13.1) | >0.9 |
| *Range* | 7.4–17.3 | 10.4–13.9 | |
| **Sex** | | | |
| Male | 15 (78.9%) | 5 (62.5%) | 0.6 |
| Female | 4 (21.1%) | 3 (37.5%) | |
| **Frequency of asthma** | | | >0.9 |
| Episodic | 13 (68.4%) | 6 (75.0%) | |
| Persistent | 6 (31.6%) | 2 (25.0%) | |
| **Allergic asthma** | | | >0.9 |
| Yes | 17 (89.5%) | 8 (100%) | |
| **BMI z-score** | 2.5 (2.0, 2.9) | 2.4 (2.3, 2.4) | 0.6 |
| *Range* | 1.6–4.0 | 1.9–2.5 | |
| **TMI** | 17.2 (16.1, 18.6) | 17.1 (16.6, 17.6) | 0.5 |
| *Range* | 14.5–23.7 | 15.3–17.6 | |
| **WHtR** | 0.6 (0.5, 0.6) | 0.6 (0.5, 0.6) | 0.8 |
| *Range* | 0.5–0.7 | 0.5–0.6 | |
| **Basal $FEV_1$/FVC z-score** | | | 0.14 |
| Normal | 17 (89.5) | 5 (62.5) | |
| **Basal $MMEF_{75–25}$z-score** | | | 0.6 |
| Normal (%) | 16 (84.2) | 6 (75.0) | |
| **Airway dysanapsis** | | | 0.6 |
| Dysanapsis (%) | 2 (10.5) | 2 (25.0) | |
| **Basal total %GI index** | 40.0 (38.0, 42.0) | 40.5 (37.8, 42.3) | 0.8 |
| *Range* | 35.0–43.0 | 35.0–44.0 | |
| **Basal total %RVD40** | 5.3 (4.9, 6.1) | 6.8 (4.7, 7.7) | 0.2 |
| *Range* | 3.4–7.8 | 4.5–9.3 | |

*Data are reported as median (I quartile, III quartile) or range (min-max) or counts or percentages (%)

°Wilcoxon rank sum test; Fisher's exact test

BMI = body mass index; TMI = triponderal mass index; WHtR = waist-to-height ratio; LLN = lower limit of normal; $FEV_1$ = forced expiratory volume in the first second; FVC = forced volume capacity; $MEF_{25–75}$ = mean flow between 25 and 75%; GI = global inhomogeneity index; RDV = regional ventilation delay; BD = bronchodilator

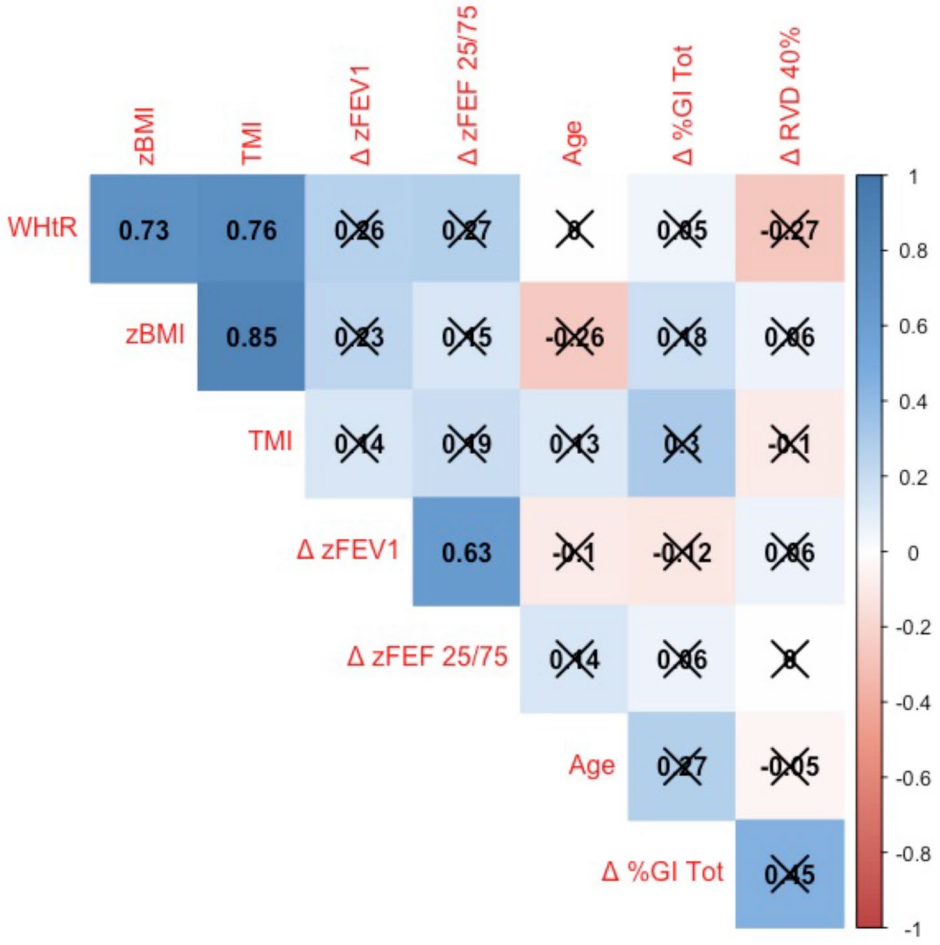


**Fig. 1** Correlation plot. Correlations not surviving correction for multiplicity are crossed. Direction and strength of correlation is displayed also by colors. Δ denotes difference as post-pre

showed a distinct regional ventilation pattern, with BD use leading to a suboptimal spirometric response and minimal changes in EIT measurements.

Obese asthmatic adults typically experience altered breathing mechanics, resulting in reduced expiratory reserve volume, functional residual capacity (FRC) and lung compliance, due to the abdominal and chest wall fat compression [4]. However, the impact of obesity on ventilation distribution during spontaneous breathing in children remains unexplored, with most data focusing on obese adults or critically ill children. Using EIT, we analyzed the ventral-to-dorsal ventilation distribution in the sitting position, finding higher dorsal ventilation compared to the ventral regions despite high inter-subject variability. This may be due to greater diaphragm excursion, leading to higher variation in the pleural pressure and greater ventilation in the dorsal regions [32, 33]. In a recent study [32] including twenty lung-healthy children younger than 5 years who underwent non-thoracic surgery, EIT documented a greater ventilation distribution in the posterior regions of the lungs during spontaneous breathing before the anaesthesia induction. Our findings suggest that obesity in children may not significantly alter the pattern of ventilation distribution, at least in the sitting position. However, while the dorsal regions were more ventilated, they also showed greater inhomogeneity (higher %GI index). In 2013, Mahadev et *al.* [34] demonstrated that increased BMI in adults is associated with greater diffusion-dependent ventilation heterogeneity, as measured by multiple breath nitrogen washout, regardless of FRC. Similarly, in 2021, Yang et al. [35] found a weak but significant correlation between GI index and BMI in healthy adults in the supine position, likely due to fat accumulation leading to increased airway resistance, gas trapping, ventilation/perfusion mismatch and ventilation heterogeneity [4, 7, 36]

Regarding spirometric parameters, we found that mean values of $FEV_1$, $FEV_1/FVC_{ratio}$ and $FEF_{25–75}$ were generally within the normal range. In obese adults, studies typically show an inverse relationship between increased BMI and lower $FEV_1$ and FVC, while the $FEV_1/FVC_{ratio}$ remains unaffected [4]. In children, however, excess

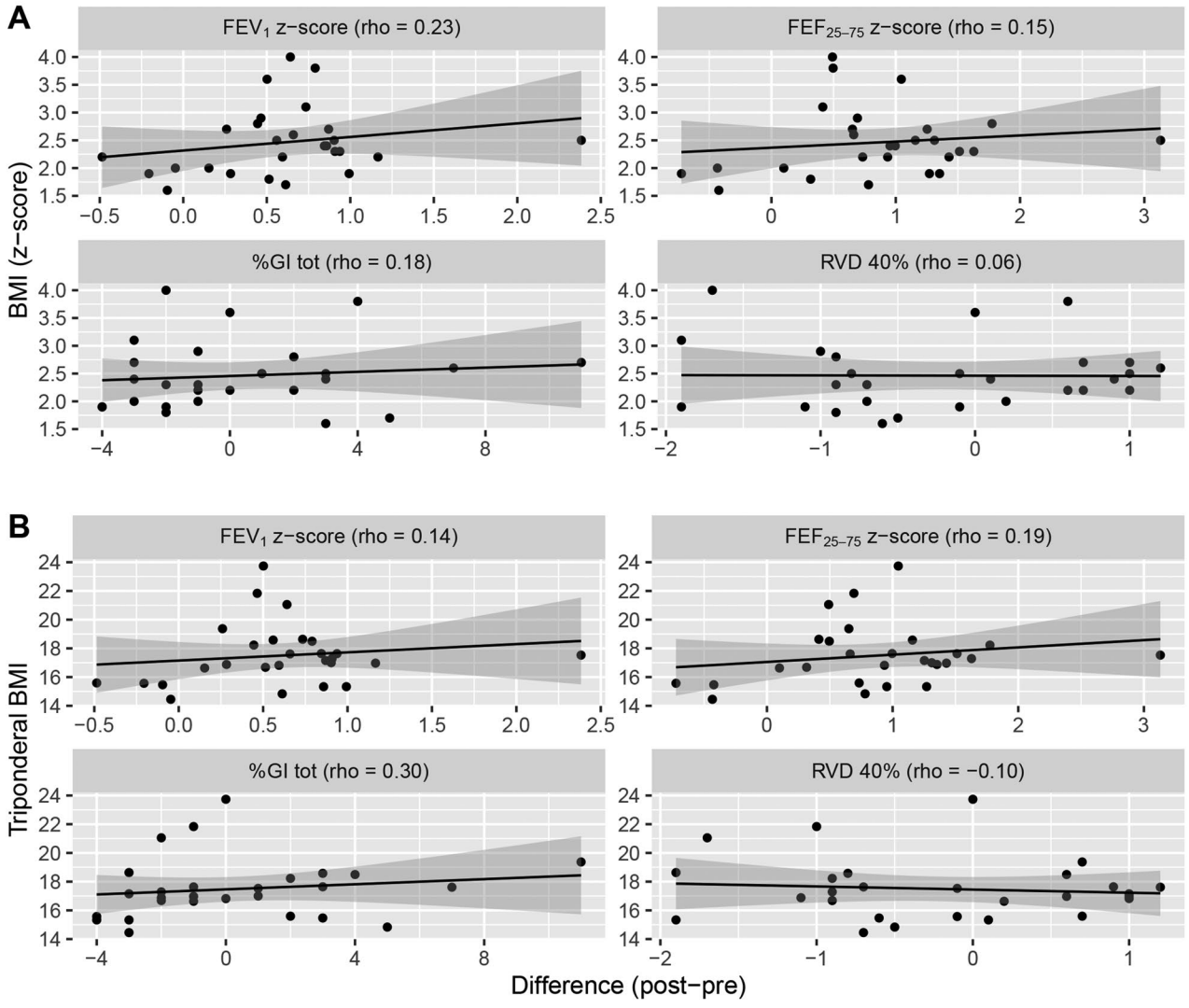


**Fig. 2** Correlation between BMI (**A**) or TMI (**B**) and respiratory/EIT parameters. Solid line denotes regression line with 95% CI bands (gray). CI, confidence interval; BMI, body mass Index; TMI, triponderal BMI; GI tot, total global inhomogeneity; %RVD40, global regional ventilation Delay; $FEV_1$, forced expiratory volume in the first second; $FEF_{75-25}$, forced expiratory flow between 25 and 75% of the forced vital capacity

weight appears to affect lung volumes and airflow differently. For instance, a large study of healthy Italian children found that FVC and $FEV_1$ were positively correlated with weight, but $FEV_1$ increased less than FVC, resulting in a negative correlation between $FEV_1/FVC_{ratio}$ and weight, regardless of respiratory symptoms [37]. This may indicate a disproportionate growth between airways and lung parenchyma, or dysanapsis, where lung size increases without a corresponding increase in airway caliber. In our study, 15% of participants met the criteria for airway dysanapsys. Although data on the prevalence of this condition in obese asthmatic children are limited, it is known that obesity-related dysanapsis can negatively affect lung function overtime. Particularly, overweight and obese children had up to a twofold increased risk of dyasanapsis compared with normal-weight children. This condition can make symptoms control more challenging and reduce the effectiveness of medications [5], which may help explain the observed lack of response to BD. A recent prospective study in healthy infants found that airway dysanapsis could originate early in life: higher BMI z-scores and rapid weight gain were significantly associated with early dysanapsis, even in the absence of obesity, indicating that the imbalance between airway and lung growth begins in infancy [38]. Our findings highlight that dysanapsis can originate early in life, can be associated with overweight-obesity, and can play a pivotal role in the obese-asthma interplay.

In our pediatric sample, BD administration led to a global increase in $\%FEV_1$, $FEV_1$ z-score and $FEF_{25-75}$ z-score. However, a clinically significant BD response was observed in only 30% of obese asthmatic children.

The response to BD in obese asthmatics has been widely studied, often with inconclusive results. For instance, McGarry et al. [9] found that obese children and adolescents had a 24% higher likelihood of being unresponsive to BD compared to their non-obese peers in a large cohort of 2963 Black and Hispanic children. Conversely, a recent study of 415 symptomatic non-smoker adults showed that the fluticasone/salmeterol combination led to greater improvements in $FEV_1$ and $FEV_1$/FVC, compared to salbutamol, particularly in obese individuals [39]. In our study, the suboptimal BD response observed in 70% of the sample was further confirmed by EIT, which showed no significant changes in total and regional %GI index and %RVD40 after BD. These parameters are particularly effective for assessing air distribution in the lungs, reflecting airway patency. Since its development over 30 years ago, EIT has primarily been used in intensive care settings to customize mechanical ventilation parameters. More recently, EIT has been adopted to detected and monitor lung diseases in non-critically ill children, with strong evidence supporting its reliability in assessing lung function and treatment response in asthmatic children [18]. Compared to spirometry, EIT appears to be more sensitive in detecting small regional changes induced by the BD [40]. In our study, we observed a reduction in ventilation percentage in the VL region after BD, likely reflecting a redistribution of ventilation across the other three ROIs, consistent with a suboptimal therapeutic response.

The poor response to BD in many obese asthmatic children can be attributed to several factors. Obesity is linked to altered respiratory mechanics, leading to reduced lung compliance and fixed airway obstruction. However, the absence of significant spirometric anomalies in our sample suggests that weight-induced mechanical changes may play a limited role, as also observed in the ventilation distribution. Additionally, insulin resistance, compensatory hyperinsulinemia, and systemic inflammation associated with obesity may further impair asthma control, diminishing the effectiveness of BD treatment. A recent mouse model study highlighted the role of hyperinsulinemia in promoting β2- adrenergic receptor (β2-AR) desensitization in airway smooth muscles [41]. Unfortunately, we can only speculate that the abnormal WThR observed in most of our patients – an indicator of abdominal obesity and increased risk for metabolic syndrome - might contribute to impaired β2-AR response, as we did not assess the metabolic profiles of our sample. Conversely, in this cohort with a high prevalence of allergic sensitization, we cannot rule out the possibility that long-term maintenance treatment may have influenced the inflammatory pattern and respiratory function, suggesting that well-controlled $TH_2$ inflammation, rather than excess adiposity, could be a key factor in the limited BD response. This hypothesis aligns with pur previous findings, where we observed a similar spirometric pattern between obese and normal-weight asthmatic children, both with comparable prevalence of the allergic phenotype [42]. However, we did not directly assess these factors in our study and our hypotheses remain speculative. Further research is needed to clarify which of these factors play the most significant role.

We did not find significant correlations between pre-post BD differences in respiratory parameters and anthropometric indicators (BMI z-score, TMI, WThR). However, we did observe a stronger association between linear increases in total %GI following BD administration and higher TMI. Unlike BMI, which does not distinguish between muscle mass and body fat, TMI offers a more accurate estimation of adiposity, particularly in adolescents, whose body proportions and fat levels can fluctuate [25]. Clinical applications of TMI have primarily focused on early identification of metabolic and cardiovascular risks in childhood obesity, but no studies have yet explored its relationship with lung function or therapeutic response in obese children. Despite the limitation of our small sample, our findings suggest that TMI may be a useful measure of BD reversibility in obese asthmatic children.

To our knowledge, this is the first study to use EIT to assess ventilation distribution and BD response in obese asthmatic children. However, the absence of a non-overweight asthmatic control group limits the internal validity of our findings. Addtionally, the study was based on a convenience sample without formal sample size calculation that could increase the risk of type II error. The participants, primary allergic asthmatics with early diagnosis and consistent ICS or ICS/LABA therapy, may have had their lung function measurements influenced by long-term treatment. Moreover, chest wall fat in obese patients can reduce electrical conductivity, potentially lowering EIT image resolution. Few studies have examined the impact of obesity on EIT image quality. Recent numerical modeling suggests that as obesity increases, a wider gap between current injection electrodes may improve image accuracy compared to the standard voltage setup [43]. While our sample's BMI was below the threshold for poor image quality [44] (i.e., 50 $kg/m^2$), further research is needed to optimize EIT in this population.

This study was conceived as a preliminary investigation with the primary aim of testing the feasibility of EIT in obese asthmatic children. Although the sample size was limited, we observed consistent trends—including airway dysanapsis, reduced bronchodilator responsiveness, and altered regional ventilation—that align with prior literature and reinforce the validity of our findings. These preliminary results provide valuable hypotheses that require testing in prospective, well-powered studies.

## Conclusion

Children with asthma and excess weight generally showed normal spirometry in our small cohort; however, some demonstrated a dysanaptic pattern, suggesting disproportionate lung and airway growth in the obesity–asthma phenotype. EIT revealed dorsal-predominant ventilation, similar to healthy peers. While one-third of obese asthmatic children showed bronchodilator responsiveness by spirometry, EIT detected no parallel ventilation changes.

These findings highlight dysanaptic lung growth and impaired BD responsiveness as core features that may limit treatment effectiveness, underscoring the need for tailored therapies. EIT offers a promising tool to capture regional ventilation and early pathophysiological changes in pediatric asthma.

### Abbreviations

| | |
|---|---|
| BD | Bronchodilator |
| EIT | Electrical impedance tomography |
| PEEP | Positive end-expiratory pressure |
| ARDS | Acute respiratory distress syndrome |
| $FEV_1$ | Forced expiratory volume in the first second |
| FVC | Forced vital capacity |
| BMI | Body mass index |
| ICS | Inhaled corticosteroids |
| LABA | Long-acting beta-agonist |
| SPTs | Skin prick tests |
| IgE | Immunoglobulin E |
| FFM | Free fat mass |
| TMI | Triponderal mass index |
| WC | Waist circumferences |
| WHtR | Waist-to-height ratio |
| TV | Tidal Volume |
| ROIs | Region of interests |
| VL | Ventral left |
| VR | Ventral right |
| DL | Dorsal left |
| DR | Dorsal right |
| TV | Tidal variation |
| GI | Global inhomogeneity |
| RVD | Regional ventilation delay |
| $FEF_{25-75}$ | Forced expiratory flow between 25% and 75% of the FVC |

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### Author contributions

Antonella Gambadauro: Conceptualization; investigation; writing –original draft; software; data curation. Simone Gambazza: Methodology; formal analysis; visualization; writing – original draft. Sara Manti: Data curation; investigation. Mara Lelii: Investigation; supervision. Barbara Madini: Investigation; supervision. Alessia Rocchi: Investigation; supervision; writing – original draft. Beatrice Andrenacci: Investigation. Giovanna Chidini: Investigation. Maria Francesca Patria: Conceptualization; resources; project administration; writing - original draft; writing – review & editing; methodology.

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### Data availability

The data presented in this study are available on request from the corresponding author.

## Declarations

### Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico (Ethic Committee, Milan, Area 2, approval number 333_2016).

### Consent for publication

Not applicable.

### Competing interests

The authors have no conflicts of interest to disclose.

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