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REVIEW ARTICLE

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Comparison of lung volumes measured with computed tomography and whole-body plethysmography – a systematic review

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ABSTRACT

Introduction: Whole-body plethysmography is the preferred method for measuring the static lung volumes: total lung capacity (TLC), functional residual capacity (FRC) and residual volume (RV), as it also incorporates trapped gas – a common finding in chronic obstructive pulmonary disease (COPD). Quantitative computed tomography (CT) is a promising alternative to plethysmography, which can be challenging to perform for patients with severely impaired lung function. The present systematic review explores the agreement between lung volumes measured by plethysmography and CT, as well as the attempts being made to optimize alignment between these two methods.

Methods: A literature search was performed on the PubMed database using the block search strategy. Articles were included if they provided both CT based and plethysmography based TLC. Risk of bias was evaluated using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) checklist.

Results: 22 articles were included. On average, CT-derived TLC (CT-TLC) was 709 mL lower compared to plethysmography TLC (p-TLC) with a 12.1% deviation from the reference standard, p-TLC. This discrepancy (ΔTLC) appeared slightly larger in obstructive patients (obstructive: 781 mL, non-obstructive: 609 mL), whereas percent deviation was slightly smaller (obstructive: 11.4%, non-obstructive: 13.5%). CT-based RV analyses primarily based on COPD patients measured 603 mL higher than plethysmography (p-RV) with 17.8% deviation from p-RV. Studies utilizing spirometry-gating for CT acquisition reported good agreement between modalities (ΔTLC: 70–280 mL), and one study demonstrated noticeable improvements compared to conventional breath-hold instructions in an otherwise identical study setting.

Conclusion: CT quantifications routinely underestimate TLC and overestimate RV in comparison to plethysmography. Spirometry gating reduces the level of disagreement and can be of assistance when patients are already undergoing CT. However, further studies are needed to confirm these results.

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Systematic review; total lung capacity; functional residual capacity; residual volume; static lung volumes; computed tomography; body box; whole-body plethysmography

Introduction

After its introduction in 1956 [1], whole-body plethysmography has been regarded as gold standard for measuring static lung volumes including residual volume (RV), functional residual capacity (FRC) and total lung capacity (TLC). Methods based upon multiple-breath gas dilution or washout techniques depend on communicating gas and thus only measure a subject's ventilated lung volumes. In contrast, plethysmography includes also trapped air so it is applicable for patients with lung diseases characterized by air trapping such as chronic obstructive pulmonary disease (COPD) [2]. Performing the necessary respiratory maneuvers correctly requires meticulous coaching and multiple attempts [3]. This can be especially demanding for patients with severely impaired lung function and might not be suitable for patients (e.g. children) who find it challenging to follow instruction. In addition, the intermittent closure of air flow and compact dimensions of the body box can induce panic attacks in patients suffering from claustrophobia.

CT lung volumetrics is promising as an alternative tool for assessing pulmonary function and volumes. Furthermore, software can both quantify degree of emphysema and segment the lung into pulmonary lobes, which is helpful when selecting lobes as target for lung volume reduction therapy.

A technician or voice recording usually instructs the patient to fully inhale or exhale and hold still as the CT scan is performed. Patient cooperation and scan timing

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is among the challenges faced and can be managed by spirometry-gating and other solutions.

The aim of this systematic review is to assess the agreement between static lung volumes measured by quantitative CT volumetrics and body plethysmography and explore the attempts being made to optimize alignment. It is hypothesized that inspiratory CT-based volumes underestimate TLC and expiratory CT-based volumes overestimate RV whereas spirometry gating reduces the level of disagreement.

Methods

Search and study selection

The research question was *'What is the agreement between lung volumes measured with CT and body box?'* A systematic search strategy was applied on PubMed using block-searching strategy with the entries: (TLC OR RV) AND CT AND plethysmography. The first broad search identified 1405 results (Table A1. *Search Protocol #1*) and a second, narrower search yielded 111 results (Table A2. *Search Protocol #2*). Titles and abstracts were screened, and articles were assessed for eligibility by screening the full-text version. Reference lists were searched for additional relevant articles. Articles had to include human subjects and TLC derived from CT acquired at maximum inspiration as well as plethysmography TLC as comparator. Results had to be original studies in English or a Scandinavian language and include an abstract and a full-text version.

The selection process is visualized using a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram (Figure 1) [4].

Since whole-body plethysmography is the gold standard for measuring static lung volumes, articles based on multiple-breath gas dilution or washout methods were excluded. If studies provided data from before and after thoracic surgery, only pre-surgery data was included to avoid patients contributing to the result multiple times.

Risk of bias

The Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool was used for evaluating the risk of bias and method quality (Figure 2) [5]. For each article, the following domains were evaluated: patient selection, index test, reference standard, and flow and timing.

It was considered appropriate if plethysmography was performed according to guidelines, such as from the American Thoracic Society and European Respiratory Society [3], or if the described method of static spirometry followed the same standards. A maximum time interval of 30 days between pulmonary function testing and CT acquisition was considered appropriate. However, the acceptable interval was shortened if patients had fluctuating lung function impairment such as in asthma.

Results

Search

We identified 115 articles via the database search (Figure 1) comprising 111 from the final search and additionally four from the original search (Tables A1 and 2). Nineteen articles met the inclusion criteria described in *Search and Study Selection*. An additional three eligible articles were uncovered by screening the reference list of these articles. In total, 22 articles were included for revision; eight studies were prospective and 14 retrospective (Table 1).

Differences in lung volumes measured by CT and Plethysmography

In the 17 articles that provided absolute TLC volumes derived from plethysmography (p-TLC) and CT (CT-TLC), plethysmography measured a larger volume than quantified in a corresponding inspiratory CT image (Table 2 and Figure 3). On average, p-TLC was 709 mL larger than CT-TLC (maximum: 1380 mL, minimum: 70 mL) and the mean percent deviation was 12.1% (maximum: 23.7%, minimum: 3.7%) with p-TLC as reference.

All except one study (*O'Donnell CR* et al. [1]) calculated a correlation coefficient between results from both modalities [1]. In general, CT-TLC correlated well with p-TLC averaging 0.83 (maximum: 0.98, minimum: 0.38). *Gawlitza J* et al. [6] were the only ones observing a weak association (0.38) between plethysmography- and CT-derived lung volumes.

Seven articles provided absolute measurements of RV [7–13] (Table 3). The mean difference between p-RV and CT-RV was −603 mL (maximum: −1060 mL, minimum: −290 mL), and the average percent deviation was −17.8% (maximum: −39.1%, minimum: −6.0%). Correlations for the RV assessments were somewhat weaker but still good as indicated by an average correlation coefficient of 0.76 (maximum: 0.84, minimum: 0.65).

Five out of the seven articles on RV studied patients with COPD exclusively [7,8,10,11,13] (Table 3). When

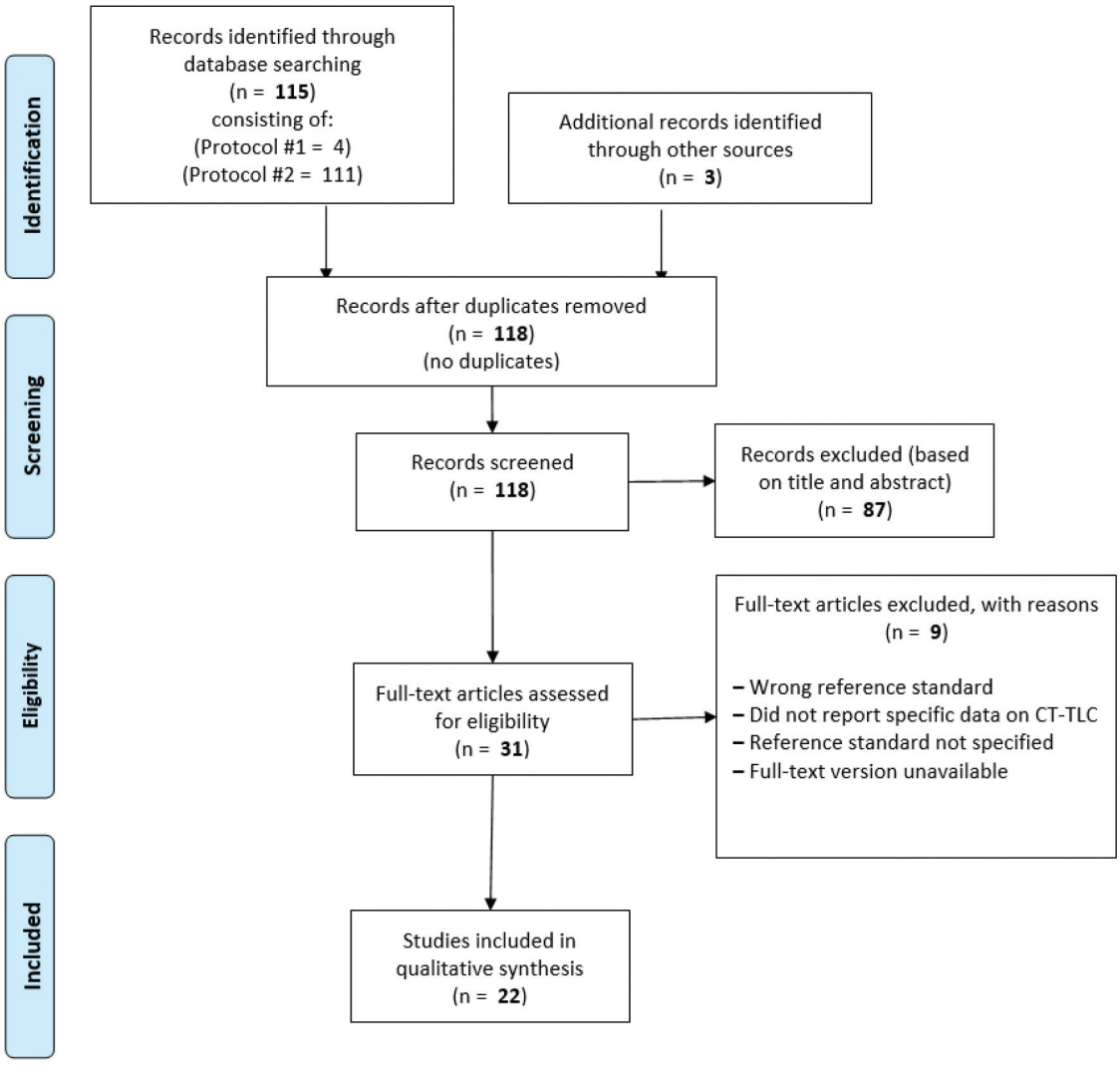

Figure 1. PRISMA flow diagram.

comparing pooled volumes in subjects with COPD and non-COPD subjects (these included healthy subjects and patients with suspected lung disease, respectively), it is evident that a moderate disagreement in mean absolute difference between the groups (COPD: −561 mL, non-COPD: −730 mL) contributes to a significant discrepancy in percent deviation from the reference standard, p-RV (COPD: 12.2%, non-COPD: 31.8%) (Figure 4).

When TLC data is divided into an obstructive and a non-obstructive group, ΔTLC appears slightly larger in obstructive patients (obstructive: 781 mL, non-obstructive: 609 mL), whereas percent deviation is slightly smaller (obstructive: 11.4%, non-obstructive: 13.5%) (Figure 3).

Three studies stated that a bronchodilator was administered before performing body plethysmography and CT [7,11,14]. In contrast, *Tantucci C* et al. stated that when relevant, inhalations were withdrawn 24–48 h beforehand [15]. However, results from these articles did not seem to differ noticeably from other articles on obstructive patients.

Jung WS et al. and *Tantucci C* et al. categorized subjects into restrictive, obstructive and control groups according to dynamic spirometry results. In the study conducted by *Jung WS* et al. patients with a restrictive pattern had the smallest ΔTLC, percent deviation and correlation coefficient [16]. In contrast, *Tantucci C* et al. reported an excellent correlation (0.98, 0.97 and 0.98) and minimal ΔTLC (110 mL, 70 mL and 80 mL) in all patient groups showing no noteworthy variation in the groups [15].

This was also one of only two studies utilizing a spirometer to gate CT acquisition – all other studies gave conventional breath-hold instructions. *Bakker JT* et al. aimed to investigate the effects of spirometric gating

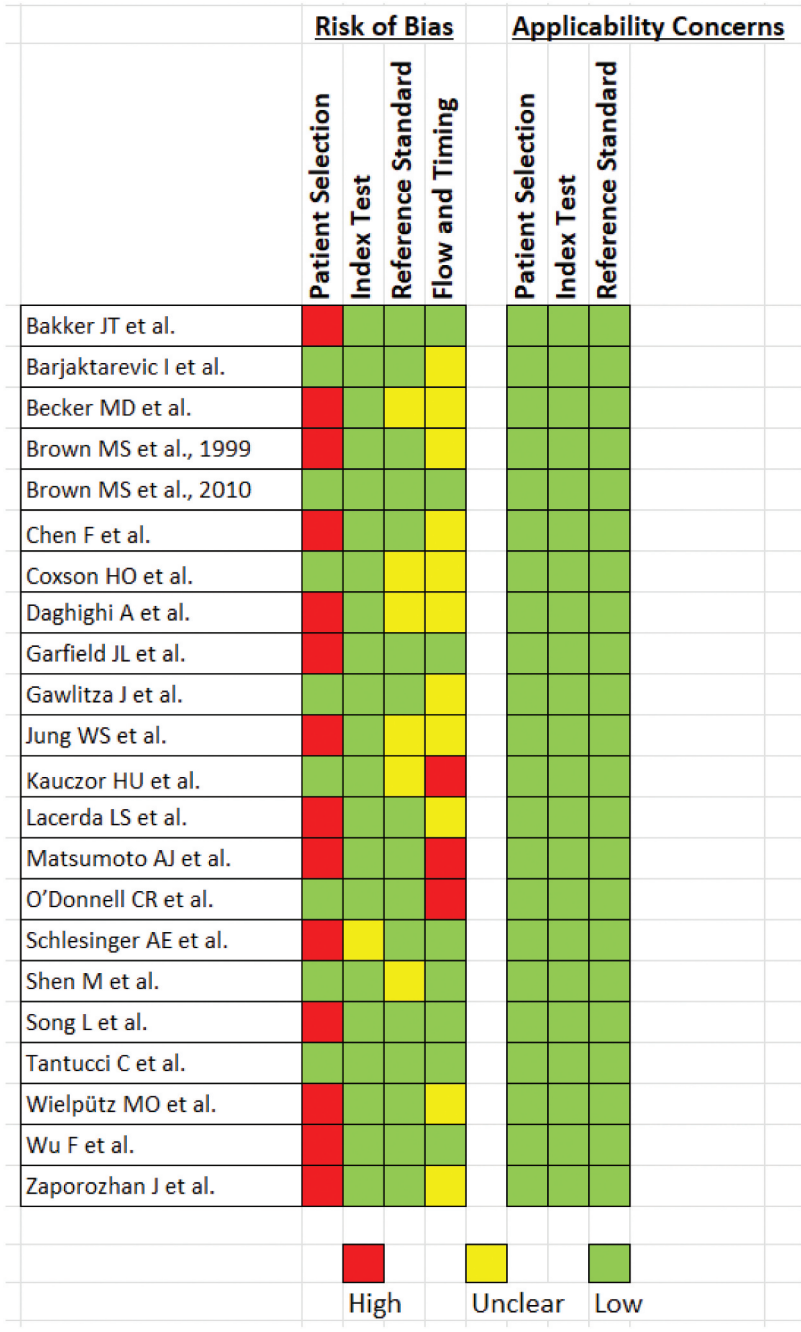

Figure 2. Risk of bias and applicability assessment using the QUADAS-2 tool.

on patients with COPD by comparing it to instructing patients to hold their breath [7]. This technique rendered noticeable improvements in all parameters in an otherwise identical study setting (Tables 2 and 3).

Discussion

The findings of the present review suggest that discrepancy between plethysmography- and CT-derived lung volumes is a universal phenomenon. Specifically, quantitative CT routinely underestimates TLC and overestimates RV in comparison to body plethysmography. Utilizing a spirometer to gate CT acquisition reduces disagreement noticeably though it does not eliminate it entirely.

TLC can be defined as the total gas volume in the lung after a full inspiratory maneuver [3]. It has been challenging to determine whether gas in the conductive airways is included in this definition. Even though it might seem trivial, this appears to be an import factor to consider. Body plethysmography incorporates volumes in the oropharynx, trachea,

Table 1. Study characteristics.

Study	Study Type	Publishing Year	No. of Participants	Age, years (Mean±SD)	Indication, type of subjects
Bakker JT et al.	Retrospective, single-center	2022	200	62 ± 8	COPD
Barjaktarevic I et al.	Prospective, multi-center	2015	460	64 ± 7	COPD
Becker MD et al.	Retrospective, single-center	1997	28	65 ± 7	COPD
Brown MS et al.	Retrospective, single-center	1999	43	–	21 normal 9 asthma 9 scleroderma 4 COPD
Brown MS et al.	Prospective, multi-center	2010	486	63 ± 7	COPD
Chen F et al.	Retrospective, single-center	2011	21	42 ± 11	Healthy lung donation candidates
Coxson HO et al.	Prospective, multi-center	2008	57	–	COPD
Daghighi A et al.	Retrospective, Multi-center	2018	61	–	Thoracic scoliosis
Garfield JL et al.	Retrospective, single-center	2012	59	63 ± 9	COPD
Gawlitza J et al.	Prospective, single-center	2017	46	66 ± 10	COPD
Jung WS et al.	Retrospective, single-center	2016	264	61 ± 14	LTx candidates grouped according to PFT results: Normal Obstructive Restrictive
Kauczor HU et al.	Prospective, single-center	1998	72	59	Suspected lung disease
Lacerda LS et al.	Retrospective, single-center	2018	43	Cystic fibrosis: 31 Controls: 24 Mean: 27	21 Cystic fibrosis 22 Controls
Matsumoto AJ et al.	Retrospective, single-center	2017	118	54 ± 11	LTx recipients before transplantation
O'Donnell CR et al.	Prospective, multi-center	2010	132	60 ± 11	Various indications for CT
Schlesinger AE et al.	Retrospective, single-center	1994	21	11	Follow-up of LTx children
Shen M et al.	Prospective, multi-center	2019	29	62	COPD
Song L et al.	Retrospective, single-center	2020	172	66 ± 7	COPD
Tantucci C et al.	Prospective, single-center	2016	37	Control:57 ± 11 Obstructive: 70 ± 9 Restrictive: 66 ± 13	Subjects grouped according to PFT results: Controls Obstructive Restrictive
Wielpütz MO et al.	Retrospective, multi-center	2014	49	64 ± 9	COPD
Wu F et al.	Retrospective, single-center	2021	65	56	Healthy
Zaporozhan J et al.	Retrospective, multi-center	2005	31	60 ± 8	COPD

Note: Study characteristics of all included studies [1,6–26]. COPD: Chronic Obstructive Pulmonary Disease, LTx: Lung transplantation, PFT: Pulmonary function test.

and anatomic dead space in the main conducting airways [10]. Some types of CT segmentation software include gas volumes in the tracheobronchial tree, others do not. For instance, the post-processing software used in *Shen M* et al.'s study excluded these volumes [10]. In contrast, *Tantucci C* et al. included anatomic dead space of 150 mL in their CT-TLC calculations [15]. Compressed gas in the upper gastrointestinal tract might also further increase FRC, which forms the basis for TLC and RV calculations [3].

Another important factor to note is the difference in posture (supine in CT vs. upright position in body plethysmography). By comparing conventional supine CT with upright CT in a specialized CT scanner, a study demonstrated that CT-based inspiratory and expiratory volumes were significantly smaller in the supine position than in the standing and sitting position in healthy subjects [27]. This is largely due to abdominal content pressing up against the diaphragm in the supine position, which has been shown by other studies to reduce vital capacity by less than 10% in normal subjects [17]. This is consistent with the results from the present review showing that CT-TLC is smaller than p-TLC.

However, the above studies contradict the present findings of a generally negative ΔRV (Table 3). This may be due to various CT software packages include lung tissue and blood vessels in their TLC volumetrics, which proportionally makes up more of the total lung volume at full expiration. ΔRV was largely based on data from COPD patients, a disease characterized by hyperinflation and an impaired ability to fully expire. Perhaps, the supine position exacerbates an already present muscle weakness, such as in the accessory expiratory muscles.

Tantucci C et al. calibrated CT and plethysmography TLC results by adding or subtracting the difference between vital capacity obtained in the seated and supine position, respectively, and presented excellent correlations [15] (Table 2).

Body plethysmography measures pressure changes at the mouth opening based on the assumption that these reflect pressure changes in the alveoli during shutter valve occlusion. In the presence of airway obstruction, however, this assumption might fail.

Table 2. Total lung capacity data.

Study		Subcategory	P-TLC (ml) (mean ± SD)	CT-TLC (ml) (mean ± SD)	ΔTLC (mL) (mean ± SD)	Percent Deviation (%)	Correlation Coefficient
Bakker JT et al.		Spirometry gated (*n*=100)	7640 ± 1450	7370 ± 1450	280 ± 340	3.66	0.95 (p <0.001)
		Breath-hold (*n*=100)	7360 ± 1470	6780 ± 1480	590 ± 430	8.02	0.92 (p <0.001)
Barjaktarevic I et al.			7562 ± 1512	6717 ± 1349	841	11.12	0.82 (p <0.0001)
Becker MD et al.							0.90 (p <0.0001)
Brown MS et al., 1999			5830	4450	1380	23.67	0.91
Brown MS et al., 2010			7620 ± 1480	6990 ± 1380	630	8.27	0.86 (p <0.001)
Chen F et al.			5429 ± 1334	4526 ± 1100	903	16.63	0.62 (p <0.0001)
Coxson HO et al.			7780 ± 1400	6840 ± 1375	940	12.08	0.77
Daghighi A et al.							0.71
Garfield JL et al.			6460 ± 1280	5340 ± 1200	1120	17.34	0.92 (p <0.01)
Gawlitza J et al.				5421 ± 1441			0.38
Jung WS et al.		Normal (*n*=117)	5250 ± 1180	4450 ± 1050	800	15.24	0.77
		Obstructive (*n*=110)	5730 ± 1250	4910 ± 1140	820	14.31	0.70
		Restrictive (*n*=37)	3980 ± 850	3570 ± 780	410	10.30	0.64
Kauczor HU et al.			5690 ± 1620	5020 ± 1560	670	11.78	0.89
Lacerda LS et al.							0.71 (p <0.001)
Matsumoto AJ et al.			5370 ± 2290	5010 ± 2070	360 ± 560	6.70	0.88 (p <0.001)
O'Donnell CR et al			6180 ± 1690	5310 ± 1470	870	14.08	
Schlesinger AE et al							0.92
Shen M et al					1118		0.82
Song L et al			7361 ± 1374	6751 ± 1383	610	8.29	0.81 (p <0.001)
Tantucci C et al.		Control (*n*=10)			110 ± 260		0.98 (p <0.01)
		Obstructive (*n*=20)			70 ± 420		0.97
		Restrictive (*n*=7)			80 ± 380		0.98
Wielpütz MO et al.		YACTA	7700 ± 1700	6824 ± 1255	876	11.38	0.85 (p <0.001)
		LowATT		6657 ± 1251	1043	13.55	0.77 (p <0.001)
		Pulmo3D		6689 ± 1356	1011	13.13	0.91 (p <0.001)
Wu F et al.			5170	4660	510	9.86	0.89 (p <0.001)
Zaporozhan J et al.			8190 ± 1400	7210 ± 1300	980	11.97	0.90
Averages from pooled data					**ΔTLC [mL]**	**Percent Deviation (%)**	**Correlation Coefficient**
				Obstructive	781	11.35	0.83
				Non-obstructive	609	13.53	0.82
				Mixed	*585*	*13.63*	*0.83*
				Healthy	*707*	*13.25*	*0.76*
				Total	709	12.07	0.83

Note: Total lung capacity (TLC). ΔTLC: difference between Plethysmograpic-TLC and CT-TLC. In cases where difference was not provided, the authors calculated it as: ΔTLC = P-TLC − CT-TLC. Percent Deviation = (ΔTLC/P-TLC)*100. YACTA, LowATT and Pulmo3D are different CT software packages. Each colour represents a patient group. Blue: mixed. Red: restrictive. Green: healthy. Black: obstructive [1,6–26].

Table 3. Residual volume data.

Study		Subcategories	P-RV (ml) (mean ± SD)	CT-RV (ml) (mean ± SD)	ΔRV [mL]	Percent Deviation (%)	Correlation Coefficient
Bakker JT et al.		Spirometry gated	4640 ± 1090	4940 ± 1100	-300 ± 470	-6.47	0.82
		Breath-hold	4450 ± 1040	5140 ± 1290	-700 ± 720	-15.73	0.69
Becker MD et al.							0.84 (p <0.0001)
Brown MS et al., 2010			4830 ± 1210	5120 ± 1260	-290	-6.00	0.67 (p <0.001)
Gawlitza J et al.				4417 ± 1279			0.65 (p <0.0001)
Kauczor HU et al.			2560 ± 1250	3550 ± 1270	-1000	-39.07	0.81
Shen M et al.					-405		0.82
Song L et al.			5019 ± 1136	5631 ± 1227	-612	-12.19	0.66 (p <0.001)
Wu F et al.			1870	2330	-460	-24.60	0.81 (p <0.001)
Zaporozhan J et al.			5170 ± 1250	6230 ± 1260	-1060	-20.50	0.83
Averages from pooled data					**ΔRV [mL]**	**Percent Deviation (%)**	**Correlation Coefficient**
				COPD	-561	-12.18	0.75
				Non-COPD	-730	-31.84	0.81
				Total	-603	-17.79	0.76

Residual volume (RV). ΔRV: difference between Plethysmographic-RV (p-RV) and CT-RV. In cases where difference was not provided, the author calculated it as: ΔRV = P-RV − CT-RV. Percent Deviation = (ΔRV/P-RV)*100. Each colour represents a patient group. Blue: mixed. Green: healthy. Black: obstructive [6–13,25].

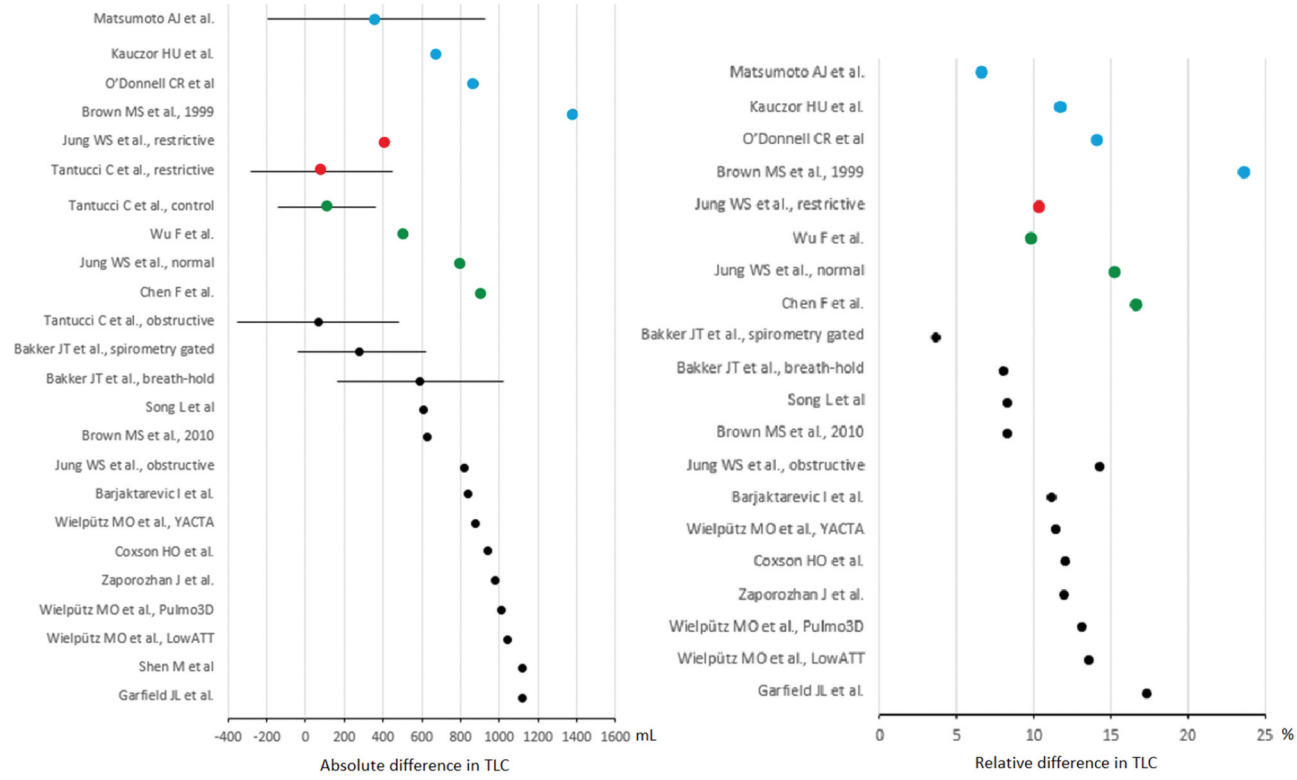

Figure 3. Total lung capacity (TLC) plot. *plotted values of differences between TLC (in ml) measured with plethysmography and* CT (ΔTLC) *and given as percent deviation (100% * (plethysmography - CT)/Plethysmography). Black line represents standard deviation when available. Each colour represents a patient group. Blue: mixed. Red: restrictive. Green: healthy. Black: obstructive*. [1,7–17,20–24].

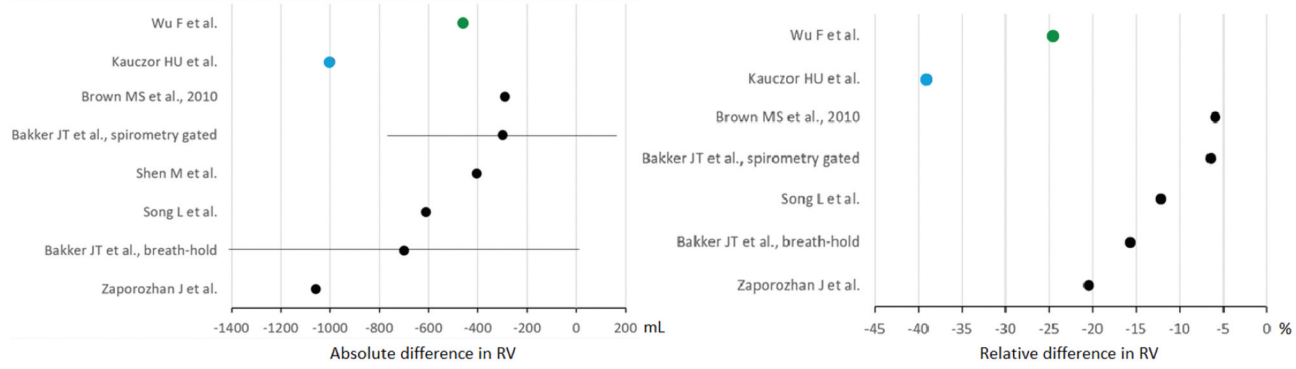

Figure 4. Residual volume (RV) plot. *plotted values of differences between RV (in ml) measured with plethysmography and* CT (ΔRV) *and given as percent deviation (100% * (plethysmography - CT)/Plethysmography). Black line represents standard deviation when available. Each colour represents a patient group. Blue: mixed. Green: healthy. Black: obstructive*. [7–13].

O'Donnell CR et al. find that a worsening in airway obstruction leads to increasing overestimation of TLC, which might be due to an incomplete transmission of alveolar pressure changes to the mouth [28]. This may be part of the reason for ΔTLC being slightly larger in studies with data from obstructive patients.

Plethysmography is a very standardized method of determining lung volumes with universally applied guidelines by the American Thoracic Society and the European Respiratory Society [3]. A skilled technician instructs the patient to perform a sequence of respiratory maneuvers, and multiple attempts are made to obtain repeatability of the volume results to correct for variability in patient effort and cooperation, which can be monitored simultaneously.

Due to radiation concerns, CT acquisition is rarely repeated, and thus such unpredictable errors cannot be rectified. This becomes increasingly relevant in patients

having difficulty maintaining inspiratory and expiratory breath-hold during the scan due to dyspnea. It is not possible to confirm with certainty the amount of effort patients put into following instructions. As CT accuracy depends on subject performance, being able to monitor patient effort becomes crucial in determining reliability of volume quantifications as well as certain qualitative radiological descriptions.

Bakker JT et al. showed that utilizing a spirometer can help bring CT-based volumes to a closer alignment with plethysmography measurements in patients with severe emphysema [7].

Spirometry gating is an easily applicable tool and largely tolerant to subject's cooperation. Although studies on this are limited, the technique shows great promise in minimizing disagreements ascribable to patient effort or cooperation between patient and instructor. This would be relevant for patients already undergoing inspiratory and expiratory CT evaluation, such as candidates for lung volume reduction surgery or lung transplantation. For patients without a CT appointment, these improvements do not justify body plethysmography being replaced by spirometry-gated CT as radiation is still a concern.

Spirometers with a shutter valve are also available ensuring total control of airflow. However, *Kauczor HU* et al. had to discontinue spirometry gating with shutter occlusion as four out of five subjects took the device out of their mouth for both inspiratory and expiratory CT acquisition [9]. Sudden blockage of airflow may not be tolerated by all patients, in particular children, patients suffering from claustrophobia, and patients prone to anxiety, which many people with COPD experience [29].

CT machines differ in scan time ranging from one to several seconds. Many patients with severe lung disease are not capable of holding their breath for the required amount of time – regardless of spirometry gating. The studies using a spirometer scanned their patients within 6 seconds. Thus, their results may not be applicable in hospital departments with slow scanners. Other CT specifications, such as a difference in slice thickness, do not seem to have a significant impact on the results (Table A3).

The limitations of the present review need to be addressed. It was decided to narrow down the literature search, which entails a risk of missing eligible articles. In addition, this review is based on results from one single database, PubMed. It is possible that the results would be different if the search had included more databases e.g. Embase. The good congruence between both modalities may be attributed to the fact that publishers tend to exclude studies if their findings contradict current research in the area.

Another limitation may stem from individual variations in age distribution. Most studies predominantly involved middle-aged patients in their 50s and 60s. However, three studies by *Chen F* et al. *Lacerda LS* et al. and *Schlesinger AE* et al. included younger groups with mean ages of 42, 27 and 11 years, respectively [18–20]. As expected, the first two studies aligned well with overall findings, as they included adult participants whose body composition and size are comparable to those of middle-aged patients.

It might be anticipated that the smaller lung volume of *Schlesinger AE* et al.'s group, consisting of children with lung transplants aged 3 to 18 years, would result in a smaller absolute difference in total lung capacity, while percentage deviation would likely remain consistent with general outcomes of this study [18]. However, only a correlation coefficient for TLC was provided, which stood at 0.92, indicating a strong correlation as expected.

Based on the QUADAS-2 risk of bias assessment, 16 articles included domains with high risk of bias, whereas two articles demonstrated a low risk of bias. An inappropriately long time interval between plethysmography and CT leads to a high risk rating in the flow and timing domain. Four studies were unclear, as they did not provide sufficient information to assess the domains of interest. The majority of studies were retrospective and they used data originally collected for other purposes. Moreover, there is a risk of extracting patient data out of convenience rather than relevance in this type of study. For instance, *Lacerda LS* et al. scored a high risk of bias in the patient selection domain due to their study being based on a convenience sample of patients [19]. Yet, there seems to be no difference between retrospective and prospective studies regarding their results.

Conclusion

CT-based volume quantifications align well with lung volumes measured in the whole-body plethysmograph, although a clear tendency to underestimate TLC and overestimate RV in comparison to gold standard plethysmography is evident. Spirometry gating continues to be a suitable tool to reduce disagreement and can be of assistance when patients are already undergoing CT. However, research on this instrument is scarce and limitations of the present review should be considered. Standardization of CT software and further research is needed before evaluation of the static volumes of pulmonary function can be fully based on CT.

Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request in anonymized form.

Disclosure statement

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Appendix

Table A1. Search protocol #.

Database	Search Strings	Hits
PubMed 1966 -	**#1**:("Lung Volume Measurements"[Mesh]) OR ("Lung volume*" OR "Total lung capacity" OR "TLC" OR "Residual volume" OR "RV" OR "Total lung volume" OR "Functional residual capacity" OR "FRC" OR "Inspiratory lung volume" OR "Expiratory lung volume" OR "Lung-volume quantification" OR "end-inspiratory lung volume" OR "end-expiratory lung volume" OR "Lung volume measurement*" OR "Static lung volumes" OR "Lung Capacity")	91782
	#2:("Tomography, X-Ray Computed"[Mesh]) OR ("Computer tomography" OR "computer-assisted tomography" OR "Chest computed tomography" OR "CT" OR "Inspiration CT" OR "Expiration CT" OR "CT-derived lung volumes" OR "Multidetector Computed tomography" OR "computed tomography segmentation" OR "computed tomography" OR "Computerized tomography" OR "Volumetric chest CT" OR "CAT scan" OR "low-dose CT" OR "high-resolution CT" OR "tomodensitometry" OR "quantitative CT")	903743
	#3:("Plethysmography, Whole Body"[Mesh]) OR ("Body plethysmography" OR "plethysmography analysis" OR "plethysmographic" OR "plethysmographic methods" OR "Respiratory function tests" OR "Static spirometry" OR "Body box" OR "Plethysmograph*" OR "Whole Body Plethysmography" OR "Pulmonary function test*")	80527
	#1 AND **#2** AND **#3**	1405

Note: Protocol 1: the original search on PubMed using the block searching strategy.

Table A2. Search Protocol #2.

Database	Search Strings	Hits
PubMed 1966 -	**#1**: ("Total Lung Capacity"[Mesh]) OR ("Total Lung Capacity" OR "TLC")	47199
	#2: ("Tomography, X-Ray Computed"[Mesh]) OR ("Computer tomography" OR "computer-assisted tomography" OR "Chest computed tomography" OR "CT" OR "Inspiration CT" OR "Expiration CT" OR "CT-derived lung volumes" OR "Multidetector Computed tomography" OR "computed tomography segmentation" OR "computed tomography" OR "Computerized tomography" OR "Volumetric chest CT" OR "CAT scan" OR "low-dose CT" OR "high-resolution CT" OR "tomodensitometry" OR "quantitative CT")	903743
	#3:("Plethysmography, Whole Body"[Mesh]) OR ("Body plethysmography" OR "plethysmography analysis" OR "plethysmographic" OR "plethysmographic methods" OR "Static spirometry" OR "Body box" OR "Plethysmograph*" OR "Whole Body Plethysmography")	25428
	#1 AND **#2** AND **#3**	111

Note: Protocol 2: the narrowed search on PubMed using the block searching strategy.

Table A3. CT Specifications.

Study	Gating	CT Scanner	Slice Thickness (mm)	Scan Time (sec)	Volumetric Software
Bakker JT et al.	Gated group: Spirometric gating without shutter occlusion. Non-gated group: Breath-hold.	Second-generation dual source CT scanner (CT Somatom Definition Flash; Siemens, Erlangen, Germany)	1	1.5	LungQ; Thirona, Nijemegen, The Netherlands
Barjaktarevic I et al.	–	Multislice CT scanning (GE Healthcare or Siemens healthcare scanners)	1, 1.25	–	Pulmonary Workstation 2.0 software (VIDA Diagnostics Inc)
Becker MD et al.	Breath-hold	Conventional scanner (GE 9800 HiLite; GE Medical Systems, Milwaukee, W1)	10	–	Custom software written in Visual C++ (Microsoft, Redmond, WA)
Brown MS et al. 1999	Breath-hold	Either helical or electron beam CT. Helical: GE HiSpeed Advantage or CT/I scanners (GE Medical Systems, Milwaukee, WI, U.S.A.). Electron beam: Siemens Evolution scanner (Siemens Medical Systems, Iselin, NJ, U.S.A.)	6, 8, 10	–	Custom software
Brown MS et al. 2010	Breath-hold	Multicenter study with different scanners (GE, Siemens, Philips, Toshiba)	5–10	–	Custom made knowledge-based segmentation software
Chen F et al.	Breath-hold	multidetector Aquilion 64 CT scanner (Toshiba Medical Systems, Tochigi, Japan)	0.5	–	AZE Virtual Place Lexus workstation (AZE Ca, Ltd, Tokyo, Japan)
Coxson HO et al.	–	High-resolution CT, Multislice CT or thick slice protocol	1, 1.25, 5	–	Custom software (EmphylxJ, Vancouver, BC, Canada)
Daghighi A et al.	Breath-hold	SOMATOM Definition Flash, Siemens Medical Solutions, Forchheim, Germany	4	–	MIALite

(*Continued*)

Table A3. (Continued).

Study	Gating	CT Scanner	Slice Thickness (mm)	Scan Time (sec)	Volumetric Software
Garfield JL et al.	Breath-hold	16 or 64 MDCT scanner (Somatom Sensation; Siemens Medical Systems, Erlangen, Germany)	0.75, 5	–	Custom software (Pulmonary Workstation Plus, VIDA Diagnostics, Inc, Coralville, IA)
Gawlitza J et al.	Breath-hold	3rd generation dual-source CT (Somatom FORCE, Siemens Healthineers, Forchheim, Germany)	1.5	–	Dedicated semiautomatic software (SyngoViaB10, Pulmo3D, Siemens Healthineers, Forchheim, Germany)
Jung WS et al.	Breath-hold	128-slice (Somatom Definition AS+) or 64-slice (Somatom Sensation 64) or 16-slice (Somatom Sensation 16; Siemens Medical Solutions, Erlangen, Germany) multidetector CT	3, 5	–	Aquarius iNtuition version 4.4.6; TeraRecon, Foster City, CA
Kauczor HU et al.	Breath-hold	Unenhanced helical CT using Somatom Plus-S scanner (Siemens, Erlangen, Germany)	8	–	Pulmo-CT Siemens or Allegro workstation (ISG Technologies, Mississauga, Ontario, Canada)
Lacerda LS et al.	Breath-hold	64-channel Multislice Philips system (Brilliance 40, Philips Medical Systems, Cleveland, Ohio)	2	–	OsiriX program (OsiriX 64-bits, Pixmeo Sarl, Geneva, Switzerland)
Matsumoto AJ et al.	Breath-hold	Multicenter, retrospective with different spiral-CT scanners (Siemens, GE, Imatron, Toshiba)	1–5	–	CALIPER
O'Donnell CR et al.	Hospital 1: Spirometric gating Hospital 2: Breath-hold Hospital 3: Breath-hold	Three centers with spiral-CT scanners	–	–	Custom software
Schlesinger AE et al.	Breath-hold	Helical CT in 17 patients and conventional in remaining four (Somatom Plus S, Siemens, Erlangen, Germany)	–	–	Manual tracing
Shen M et al.	Breath-hold	64-slice multiple-detector CT scanner (Somatom Sensation 64; Siemens, Erlangen, Germany)	1	–	The LungSeg Toolbox (The Hamlyn Centre, Imperial College London, UK) or Syngo CT Pulmo 3D (Siemens Healthineers GmbH, Erlangen, Germany)
Song L et al.	Breath-hold	Noncontrast multislice CT (MSCT) scanning (Light Speed Ultra 8 or Revolution EVO, both General Electric Healthcare, Chicago, IL, USA)	0.625, 1.25	–	MeVis PULMO3D software (v 3.7.1, Fraunhofer MEVIS, Bremen, Germany)
Tantucci C et al.	Spirometric gating with shutter occlusion	Multidetector CT scanner (Somatom Definition Flash, Siemens Medical Solutions, Forchheim, Germany)	1	5.7	Aquarius iNtuition version 4.4.6; TeraRecon, Foster City, CA
Wielpütz MO et al.	Breath-hold	4-slice Volume Zoom helical computer tomograph (Siemens Medical Solutions AG, Forchheim, Germany)	1.25	–	YACTA (in-house software) or LowATT (Aquarius) or Pulmo 3D (Syngo.Via)
Wu F et al.	Breath-hold	64-detector scanner (IQon Spectral CT, Philips Healthcare, Best, The Netherlands)	1	–	Philips IntelliSpace Portal post-processing workstation (version 12.0) using Chronic Obstructive Pulmonary Disease (COPD) analysis software
Zaporozhan J et al.	Breath-hold	16-detector CT (Aquilion-16; Toshiba Medical Systems, Tochigi, Japan)	1	–	Self-written software (YACTA; Mainz, Germany)

Note: CT specifications and gating techniques used in all included articles [1,6–26].