Evaluation of computed tomography in the diagnosis of ultrasound-proven diaphragm dysfunction

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Research Article

Keywords: Diaphragm, Ultrasonography, X-Ray Computed Tomography, Physiology, Respiratory Physiological Phenomena, Musculoskeletal Physiological Phenomena, Respiratory Function Tests

Posted Date: December 12th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3721354/v1

Additional Declarations: No competing interests reported.

Abstract

Introduction: Computed tomography (CT) is routinely performed to assess dyspnea, but few data are evaluating diaphragmatic muscle using CT. This study aimed to assess CT in the diagnosis of diaphragmatic dysfunction.

Methods: We retrospectively collected diaphragmatic ultrasounds performed between 2018 and 2021 at our center (Marseille, France). We measured diaphragmatic pillars on CT at the level of L1 and the celiac artery, as well as the difference in height between the two diaphragmatic domes in diaphragmatic dysfunctions and controls, and compared with ultrasound measurements.

Results: 65 patients were included, 24 with diaphragmatic paralysis, 13 with diaphragmatic weakness, and 28 controls. The CT thickness of the pillars in the case group (paralysis and weakness) of left dysfunctions (n=24) was significantly thinner at the level of L1 and the celiac artery compared with controls (2.0mm vs. 7.4mm and 1.8mm vs. 3.1mm, p<0.001 respectively), and significantly different for paralysis (and not weakness) when right dysfunction (n=15) (2.6mm vs. 7.4mm and 2.2mm vs. 3.8mm, p<0.001 respectively for paralysis vs controls). Whatever the side of dysfunction, there was a significant difference in diaphragmatic height between cases and controls (7.70cm vs. 1.16cm and 5.51cm vs. 1.16cm, p<0.001 right and left dysfunction respectively). The threshold values (ROC curve analyses) for height differences between the two domes in favor of paralysis or weakness on the right dysfunctions were 4.44cm and 3.51cm respectively; and 2.70cm and 2.48cm on the left dysfunctions respectively, with good performances.

Conclusion: The thickness of the pillars on CT was thinner in left diaphragmatic dysfunction and in paralysis in right diaphragmatic dysfunction. An increase in the difference in the diaphragmatic height may strongly identify diaphragmatic dysfunction with precise thresholds.

Introduction

Diaphragmatic dysfunction (DD) is associated with a loss of diaphragm motion that may be complete (paralysis) or partial (weakness). Today, this condition is an underdiagnosed cause of respiratory dyspnea and should always be considered as a differential diagnosis in the case of unexplained breathlessness. DD can lead to restrictive ventilatory disorders, dyspnea, sleep disturbances, atelectasis, and even chronic respiratory failure [1].

Several validated methods are used for diagnosing DD, but they are not always accessible and may have several drawbacks [2–6]. The easier method is diaphragmatic ultrasound. A rapid, non-invasive, and reproducible examination, with some limitations (it is operator-dependent, position-dependent, and there may be difficulties in perfectly visualizing the diaphragm, particularly on the left side and in obese patients) [7, 8]. Thoracic computed tomography (CT) is not yet used to diagnose DD, although is often performed as part of the diagnostic workup for dyspnea. Compared with diaphragmatic ultrasonography, CT is capable of fully describing the anatomy of the diaphragm [9], is more available, not operator-dependent, and reproducible. In unilateral diaphragmatic paralysis, it has been shown that the pillars of the diaphragm become thinner and can be measured by CT [10]. In addition, measurement of pillar thickness at the level of the celiac artery and L1 has shown good intra- and inter-observer reproducibility [11].

We hypothesized that CT could play a role in the diagnosis of DD (paralysis or weakness). The aim of this study was therefore to assess the diagnostic performance of CT for the diagnosis of DD, in comparison with diaphragmatic ultrasound.

Methods

Study population

This was a retrospective observational study carried out at the North Hospital, Marseille, France. All patients with a diaphragmatic ultrasound performed in our center between 2018 and 2021 were included for analysis. Patients were classified by the diaphragm ultrasound into 3 groups: paralysis, weakness, or controls if no DD. Patients who did not have a concomitant CT scan (to assess diaphragmatic pillars) as part of their respiratory functional exploration were excluded.

Clinical data were collected from the medical chart (age, sex, height, weight, BMI, blood albumin, cause of DD, and patient history).

The Institutional Review Board of the French Learned Society for Respiratory Medicine -Société de Pneumologie de Langue Française- approved the protocol (CEPRO 2022-043), and a notice of information and non-objection was given to all participants according to French law. The study was performed in accordance with the ethical standards laid down in the 2008 Declaration of Helsinki.

Ultrasound evaluation

The diaphragm ultrasound measurements were performed with the patient in a seated position, on the right and the left side, from the same ultrasound device (Vivid S60N, GE Healthcare, Milwaukee, WI, USA). A single experienced operator (AB) performed all the measurements (cases

and controls). To strengthen the accuracy of the results, all measurements were averaged from at least three different breathing cycles.

The excursions (amplitudes) of the diaphragm were studied in M-mode during quiet breathing (QB), voluntary sniffing (VS), and deep breathing (DB) according to a previously published method [12]. Diaphragmatic thickness and maximal thickening fraction (TF_{max}) were measured in B-mode according to a previously published method [13].

Diaphragmatic weakness was defined as an amplitude during DB below normal range and severe weakness by an amplitude during DB below normal and TF_{max} <40% [13, 14]. Lower limits of the diaphragmatic amplitude during DB were 3.3cm in women and 4.1cm in men on the right side, and 3.2cm in women and 4.2cm in men on the left side [15]. Diaphragmatic paralysis was defined by a paradoxical movement during VS (cranial movement of the paralyzed dome on sniffing) and at the start of deep inspiration without inspiratory thickening (TF_{max} <20%) [5, 12, 16]. During quiet breathing, movement of the paralyzed dome may be absent or paradoxical [17, 18].

CT scan evaluation

The CT scans were reviewed by a chest radiologist (PH). All thoracic CTs were performed in inspiration according to the following parameters: 120 kV and 1 mAs/kg with care dose modulation and reconstruction in joint slices of 1:1 mm. Doses were adjusted manually according to the patient template: 100 kV if they weighed < 60 kg, if above 120 kV. The thoracic CT scans were acquired during breath-hold inspiration from the adrenal glands to the neck. CT scans were performed on various systems (Revolution EVO, Revolution Frontier, Revolution CT, GE Healthcare, WI, USA).

Diaphragmatic pillars were measured in axial and coronal images. On axial images, the right and left pillars were measured at the level of the origin of the celiac artery and the minimal thickness was recorded (Fig. 1A). On coronal images, the right and left pillars were measured along the middle of the anterior part of L1 (Fig. 1B), according to the results found in the study of Sukkasem et al. [10]. On coronal images, the difference in height between the two domes was measured in the anterior part of L1 (Fig. 1C).

Statistics

Continuous variables were described in terms of mean and standard deviation, or median and interquartile range, depending on their distribution (Shapiro test). Categorical variables were described in terms of proportions. Group comparisons (control versus DD) were made using the Chi-2 test for categorical variables, and Student's t-test or a non-parametric Mann-Whitney-Wilcoxon test, depending on the distribution, for continuous variables. ROC curves were constructed to assess the probability of having DD from CT measurements, using ultrasound as the reference for the diagnosis of DD. Areas under the curve were calculated, as were the diagnostic performances of each CT measurement (sensitivity, specificity, positive and negative predictive value) according to the optimal diagnostic thresholds defined by the ROC curves. All tests were bilateral. A p-value < 0.05 was considered significant. Analysis was performed using R software version 4.2.1 (2022-06-23) (R Core Team (2018). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/).

Results

We identified 92 diaphragmatic ultrasounds performed during the study period. Among them, 27 were excluded (21 paralysis, 3 weakness and 3 control) and 65 patients were analyzed as they had benefited from a concomitant thoracic or abdominal CT scan allowing measurement of the diaphragmatic parameters (median time between CT scan and diaphragmatic ultrasound of 31 days, 1st and 3rd quartiles [14; 66]. Among the 65 patients, 24 had diaphragmatic paralysis (7 right, 16 left, and 1 bilateral), 13 had diaphragmatic weakness (6 right, 6 left, and 1 bilateral), and 28 had normal diaphragmatic ultrasound.

The characteristics of the patients analyzed in the study are detailed in Table 1. The main cause of diaphragmatic paralysis was post-surgical, while the main cause of diaphragmatic weakness was post-COVID-19. Controls were all post-COVID-19 addressed to explore dyspnea without relevant medical history. There were no differences in age, sex, height, or BMI between the DD group and the controls.

Table 1

Clinical and functional characteristics of the patients included in the study. BMI = body mass index, PFT = pulmonary function test, FVC = forced vital capacity, FEV1 = forced expiratory volume in 1 second, Tiffeneau = FEV1/CV, TLC = total lung capacity. * = Days in absolute value.

	Dysfunctions	Controls	p	Paralysis	Weakness	p
Patients, n (%)	37 (57)	28 (43)		24 (37)	13 (20)	
Side, n (%)						
Right	13 (35)			7 (30)	6 (46)	0.48
Left	22 (60)			16 (67)	6 (46)	
Bilateral	2 (5)			1 (4)	1 (8)	
Cause						
Traumae	8 (21)	0 (0)		6 (25)	2 (15)	0.001
Surgery	13 (35)	0 (0)		13 (54)	0 (0)	
Cancer	2 (5)	0 (0)		2 (8)	0 (0)	
Parsonage Turner	1 (3)	0 (0)		0 (0)	1 (8)	
Eventration	1 (3)	0 (0)		1 (4)	0 (0)	
COVID-19	7 (19)	28 (100)		1 (4)	6 (46)	
Pneumonia	1 (3)	0 (0)		0 (0)	1 (8)	
Idiopathic	4 (11)	0 (0)		1 (4)	3 (23)	
Age	60 [47 ; 73]	56 [54 ; 60]	0.29	62 [47 ; 71]	60 [51 ; 73]	0.75
Sex (Women)	18 (49)	10 (36)	0.32	17 (71)	1 (8)	< 0.001
Height	1.66 [1.60 ; 1.78]	1.69 [1.65 ; 1.75]	0.85	1.64 [1.59 ; 1.69]	1.78 [1.67 ; 1.80]	0.012
Weight	74 ± 20	81 ± 19	0.22	66 ± 17	89 ± 16	< 0.001
BMI	26 ± 6	28 ± 6	0.14	24 ± 5	30 ± 5	0.004
Albumin	43 [39 ; 46]	45 [41 ; 47]	0.23	43 [38 ; 46]	42 [41 ; 45]	0.69
PFT						
FVC (L)	2.35 [1.91 ; 2.88]	4.05 [3.23 ; 4.68]	< 0.001	2.34 [1.91 ; 2.92]	2.35 [1.97 ; 2.80]	0.75
FVC (%pred)	69 ± 17	100 ± 14	< 0.001	76 ± 14	56 ± 12	< 0.001
FEV1 (L)	1.84 [1.45 ; 2.08]	3.32 [2.68 ; 3.74]	< 0.001	1.75 [1.34 ; 2.17]	1.97 [1.62 ; 2.08]	0.48
FEV1 (%pred)	65 [55 ; 72]	104 [96 ; 112]	< 0.001	70 [61 ; 82]	56 [55 ; 62]	0.02
Tiffeneau	78 ± 11	83 ± 5	0.045	76 ± 12	82 ± 7	0.14
TLC (L)	4.7 ± 1.2	6.1 ± 1.3	0.06	4.9 ± 1.2	4.1 ± 1.0	0.06
TLC (%pred)	85 [69 ; 97]	100 [93 ; 105]	< 0.001	94 [81 ; 98]	66 [56 ; 70]	< 0.001
Respiratory pattern						
None	6 (16)	26 (93)	< 0.001	5 (21)	1 (8)	0.17
Restrictive	26 (70)	2 (7)		14 (58)	12 (92)	
Obstructive	2 (6)	0 (0)		2 (8)	0 (0)	
Mixte	3 (8)	0 (0)		3 (12)	0 (0)	
Time between CT and US*	58 [20 ; 128]	23 [14 ; 32]	0.32	65 [18 ; 134]	52 [31 ; 66]	0.31

In the paralysis group, women were more represented (71% versus 8% in the weakness group, p < 0.001), and mean BMI was lower (24 versus 30 kg/m2 in the weakness group, p = 0.004). Sixty percent of patients had left-sided dysfunction, 35% right-sided, and 5% bilateral. The proportions

of paralysis and weakness did not differ according to the affected side ($p = 0.48$). In the dysfunction groups, patients with weakness had lower FVC in percentage predicted (mean of 56% versus 76% in the paralysis group, $p < 0.001$) and lower TLC in percentage predicted (mean of 66% versus 94% in the paralysis group, $p < 0.001$). Obstructive or restrictive patterns were not significantly different between the paralysis and the weakness groups ($p = 0.17$).

The diaphragmatic measurements found on ultrasound and CT scans are shown in Table 2. On ultrasound, in both right and left dysfunctions, all measurements were significantly lower between cases and controls, except for end-expiratory thickness in weaknesses that were not significantly different from controls. On CT scan, in the left dysfunctions, both the thickness of the pillars at L1 ($p < 0.001$) or the celiac artery ($p < 0.001$) were significantly lower compared with controls. In right dysfunctions, thicknesses of paralyzed patients only (and not weakness) were lower ($p < 0.001$ at the L1 level and $p = 0.004$ at the celiac artery level). In both right and left DD, the difference in median height between the two domes was significantly greater in the dysfunction group compared with controls, $p < 0.001$ for both sides.

Table 2

Analyses of ultrasound and CT scan measurements according to cases and controls. QB = quiet breathing, DB = deep breathing, VS = voluntary sniffing, Tee = thickness at end-expiration, Tei = thickness at end-inspiration, Tei,max = = thickness at the end of maximal inspiration, TFmax = maximal thickening fraction, Para. = Paralysis, Weak. = Weakness, Dys. = Dysfunction.

				Para. vs. Weak.		Dys. Vs. Controls	Para. Vs. Controls	Weak. Vs. Controls		Control Dys. Vs. Controls
Right dysfunction	Dysfunctions	Paralysis	Weakness	p	Controls	p	p	p	Controlateral	p
N (%)	15 (23)	8 (12)	7 (9)		28 (43)				13 (20)	
Ultrasound										
Amplitude during QB (cm)	0.90 [0.15 ; 1.43]	0.30 [-0.03 ; 0.84]	1.35 [1.05 ; 1.73]	0.02	2.00 [1.72 ; 2.37]	< 0.001	< 0.001	0.01	2.90 [2.60 ; 3.36]	0.005
Amplitude during DB (cm)	1.75 [-0.30 ; 2.76]	-0.30 [-0.43 ; 1.85]	2.45 [1.85 ; 3.13]	0.04	5.69 [5.23 ; 5.93]	< 0.001	< 0.001	< 0.001	5.28 [4.95 ; 5.62]	0.20
Amplitude during VS (cm)	-0.04 [-1.17 ; 1.37]	-1.15 [-1.30 ; -0.90]	1.50 [1.33 ; 1.90]	0.003	2.37 [1.96 ; 3.07]	< 0.001	< 0.001	0.004	3.30 [2.70 ; 3.56]	0.02
Tee (mm)	1.67 ± 0.49	1.55 ± 0.41	1.81 ± 0.58	0.32	2.02 ± 0.44	0.02	0.01	0.30	1.72 ± 0.52	0.21
Tei (mm)	1.80 ± 0.57	1.55 ± 0.42	2.09 ± 0.60	0.07	2.74 ± 0.59	< 0.001	< 0.001	0.01	2.51 ± 0.72	0.98
Tei,max (mm)	1.96 ± 0.73	1.49 ± 0.40	2.50 ± 0.65	0.003	4.00 ± 0.78	< 0.001	< 0.001	< 0.001	3.94 ± 0.83	0.84
TFmax (%)	17 ± 30	-3.5 ± 15	40 ± 24	0.001	100 ± 39	< 0.001	< 0.001	< 0.001	136 ± 41	0.07
CT scan										
Right dome higher, n (%)	14 (93)	7 (88)	7 (100)	1.0	19 (68)	0.13	0.52	0.21		
L1 crus thickness (mm)	3.6 [2.6 ; 8.8]	2.6 [1.5 ; 3.2]	9.4 [6.2 ; 12.1]	0.006	7.4 [4.7 ; 8.8]	0.13	< 0.001	0.17	5.0 [3.0 ; 7.1]	0.09
Celiac crus thickness (mm)	2.8 [2.2 ; 5.2]	2.2 [1.7 ; 2.6]	5.4 [4.2 ; 6.4]	0.008	3.8 [2.8 ; 2.6]	0.43	0.004	0.07	3.0 [2.5 ; 3.6]	0.39
Height difference (cm)	7.70 [4.68 ; 8.42]	8.08 [7.42 ; 8.73]	4.91 [3.94 ; 6.84]	0.13	1.16 [0.52 ; 1.73]	< 0.001	< 0.001	< 0.001		
Left dysfunction										
N (%)	24 (37)	17 (26)	7 (11)		28 (43)				22 (34)	
Ultrasound										
Amplitude during QB (cm)	0.00 [0.00 ; 0.85]	0.00 [0.00 ; 0.00]	1.20 [1.15 ; 1.30]	< 0.001	2.05 [1.62 ; 2.67]	< 0.001	< 0.001	< 0.001	3.00 [2.45 ; 3.40]	< 0.001
Amplitude during DB (cm)	-0.40 [-0.56 ; 1.85]	-0.51 [-0.65 ; -0.40]	2.30 [1.85 ; 2.55]	< 0.001	5.62 [5.00 ; 6.56]	< 0.001	< 0.001	< 0.001	5.40 [4.87 ; 6.21]	0.74
Amplitude during VS (cm)	-1.00 [-1.30 ; 1.00]	-1.23 [-1.41 ; -0.99]	1.40 [1.05 ; 1.60]	< 0.001	2.36 [1.98 ; 2.81]	< 0.001	< 0.001	< 0.001	2.90 [2.40 ; 3.78]	0.14
Tee (mm)	1.54 ± 0.35	1.48 ± 0.38	1.69 ± 0.24	0.19	1.91 ± 0.42	0.001	0.001	0.18	1.91 ± 0.36	0.34

				Para. vs. Weak.		Dys. Vs. Controls	Para. Vs. Controls	Weak. Vs. Controls		Control Dys. Vs. Controls
Tei (mm)	1.57 ± 0.45	1.39 ± 0.40	1.96 ± 0.29	0.003	2.51 ± 0.62	< 0.001	< 0.001	0.03	2.82 ± 0.73	0.66
Tei,max (mm)	1.61 ± 0.58	1.35 ± 0.47	2.20 ± 0.29	< 0.001	4.00 ± 0.85	< 0.001	< 0.001	< 0.001	4.02 ± 1.04	0.94
TFmax (%)	5 ± 24	-6 ± 20	31 ± 7	< 0.001	112 ± 37	< 0.001	< 0.001	< 0.001	111 ± 41	0.40
CT scan										
Left dome higher, n (%)	22 (92)	16 (94)	6 (86)	1.0	9 (32)	< 0.001	< 0.001	0.03		
L1 crus thickness (mm)	2.0 [1.6 ; 2.7]	2.0 [1.6 ; 2.3]	3.5 [2.6 ; 4.3]	0.03	7.4 [4.6 ; 9.0]	< 0.001	< 0.001	0.005	4.7 [4.0 ; 5.7]	0.01
Celiac crus thickness (mm)	1.7 [1.4 ; 2.2]	1.8 [1.3 ; 2.2]	1.6 [1.6 ; 2.1]	0.80	3.1 [2.7 ; 3.8]	< 0.001	< 0.001	0.001	3.4 [3.0 ; 4.2]	0.61
Height difference (cm)	5.51 [2.77 ; 7.74]	6.70 [3.00 ; 8.00]	3.51 [1.85 ; 5.58]	0.09	1.16 [0.52 ; 1.73]	< 0.001	< 0.001	0.02		

Table 3 shows the threshold values and diagnostic performances for DD of CT measurements derived from ROC curve analyses. The diagnostic performances of L1 and celiac artery measurements were good in the case of paralysis (better in left than right dysfunction). In the case of weakness, the diagnostic performances of L1 and celiac artery measurements were good for left but not right dysfunction (95% intervals for areas under the curve including 50%). The diagnostic performances of diaphragmatic cupola height differences were excellent (areas under the curve close to 100%), except for left weaknesses (area under the curve of 79%).

Table 3

ROC curve analyses. Threshold values of CT-scan measurements to diagnose diaphragm dysfunction (ultrasound as reference) at the level of the celiac artery or L1 (mm) and of the height difference (cm). R = Right, L = Left, AUC = area under the curve, 95%CI = 95% confident interval, Se = sensitivity, Spe = specificity, PPV = positive predictive value, NPV = negative predictive value.

Group	Measurement	Side	AUC	95%CI	Threshold	Accuracy	Se (%)	Spe (%)	PPV (%)	NPV (%)
Paralysis	L1 (mm)	R	0.93	84–100	4.5	0.87	87	87	95	70
	Celiac (mm)	R	0.84	70–98	3.0	0.75	71	87	94	50
	L1 (mm)	L	0.99	95–100	3.8	0.93	92	94	96	89
	Celiac (mm)	L	0.97	93–100	2.6	0.95	100	88	92	100
Weakness	L1 (mm)	R	0.67	43–92	9.4	0.81	57	87	57	87
	Celiac (mm)	R	0.73	49–96	4.9	0.84	71	84	62	91
	L1 (mm)	L	0.88	75–100	5.0	0.77	71	100	100	46
	Celiac (mm)	L	0.93	85–100	2.6	0.87	87	86	95	67
Paralysis	Height difference (cm)	R	1.00	100–100	4.4	1.00	100	100	100	100
Paralysis	Height difference (cm)	L	0.98	94–100	2.7	0.95	88	100	100	93
Weakness	Height difference (cm)	R	1.00	100–100	3.5	1.00	100	100	100	100
Weakness	Height difference (cm)	L	0.79	56–100	2.5	0.88	71	93	71	93

Discussion

This study shows a significant reduction in diaphragmatic pillar thickness at the level of L1 and the celiac artery in most cases, except for right weaknesses. CT examination also revealed a significant increase in cupola height differences irrespective of the side, or type (paralysis or weakness) of dysfunction.

The absence of diaphragmatic pillar thinning in right-sided diaphragmatic weakness may be the consequence of different factors. Among the 7 patients with right-sided diaphragmatic weakness, only 4 had severe weakness (meaning greater muscle dysfunction with less than 40% of maximal thickening on ultrasound), while the weaknesses present on the left were all severe. Indeed, the mean thickening fraction in the case of weakness was 40% on the right, compared with 31% on the left. In addition, the right diaphragmatic pillar is stronger, thicker, and longer than the left pillar [10, 19]. On can hypothesize that the right pillar change is lower in the presence of simple diaphragmatic weakness.

With regard to diagnostic thresholds for diaphragmatic pillars thickness on CT, for right-sided diaphragmatic paralysis, ROC analysis identified a threshold of 3.0mm at the level of the celiac artery, and a threshold of 4.5mm at the level of L1 with good diagnostic performances [20]. Both thresholds showed good sensitivity, specificity, and PPV, but the pillar measurement at the L1 level was more sensitive than at the celiac artery level, with a higher area under the curve. In addition, the NPV was significantly higher at the L1 level. Therefore, for the diagnosis of right diaphragmatic paralysis, pillar measurement at the L1 level seems more relevant than at the celiac artery level. For left paralysis, ROC analysis determined a threshold of 2.6 mm for the diaphragmatic pillar at the level of the celiac artery. This threshold is identical in the left diaphragmatic weaknesses, since in our study we found no significant difference in pillar thickness between the paralysis group and the weakness group at this level. In addition, at the L1 level, weakness can be differentiated from left diaphragmatic paralysis. The threshold for paralysis at L1 was 3.8mm, with good diagnostic performance. For left diaphragmatic weakness, ROC analysis determined a threshold of 5.0mm at the L1 level with excellent diagnostic performance (specificity 100% and PPV 100%), making the diagnosis of left diaphragmatic weakness certain if the thickness is below the threshold.

The study by Sukkasem et al. found a threshold of 2.5mm for the diagnosis of diaphragmatic paralysis, on both the right and left, at the level of the celiac artery and L1 [10]. In this study, diaphragmatic pillar thickness was measured in patients with diaphragmatic paralysis versus patients with normal diaphragmatic function, and diaphragmatic function was assessed by fluoroscopy. The results of these two studies cannot be compared, as they do not use the same gold standard.

In the dysfunction group, the contralateral diaphragm showed compensation by an increase in amplitude during QB and VS in both right and left dysfunctions in ultrasound. This increase in the amplitude of the healthy contralateral diaphragm has been described as a neuronal compensation for the function of the contralateral hemi diaphragm in paralysis [12, 21, 22]. However, we did not find any hypertrophy of either the right or left healthy diaphragmatic pillar. CT scans even revealed thinner pillars at the L1 level on the healthy side of patients with dysfunction, compared with controls ($p = 0.01$ on the right and $p = 0.09$ on the left), probably due to global muscle weakness.

In the case of right diaphragmatic paralysis or weakness, ROC curve analysis determined a threshold of height difference between the two domes of 4.4cm and 3.5cm respectively, with perfect diagnostic performances of 100% [20], making the diagnosis of right diaphragmatic paralysis or weakness certain if the height is greater than the threshold.

For left dysfunction, diagnostic performances were good for paralysis but not for weakness with close values of height difference between the two domes (2.7cm and 2.5cm respectively). Thus, the height difference between the domes appears in our study to be the most reliable CT measurement for diagnosing DD. To our knowledge, this is the first time that precise threshold values for the diagnosis of DD based on the difference in cupola height have been reported.

DD is generally associated with a slight decrease in vital capacity, to approximately 75%, while TLC is generally preserved [23]. The greater decrease in volumes found in this study in the weakness group may be explained by causes other than DD itself. Indeed, among the 12 patients with a restrictive pattern in the weakness group, there were 6 patients with a history of COVID-19 (including 5 severe diseases requiring intensive care), one patient with a history of talc pleurisy, 2 patients were overweight, and 6 patients were moderately obese.

This study has certain limitations. The pillar thickness is supposed to vary with breathing (it decreases with expiration) [24]. Only one radiologist performed the measurements, intra- and inter-reproducibility were not evaluated, and CT scan were both enhanced and unenhanced which make more difficult the measurements in unenhanced CT. Thus, if the scan is performed during expiration, DD may be mistakenly assumed. Also, in our study, to validate correct inspiration during thoracic scans, we checked that the posterior part of the trachea did not bulge inwards. This check could not be performed for the single abdominal scan included in our study. Moreover, the scans were performed at different times, before or after the ultrasound. This time variable may affect pillar atrophy. Finally, there were more women in the paralysis group than in the weakness group ($p < 0.001$), and we can assume that the pillars are thinner in women, as is the case in ultrasound. However, in the study by Dovgan et al. [25], pillar thickness did not vary according to gender.

Conclusion

This study found a significant reduction in diaphragmatic pillar thickness at the level of L1 and the celiac artery on CT in cases of DD (paralysis and weakness) on the left, while only in paralysis on the right. On both right and left dysfunction, there was a significant difference in height between the two diaphragm domes in cases of diaphragmatic paralysis or weakness with good diagnostic performances.

The measurement with the best diagnostic performance in favor of right paralysis or weakness was the difference in height between the two domes (4.4cm and 2.5cm respectively). On the left, in favor of paralysis, the measurement at L1 and the difference in height between the two domes were equivalent in terms of diagnostic performance (3.8 mm and 2.7 cm respectively); the measurement with the best diagnostic performance in favor of weakness was the thickness at the L1 level (5.0mm).

Abbreviations

BMI
body mass index
CT
computed tomography
DB
deep breathing
DD
diaphragmatic dysfunction
QB
quiet breathing
TF_{max}
thickening fraction
VS
voluntary sniffing

Declarations

Ethical Approval

The Institutional Review Board of the French Learned Society for Respiratory Medicine -Société de Pneumologie de Langue Française- approved the protocol (CEPRO 2022-043), and a notice of information and non-objection was given to all participants according to French law. The study was performed in accordance with the ethical standards laid down in the 2008 Declaration of Helsinki.

Funding

None

Author Contribution

PL, JB, PH, and BC conceived the study. AB, SD, and FB included the recipients in the cohort. PL and BC conducted the statistical analysis. PL, JB, and BC drafted the manuscript, and all authors critically revised the manuscript for intellectually important content.

Availability of data and materials

The data that support the findings of this study are available on request from the corresponding author.

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Figures

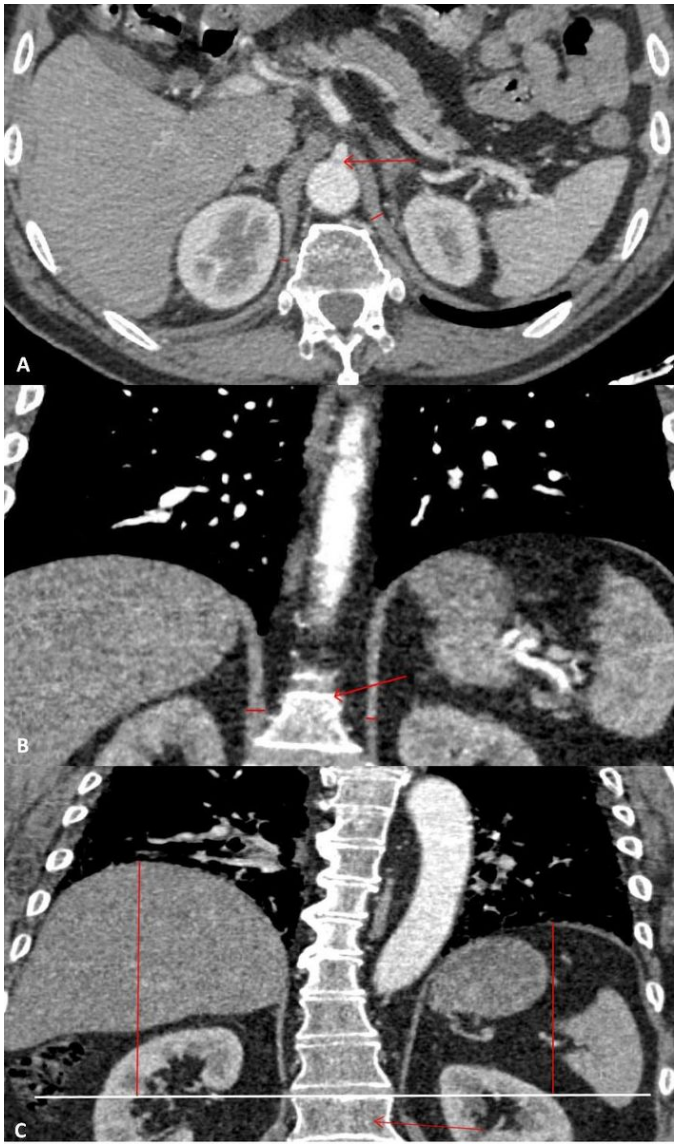

Figure 1

Measurements of the diaphragm performed on enhanced CT scan. A, Measurement of the pillars at the level of the celiac artery. Minimal diaphragm thicknesses (red lines) at the level of the origin of the celiac artery (red arrow). **B**, Measurement of the pillars at the level of L1. Diaphragm thicknesses (red lines) along the anterior part of the L1 vertebral body at mid-level (red arrow). **C**, Measurement of the diaphragm height difference. Heights (red lines) from the highest point of the diaphragmatic dome to its perpendicular intersection with a line (white line) following the upper plateau of L1 (red arrow).