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Review article

The positional change in vital capacity as a tool to identify diaphragm dysfunction: A qualitative systematic review

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ABSTRACT

Background: Sitting to supine fall in vital capacity (ΔVC) is commonly used to screen for diaphragmatic dysfunction (DD), but the predictive threshold value varies.
This systematic review aimed to compare the position-dependent change in vital capacity (VC) in patients with objectively confirmed DD.
Research question: What is the optimal predictive value of ΔVC to diagnose DD.
Study design and methods: We searched Medline/PubMed, Embase and Scopus, including backward citations, for studies from database inception to December 5, 2023. Included trials measured position change in VC in adult patients with DD, confirmed independently by a parameter other than ΔVC. Risk of bias was assessed using the Downs and Black checklist.
Results: Of 497 records identified, 10 studies were included, totalling 393 adults, of which 284 had DD. In patients with confirmed unilateral diaphragmatic paralysis, mean change in VC ranged from 7 to 23%, and in those with bilateral diaphragmatic paralysis, from 19 to 37%. In studies providing only values for DD without specifying unilateral or bilateral involvement, it ranged from 31 to 42%. In control groups, it ranged from 3 to 9%.
Interpretation: The change in VC appears to be a valid test for confirming DD when using a cut-off value of 20%, though this approach results in very low sensitivity.
A cut-off value of 15% should be used in a screening setting as an initial approach of a multimodal strategy, without being sensible enough to exclude milder forms of DD.

Introduction

Diaphragmatic dysfunction (DD) is part of the differential diagnosis of unexplained dyspnoea and should be screened for and monitored on a regular basis in a vast number of neuromuscular diseases (NMD) known to affect the diaphragm. Indeed, the incidence of DD in dyspnoeic patients in the emergency department ranged from 22.4 to 32.1%, depending on the measurement technique [1].

The gold standard for the diagnosis is the measurement of transdiaphragmatic pressure in response to phrenic nerve stimulation. However, this modality is invasive and poorly compatible with clinical routine. Some screening tests were validated, such as diaphragm fluoroscopy or sniff nasal inspiratory pressures [2,3], but they have low specificity for unilateral (UDP) or bilateral diaphragmatic paralysis (BDP) [4]. More accessible imagery modalities like the evaluation of thickening fraction of the diaphragm measured by ultrasonography have shown promising results in identifying DD but require a certain expertise.

Since pulmonary function testing (PFT) is still one of the most used paraclinical exams in pneumology, and patients with DD typically have a restrictive pattern that worsens in the supine position [5], a functional measurement such as sitting to supine fall in vital

Abbreviations: DD, diaphragmatic dysfunction; UDP, unilateral diaphragmatic dysfunction; BDP, bilateral diaphragmatic dysfunction; VC, vital capacity; ΔVC, sitting to supine fall in vital capacity; NMD, neuromuscular disease; TFDI, diaphragm thickening fraction; IQT, Interquartile range; SD, standard deviation; SVC, slow vital capacity; FVC, forced vital capacity; PFT, pulmonary function testing

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capacity (ΔVC) has been used and became a cornerstone in screening and diagnostic evaluation of DD [6,7].

In contrast, the number of studies evaluating the predictive value of this ΔVC based on patients in which the diagnosis of diaphragmatic dysfunction has been objectively confirmed beforehand, is very sparse.

To our knowledge there are neither evidence-based recommendations nor accepted threshold values for ΔVC available to confirm the presence of DD. The aim of this systematic review was to highlight the position dependent change in vital capacity (VC) in adult patients in which the diagnosis of DD has been objectively confirmed beforehand.

Method

This study adhered to the PRISMA statement and the Synthesis Without Meta-analysis (SWiM) reporting guidelines [8,9].

Literature search

Medline (via PubMed), SCOPUS and EMBASE databases were systematically searched for articles from inception to December 5th, 2023. The terms related to diaphragmatic dysfunction, pulmonary function testing and ΔVC were combined (Appendix 1). Finally, we used snowballing to include additional studies.

Eligibility criteria

In this study, we utilized the PICOS framework (Population, Intervention, Comparison, Outcome, and Study design) to systematically structure our research question and methodology: all studies (S) in which a measurement of either slow or forced ΔVC (O) was available for adult (age >= 18 years) patients in which DD (P) had been confirmed beforehand, regardless of aetiology of DD. If a study was composed of a mixed population of adults and children, it was excluded if measurements of fall in VC were not available only for the children.

No further inclusion criteria were required.

There were no prior restrictions concerning the criteria used in the studies to confirm the presence of DD. Abstracts and studies in other languages than French, German or English were excluded.

Selection process

The assessment of records was performed independently by three reviewers using “Rayyan” (https://new.rayyan.ai). No automation tools or artificial intelligence tools were used.

Discordant results (45) were resolved by consensus, after reading the abstract or, when necessary, the hole study.

Data were extracted by one reviewer (HK) and checked by another (GR).

Main outcomes and measures

The main outcome was sitting to supine ΔVC% (either forced or slow) in patients with confirmed diaphragmatic dysfunction.

Other data extracted for the study and per subgroup were number of patients, age, body mass index (BMI), sex, comorbidities, smoking status, dyspnoea (via the Modified Medical Research Council Dyspnoea Scale), aetiology of DD, type of VC measurements (forced or slow), method used to calculate ΔVC, diagnostic criteria of DD and inclusion criteria, and is summarized in Table 1.

Risk of bias and data synthesis

The quality of the included studies was assessed using the modified version of the Downs and Black Quality Assessment Checklist (Table 2), mainly because of its versatility and the possibility to evaluate different study designs. Risk of bias was assessed regarding Reporting (1), External validity (2) and Internal validity – Confounding (selection bias) (3). Since only observational studies were included, all criteria related to interventional studies were not taken into consideration and the overall grading score was adapted to the number of points concerning each individual study.

Results

Selected studies

Out of the 499 records screened, 54 were assessed for eligibility through a full-text review. Ultimately, ten studies met all the criteria and were included in this review. These papers comprised 3 retrospective and 7 prospective studies.

The study selection process is summarized in the Prospero flow chart below (Fig. 1).

Characteristics and results of the included studies

The overall number of patients included was 393, of which 284 had DD and the remaining 109 patients were part of the control groups. Sample size ranged from 8 to 84 patients, with a median of 30.5 patients per study.

The average age of patients with DD ranged from 54 to 68 years, while the average age in the control group ranged from 31 to 62 years. The male to female ratio was 1.30 in the control group (60 males to 49 females), and it was 2.04 in patients with DD (178 males to 92 females), with no data concerning gender repartition available for Laroche et al. [10].

The average BMI, available in 5 of the included studies, ranged from 28.4 to 31.7 kg/m^2 in patients with DD and from 25.0 to 28.6 kg/m^2 in the control groups. Smoking status was retrieved in 6 studies, comorbidities and underlying lung diseases were retrieved only in 3 studies.

Diaphragmatic dysfunction was diagnosed by various methods: ultrasound (mainly diaphragm thickening fraction (Tfdi)) in 2 studies; by chest X-ray or computed tomography (CT) and confirmed by ultrasound (US) if needed in three studies; neurophysiological measurements compatible with phrenic neuropathy, neuromuscular transmission deficiency or neuromuscular transmission defect in one study; gastric pressure decrease/transdiaphragmatic pressure decrease (ΔPga/ΔPdi) and/or transdiaphragmatic pressure during maximal sniff test (Pdi sniff) in one study; or a combination of diagnostic criterions in 2 studies.

The aetiology of DD was noted in 8 studies. Out of 219 patients with an aetiology for DD, the main cause was idiopathic (29.2%), followed by neuromuscular (21.0%), iatrogenic (22.3%) and traumatic (15.1%). The causes were from various isolated origins in 12.3% of the patients, such as chest infection, borreliosis, diabetes mellitius, herpes, Pompe or other congenital disease. The great overall number of NMD is explained by the inclusion criteria of only NMD in two studies.

Only 2 studies [4,11] included exclusively patients with suspected DD (either UDP or BDP) in the context of new onset dyspnoea and evaluated the predictive value of sitting to supine ΔVC as a main outcome.

Forced VC (FVC) was used to calculate ΔVC in 5 studies [10,12–15], slow VC (SVC) only in one [16], and was not further specified in the remaining 4 studies [4,11,17,18].

No information was available regarding whether ΔVC was based on changes in VC values expressed as a percentage of predicted or as raw values (litres), except for one study [13] that used the former method. All authors used relative variation of VC to calculate ΔVC%,

Table 1
Subject characteristics, study design and main outcomes of included studies.

Diaphragm dysfunction and ΔVC	Subgroup: n	Age	BMI	Sex (M/F)	Relevant comorbidity/ underlying lung disease	Smoking status	mMRC	Confirmation criteria for DD	Selection criteria for patients with DD	Outcome ΔVC (%)	Calculation of ΔVC	Type of VC (Forced/Slow)	Study type	(Suspected) cause of DD	Publication year	Main outcome
Pereira	UDP: 35; control: 20	Mean +/- SD: DD 55,8 +/- 9,9 (32 −77); control: 49,8 +/- 6,4 (40 −58); P 0,03	Mean +/- SD: DD: 28,4 +/- 3,4 (22,2 −35,6); control 27,9 +/- 2,1 (22,5 −29,8); P 0,49	DD: 17/18; control 10/10; P 0,92	patients with comorbidity suspected to have an impact on respiratory function excluded	/	DD: mMRC 1 =11; mMRC 2=14; mMRC 3 = 9; mMRC 4 = 1; mMRC 5 = 0; control mMRC 1 = 20	pneumologist via CT or chest x-ray (if doubt: US)	presence of UDP (tertiary centre)	Mean +/- SD: UDP 12 +/- 8 (no data available for control group)	- Relative change between sitting and supine VC. - No information if calculated based on raw data (L) or percentage predicted	FVC	cross-sectional	idiopathic 10 (29%), trauma 13 (37%), after cardiac surgery 8 (23%), after thoracic surgery 4 (11%)	2021	investigate the diaphragm contraction mechanisms and nondiaphragmatic inspiratory muscle activation during exercise in patients with UDP, compared with healthy individuals
Koo	total: 76; control: 23; UDP: 40; BDP: 13	median (IQR): total 65,6 (56,0 −73); control: 61,5 (52,0 −67,0), UDP 68,0 (59,0 −79,0); BDP 63 (59,0 −73,0); P 0,030	median (IQR): total 30,9 (26,9 −35,4); control 28,6 (25,6 −33,7); UDP 31,7 (26,9 −37,6); BDP 30,1 (27,3 −31,5); p 0,323	Total 54/22; control 15/8; UDP 27/13; BDP 12/1; P 0,189	neuromuscular disease excluded	Total (n=76) vs control (n=23) vs UDP (n=40) vs BDP (n=13): never smoked 32 vs 13 vs 14 vs 5; current smoker 4 vs 1 vs 3 vs 0, former smoker 32 vs 8 vs 18 vs 6	/	US (TFdi)	referred for dyspnoea workup	median (IQR) total 11,6 (5,4 −22,1); control 5,3 (3,8−8,9); UDP 13,8 (6,9 −21,0); BDP 37,0 (22,1 −41,8); P < 0,001	- Relative change between sitting and supine VC. - No information if calculated based on raw data (L) or percentage predicted	Not specified	cross-sectional	idiopathic 36,9%, other aetiologies included diabetes mellitius, idiopathic brachial plexopathy, post-polio syndrome, neck injury and post-operative	2016	examine if the ratio of maximal expiratory pressure to maximal inspiratory pressure (MEP/MIP) may provide an alternative to ΔVC when screening patients for DD
Safavi	control 20; BDP 6; COPD 5	mean +/- SD: control 34 +/- 9,7; BDP 61,3 +/- 11; COPD 67 +/-7,7	mean +/- SD: control 25 +/-5; BDP 29,4 +/- 7,8; COPD 24,6 +/- 2,8	control 9/11; BDP 1/5; COPD 2/3	Healthy control group excluded chronic respiratory disease or smoking history	Control (n=20) vs BDP (n=6) vs COPD (n=5): active smoker 0 vs 0 vs 1; ex-smoker (>= 2 PY) 3 vs 3 vs 4; never-smoker 17 vs 3 vs 0	Mean +/- SD: control 1; BDP 2,7 +/- 0,8; COPD + hyperinflation 3 +/- 1	pneumologist via PFT or chest CT	BDP supporting supine position	mean +/_ SD: control 3,9 +/- 3; BDP 19,3 +/- 5,7; COPD 11 +/- 8	- Absolute change between sitting and supine VC. - No information if calculated based on raw data (L) or percentage predicted	Not specified	prospective	/	2020	evaluate the use of an open-configuration upright low-field MRI system to assess diaphragm morphology and function in patients with BDP and COPD with hyperinflation
Brault	control 36; UDP 31; BDP 17	mean +/- SD: control 61 +/- 11; UDP 57 +/- 13; BDP 60 +/- 12; p 0,36	mean +/- SD: control 28,3 +/- 6,3; UDP 30,9 +/- 4,9; BDP 29,9 +/- 4,4	control 18/18; UDP 19/12; BDP 14/3; p 0,08	comparing control (n=36) with DD (n=48); CAD 3 vs 9; CHF 0 vs 3; HTA 11 vs 21; DB 7 vs 10; OSA 8 vs 18; lung desease 8 vs 19; asthma 6 vs 12; COPD 1 vs 4; pulm hypertension 0 vs 2; ILD 1 vs 2	control (n=36) vs DD (n=48) active smoker 2 vs 5; ex-smoker 9 vs 21	mean (IQR): control 2 (1−3); UDP 2 (1−3); BDP 3 (3−4); p 0,001	US (Tfdi)	cross sectional, referred to tertiary university centre for suspected DD	median (IQR): ΔVC control 6 (1−12); UDP 7 (4−12); BDP 27 (21−37); *p* < 0,001	- Relative change between sitting and supine VC. - No information if calculated based on raw data (L) or percentage predicted	Not specified	cross-sectional	idiopathic 11 (23%); neuromuscular 5 (11%); mechanical/ trauma 14 (30%); auto immune 5 (11%); inflammatory 6 (13%); congenital 5 (11%); Metabolic 1 (2%)	2020	the diagnostic performance of ΔVC in identifying the presence of unilateral or bilateral DD.

(*continued on next page*)

Table 1 (*Continued*)

Diaphragm dysfunction and ΔVC	Subgroup: n	Age	BMI	Sex (M/F)	Relevant comorbidity/ underlying lung disease	Smoking status	mMRC	Confirmation criteria for DD	Selection criteria for patients with DD	Outcome ΔVC (%)	Calculation of ΔVC	Type of VC (Forced/Slow)	Study type	(Suspected) cause of DD	Publication year	Main outcome
Nafisa	UDP: 29; BDP: 31	mean +/- SD: 58± 12.9	/	38/22	Progressive neuromuscular disease was excluded after taking a personal and family history, combined with clinical neurological examination and, if indicated, neurological investigation	/	(Dyspnoea on exertion 28; Orthopnoea 32)	mainly by chest x-ray, partially by ultrasound (Tfdi)	patients with isolated diaphragmatic palsy admitted to hospital or referred as respiratory outpatients for NIV at two large teaching hospitals in the United Kingdom	available for 40 patients (others too sick) mean +/- SD: DD 42 +/- 0,16	- Relative change between sitting and supine VC. - No information if calculated based on raw data (L) or percentage predicted	Not specified	retrospective cohort	idiopathic 31; post-heart-lung transplant 18; post coronary artery bypass grafting 2; post radiofrequency cardiac ablation 2, post spinal surgery 1; post-thyroidectomy 1; post-mastectomy 1; post-radiotherapy 1; post-intensive care unit admission 1	2019	retrospective cohort data in patients with isolated diaphragmatic palsy in the absence of progressive neuromuscular disease: Clinical presentation, tests of respiratory-muscle function (sitting/ supine vital capacity, maximal expiratory pressure (MEP), maximal inspiratorypressure (MIP) and sniff nasal inspiratory pressure (SNIP)) and outcomes
Türk	UDP: 17 (left 12; right 5); BDP: 13	Median (IQR): 67 (29–82)	/	18/12	no anterior neuromuscular disorder or known DD	/	/	neurophysiologic data consistent with the diagnosis of either phrenic neuropathy, neuromuscular transmission defect or myopathy	DD and new neuromuscular disorder	mean +/-SD; ΔFVC available for 15 patients (UDP: 10; BDP: 5); UDP 23 +/- 4; BDP 32 +/- 14	- Relative change between sitting and supine VC. - Variation of percentage of predicted	FVC	retrospective longitudinal	idiopathic 8 (27%); neuralgic amyotrophy 2 (7%); iatrogenic 6 (20%); diabetes mellitius 1 (3%); Borreliosis 2 (7%); post-polio syndrome 1 (3%); multifocal motor neuropathy 1 (3%); chronic inflammatory demyelating polyneuropathy 1 (3%); spondylolysis 1 (3%); ALS 5 (17%); myasthenia gravis 1 (3%); Pompe 1 (3%)	2018	evaluate the aetiology and clinical outcome in patients, in whom uni- or bilateral diaphragmatic dysfunction was primarily diagnosed, before a specific neuromuscular disease was found
Rice	DD: 16	mean +/- SD: 55 +/- 16	mean +/- SD: 32 +/- 5	15/1	6 patients with obstructive pneumopathy, 4 patients with diabetes	7 patients with smoking history	/	via imaging without further precision	neuralgic amyotrophy followed in hospital	mean +/- SD: 40 +/- 16 (N = 14)	- Relative change between sitting and supine VC. - No information if calculated based on raw data (L) or percentage predicted	FVC	prospective	neuralgic amyotrophy	2017	Modelling the course of recovery of lung function in 16 subjects with diaphragm impairment from neuralgic amyotrophy. The first and last available vital capacity, sitting-to-supine decline in vital capacity, and maximal inspiratory pressures were compared

(*continued on next page*)

Table 1 (*Continued*)

Diaphragm dysfunction and ΔVC	Subgroup: n	Age	BMI	Sex (M/F)	Relevant comorbidity/ underlying lung disease	Smoking status	mMRC	Confirmation criteria for DD	Selection criteria for patients with DD	Outcome ΔVC (%)	Calculation of ΔVC	Type of VC (Forced/Slow)	Study type	(Suspected) cause of DD	Publication year	Main outcome
Clague	UDP left (n=4); UDP right (n=4)	mean +/- SD: 54.25 ±8.832	mean +/- SD: 74.875 **kg** ±4.756	7/1	1 patient with mild bronchographially demonstrable bronchiectasis	ex-smoker = 6; non-smoker = 2	Mean +/- SD: overall: 2 ± 0.849 (Left UDP = 2.5 ± 0.49; Right UDP = 1.5 ± 1.47	hemidiaphragm raised and paradoxical movement on sniffing	/	mean +/- SD: UDP right 19 +/- 3,34; UDP left 10,25 +/- 0,86	- Not specified if relative or absolute change between sitting and supine VC - No information if calculated based on raw data (L) or percentage predicted	FVC	retrospective	idiopathic 3; cervical spondylolysis 2; trauma 2; herpes 1	1979	studying the effects of posture on lung volume, airway closure, and gas exchange in patients with hemidiaphragmatic paralysis
Fromageot	DD 14; control 10	Mean +/- SD: Total 49+/- 11; DD 47 +/- 11; control 51+/- 12	/	Control: 8/2; DD: 10/4	generalised neuromuscular disease without obstructive ventilatory disorder	/	/	deltaPga/deltaPdi < 1 and/or Pdi sniff < 30cmH2O	generalised neuromuscular disease without obstructive ventilatory disorder referred for PFT	mean +/- SD: DD 31+/- 13; control 3+/-13	- Relative change between sitting and supine VC. - No information if calculated based on raw data (L) or percentage predicted	SVC	prospective	for patients with DD: Acid maltase deficiency 3; Limb-girdle muscular dystrophy 2; Myotonic dystrophy 2; myasthenia gravis 2; Polyradiculoneuritis 1; Facioscapulohumeral muscular dystrophy 1; Becker's muscular dystrophy 1; Idiopathic muscular dystrophy 1	2001	To determine whether diaphragmatic function can be determined by non-invasive respiratory indices in neuromuscular disease
Laroche	UDP 11	/	/	/	2 patients with emphysema, 1 ischemic heart disease, 1 moderate asthma, 1 bronchial hyperreactivity, 1 chronic bronchitis	2 ex-smokers	median 2; mean 2,55	greatly reduced or absent transdiaphragmatic pressure on stimulation of the phrenic nerve in the neck, by means of surface bipolar electrodes (unilateral twitch Pdi), compared with normal values on the contralateral side, and measuring phrenic nerve conduction time.	recent onset hemidiaphragm paralysis (normal chest x-ray the year before)	mean +/- SD: UDP 11,8 +/- 8,1	- Relative change between sitting and supine VC. - No information if calculated based on raw data (L) or percentage predicted	FVC	prospective	3 aortic valve replacements, 1 coronary artery bypass graft, 5 chest infections, 1 cervical lesion after neck manipulation, 1 idiopathic	1988	y

Abbreviations: SD, standard deviation; IQT, interquartile range; DD, diaphragmatic dysfunction; UDP, unilateral diaphragmatic paralysis; BDP, bilateral diaphragmatic paralysis; ΔVC%, sitting to supine fall in vital capacity; BMI, body mass index; PY, pack years; COPD, chronic, obstructive pulmonary disease; mMRC, Modified Medical Research Council Dyspnoea Scale; Tfdi, diaphragmatic thickening fraction; US, ultrasound; CT, computed tomography; NIV, noninvasive ventilation; PFT, pulmonary function test; ALS, amyotrophic lateral sclerosis; M, male; F, female; SVC, slow vital capacity; FVC, forced vital capacity

Table 2
Downs and black checklist.

Reporting	Yes (1)	No (0)	N/A (/)	unable to determine (0)	Perei ra	Koo	Safavi	Brault	Nafis a	Türk	Rice	Clag ue	From ageot	Laro che
1. **Is the hypothesis/aim/objective of the study clearly described?**					1	1	1	1	1	1	1	1	1	1
2. **Are the main outcomes to be measured clearly described in the Introduction or Methods section?** *If the main outcomes are first mentioned in the results section, the question should be answered as no.*					1	1	1	1	1	1	1	1	1	1
3. **Are the characteristics of the subjects included in the study clearly described?** *In cohort studies and trials, inclusion and/or exclusion criteria should be given. In case- control studies, a case-definition and source for controls should be given.*					1	1	1	1	1	1	1	1	1	1
4. **Are the interventions of interest clearly described?** *Treatments and placebo (where relevant) that are to be compared should be clearly described.*					/	/	/	/	/	/	/	/	/	/
5. **Are the distributions of principal confounders in each group of subjects to be compared clearly described? (Yes = 2; Partially = 1; No 0)** *A list of principal confounders is provided*					1/2	2	2	2	0/2	2	2	2	2	/
6. **Are the main findings of the study clearly described?** *Simple outcome data (including denominators and numerators) should be reported for all major findings so that the reader can check the major analyses and conclusions. (This question does not cover statistical test which are considered below)*					1	1	1	1	1	1	1	1	1	1
7. **Does the study provide estimates of the random variability in the data for the main outcomes?** *In non-normally distributed data the inter-quartile range of results should be reported. In normally distributed data the standard error, standard deviation or confidence intervals should be reported. If distribution data is not described, it must be assumed that the estimates used were appropriate and the question should be answered with yes.*					1	1	1	1	1	1	1	1	1	1
8. **Have all important adverse events that may be a consequence of the intervention been reported?** *This should be answered yes if the study demonstrates that there was a comprehensive attempt to measure adverse events. (A list of possible adverse events is provided).*					/	/	/	/	/	/	/	/	/	/
9. **Have the characteristics of subjects lost to follow-up been described?** *This should be answered yes where there were no losses to follow-up or where losses to follow-up were so small that findings would be unaffected by their inclusion. This should be answered no, where a study does not report the number of patients lost to follow-up.*					/	/	/	/	1	1	/	/	/	/
10. **Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?**					1	1	1	1	1	/	1	1	1	/
External validity														
11. **Were the subjects asked to participate in the study representative of the entire population from which they were recruited?** *The study must identify the source population for subjects and describe how the subjects were selected. Subjects would be representative if they comprised the entire source population, an unselected sample of consecutive patients, or a random sample. Random sampling is only feasible where a list of all members of the relevant population exists. Where a study does not report the proportion of the source population from which the subjects are derived, the question should be answered as unable to determine.*					1	1	0	1	0	1	1	/	1	0
12. **Were those subjects who were prepared to participate representative of the entire population from which they were recruited?** *The proportion of those asked who agreed should be stated. Validation that the sample was representative would include demonstrating that the distribution of the main confounding factors was the same in the study sample and the source population.*					0	0	0	1	0	0	1	1	1	0
13. **Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?** *For the question to be answered yes, the study should demonstrate that the intervention was representative of that in use in the source population. The question should be answered no if, for example, the intervention was undertaken in a specialist centre unrepresentative of the hospitals most ofthe source population would attend.*					/	/	/	/	/	/	/	/	/	/
Internal Validity														

(*continued*)

14. **Was an attempt made to blind study subjects to the intervention they have received?** *For studies where the patients would have no way of knowing which intervention they received, this should be answered yes.*	/	/	/	/	/	/	/	/	/	/	
15. **Was an attempt made to blind those measuring the main outcomes of the intervention?**	/	/	/	/	/	/	/	/	/	/	
16. **If any of the results of the study were based on "data dredging", was this made clear?** *Any analyses that had not been planned at the outset of the study should be clearly indicated. If no retrospective unplanned subgroup analyses were reported, then answer yes.*	1	1	1	1	1	1	1	1	1	1	
17. **In trials and cohort studies, do the analyses adjust for different lengths of follow-up, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls?** *Where follow-up was the same for all study subjects the answer should yes. If different lengths of follow-up were adjusted for by, for example, survival analysis the answer should be yes. Studies where differences in follow up are ignored should be answered no.*	/	/	/	/	/	/	/	/	/	/	
18. ***Were the statistical tests used to assess the main outcomes appropriate?*** *The statistical techniques used must be appropriate to the data. For example, nonparametric methods should be used for small sample sizes. Where little statistical analysis has been undertaken but where there is no evidence of bias, the question should be answered yes. If the distribution of the data (normal or not) is not described it must be assumed that the estimates used were appropriate and the question should be answered yes.*	1	1	1	1	1	1	1	1	1	1	
19. **Was compliance with the intervention/s reliable?** *Where there was noncompliance with the allocated treatment or where there was contamination of one group, the question should be answered no. For studies where the effect of any misclassification was likely to bias any association to the null, the question should be answered yes.*	/	/	/	/	/	/	/	/	/	/	
20. **Were the main outcome measures used accurate (valid and reliable)?** *For studies where the outcome measures are clearly described, the question should be answered yes. For studies which refer to other work or that demonstrates the outcome measures are accurate, the question should be answered as yes.*	1	1	1	1	1	1	1	1	1	1	
Internal Validity – confounding (selection bias)											
21. **Were the subjects in different intervention groups or were they recruited from the same population?** *For example, patients for all comparison groups should be selected from the same hospital. The question should be answered unable to determine for cohort and casecontrol studies where there is no information concerning the source of patients included in the study.*	0	1	1	1	1	1	1	/	1	/	
22. **Were study subjects in different intervention groups or were they recruited over the same period of time?** *For a study which does not specify the time period over which patients were recruited, the question should be answered as unable to determine.*	/	1	1	1	1	1	1	/	1	/	
23. **Were study subjects randomised to intervention groups?** *Studies which state that subjects were randomized should be answered yes except where method of randomisation would not ensure random allocation. For example, alternate allocation would score no because it is predictable.*	/	/	/	/	/	/	/	/	/	/	
24. **Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable?** *All non-randomised studies should be answered no. If assignment was concealed from patients but not from staff, it should be answered no.*	/	/	/	/	/	/	/	/	/	/	
25. **Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?** *This question should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat; the distribution of known confounders in the different treatment groups was not described; or the distribution of known confounders differed between the treatment groups but was not taken into account in the analyses. In nonrandomized studies if the effect of the main confounders was not investigated or confounding was demonstrated but no adjustment was made in the final analyses the question should be answered as no.*	/	/	/	/	/	/	/	/	/	/	
26. **Were losses of subjects to follow-up taken into account?** *If the numbers of subjects lost to follow-up are not reported, the question should be answered as unable to determine. If the proportion lost to follow- up was too small to affect the main findings, the question should be answered yes.*	/	/	/	/	/	/	/	/	/	/	
Power											
27. **Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?** *Sample sizes have been calculated to detect a difference of x% and y.*	/	/	/	/	/	/	/	/	/	/	
Results	11/14	14/15	13/15	15/15	14/16	14/15	15/15	12/12	15/15	8/10	

"1": Yes.
"0": No or unable to determine.
"/": N/A.

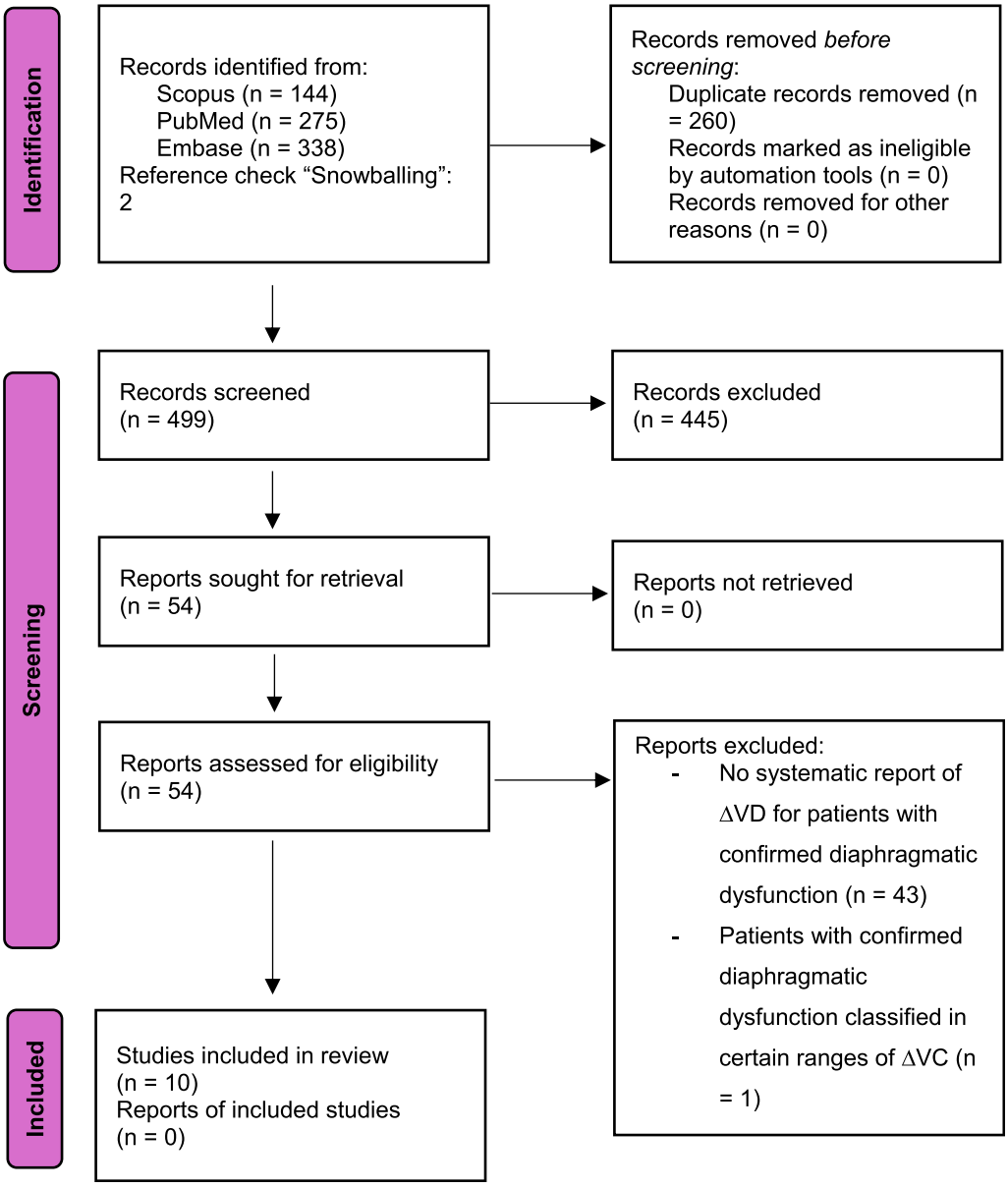

Fig. 1. Prospero flow chart.

except for Safavi et al. [17] who used absolute variation and Clague et al. [15] who did not specify how ΔVC% was calculated.

In patients with confirmed UDP, average ΔVC ranged from 7 to 23%, and in patients with BDP from 19 to 37%. In studies providing only values for patients with DD without specifying unilateral or bilateral involvement, ΔVC% ranged from 31 to 42%. The latter number was obtained in a population referred for evaluation of indication for home ventilation, explaining the extremely high fall. The sitting or supine ΔVC were compared with a control group in 4 studies, in which values ranged from 3 to 9%. Difference of ΔVC% between the control group and patients with DD was significant in all those studies beside the population analysed by Brault et al., explainable by the inclusion of less severe unilateral disease (i.e. paresis rather than phrenic paralysis).

Critical appraisal

As shown in the "Downs and Black checklist" (Table 2), no significant quality flaws were noted in the reporting section, with the exception of Nafisa [18] and Pereira [12] who either did not or only partially described the distributions of the main confounders in each subject group. Concerning the external validity, the most important potential bias originates from the fact that in several studies, subjects asked to participate or who were prepared to participate (or both) were not representative of the entire population from which they were recruited. No flaw was noted concerning the internal validity. Finally, in the "Internal Validity – confounding (selection bias)" section, no information concerning the characteristics of subjects in the control group of the study conducted by Pereira et al. [12] were available.

Since none of the included studies was interventional, several points of the original score were not applicable, and the final score for each study evaluated was expressed in terms of the number of points compatible with the study in question. To conclude, besides the insufficient external validity, which is a direct consequence of our study design, and considering the application of an incomplete form of the original score, the overall quality of the included studies was good.

Discussion

The aim of this systematic review was to study the predictive value of ΔVC in confirming the presence of DD, primarily in the context of the differential diagnosis of dyspnoea without restriction in relation to patients' comorbidities. The main results of this systematic review are that in a monomodal approach, ΔVC% is a valid test to confirm the presence of DD by choosing a relatively high cut-off value of 20%, which ensures high specificity at the cost of low sensitivity.

In a multimodal approach, using a lower cut-off value of 15% for ΔVC as initial test allows for better sensitivity, although it does not allow to rule out presence of DD.

Suspecting DD can be challenging since the anamnesis is often non-specific and the clinical examination poor. Dyspnoea on exertion can often be the only complaint of patients with undiagnosed UDP, and exercise limitation may be attributed to factors such as effort deconditioning or co-morbid conditions such as obesity or cardiopulmonary disease [19,20]. Conversely, patients with BDP have often more pronounced symptoms, including orthopnoea and dyspnoea with minimal exertion or with bending [21]. After excluding pulmonary and cardiovascular causes, DD should be considered as potential cause of unexplained dyspnoea.

No matter the aetiology of DD, the physiopathological mechanism remains similar. In healthy individuals in the supine position, gravitation shifts the abdominal content displacing the diaphragm cephalad. Blood shifts into the thorax and the intercostal muscles have a mechanical disadvantage, causing a fall in VC compared to the sitting position. In patients with DD, this effect is amplified since the diaphragm can no longer counteract this shift [20,22]. A cranial shift of the abdominal content can also be seen in obese patients even in the sitting position, secondary to the reduced ability of the diaphragm to move caudally due to increased abdominal content, causing a compression of the lungs resulting in a restrictive pattern in pulmonary function testing [23]. Partly because of concomitant exercise deconditioning, obesity is frequently part of the aetiological differential diagnosis of dyspnoea, but surprisingly no data about its impact on ΔVC were found in the review. This could be explained by the fact that obesity reduces range of diaphragmatic motion no matter the position, but an amplified impact in the supine position is from a mechanical point of view, a plausible hypothesis that needs to be further evaluated.

Furthermore, concomitant parenchymal lung desease such as chronic obstructive pulmonary disease and interstitial lung disease can impact diaphragm function and its range of motion. For example, as a result of pulmonary distension, the diaphragm is pushed in a caudal direction, and subsequently acts as a confounding factor by altering pulmonary function tests including ΔVC, as highlighted by Allen et al. [22]. These comorbidities illustrate that diaphragmatic function is part of complex respiratory mechanics that also depends on the action of accessory respiratory muscles, and that VC or ΔVC can be impacted either by these comorbidities or by DD or both. To limit the impact of confounding factors on these outcomes, we decided to include only studies in which the presence of DD had been objectively confirmed by parameters other than PFT or ΔVC, resulting in the inclusion of a limited number of studies.

Many modalities have been used in routine to assess diaphragmatic function, ranging from clinical criteria such as paradoxical abdominal movements, to iconographic assessments such as chest x-ray, CT-scanner or US assessments [6]. All of them were retrieved in this systematic review.

The measurement of transdiaphragmatic pressure in response to phrenic nerve stimulation is the gold standard in measuring diaphragmatic pressure-generating capacity and diagnose DD based on a fall of transdiaphragmatic pressure in the supine position [24]. A twitch transdiaphragmatic pressure of greater than 10 cm H2O with unilateral phrenic nerve stimulation or greater than 20 cm H_2O with bilateral phrenic nerve stimulation excludes significant weakness of the diaphragm [6]. However, it is rarely performed since it requires considerable expertise and sophisticated equipment [25], poorly compatible with the clinical routine.

Among the included studies, Türk and Laroche were the only two who used electrophysiological data to confirm the presence of DD [10,13]. Laroche confirmed DD by measuring transdiaphragmatic pressure upon phrenic nerve stimulation, while Türk included patients with neurophysiologic data consistent with phrenic neuropathy, neuromuscular transmission defects, or myopathy.

Two recent studies [4,11] from this systematic review used ultrasound measurement of the diaphragm thickening fraction (TFdi (thickness at the end of the inspiration − thickness at the end of expiration)/thickness at the end of expiration (in %))), a novel method measuring diaphragmatic thickening, which is proportional to the shortening of the muscle during contraction, with a normal lower limit accepted of 20%. [26]. The strong curvilinear relationship between ΔVC% and Tfdi reported by Brault [11] (rho = 0.67; $p < 0.001$) further confirmed the validity of this mode of evaluation.

Four studies included in this systematic review [12,14,17,18] relied on chest radiography or chest computed tomography to confirm the presence of DD, but the performance of these complementary tests to detect DD seems limited: chest radiography had high sensitivity (90%), but unacceptably high false positive findings (positive predictive value of 33%) for the diagnosis of diaphragm dysfunction [27]. Chest computed tomography was used to exclude aetiologies associated with diaphragmatic dysfunction, but exact parameters of normal diaphragm thickness were poorly defined, and patients with recent diaphragmatic paralysis may not present visible diaphragm atrophy on CT-scans [28].

The expected range of ΔVC in patients with unilateral and bilateral DD was poorly described in the literature, but reported values were usually between 10−20% for UDP [10,15,19,20] and 30−50% for BDP [20]. Reported values of ΔVC% were extremely heterogenous, reflecting the discrepancies concerning the different study designs, inclusion criteria used, and the absence of subgroups differentiating between UDP and BDP in several cases. Therefore, a quantitative comparison of values of ΔVC or even a meta-analysis would have been of little to no interest.

Furthermore, several studies did not precise if they used slow or forced vital capacity to calculate ΔVC [4,11,17,18]. FVC was mainly used [10,12−15]. Only Fromageot [16] used SVC. During a SVC manoeuvre, there is a greater lung expansion [29] and less thoracic gas compression than during a FVC manoeuvre, allowing a greater volume of air to be expired [29]. Indeed, when the intrapleural pressure exceeds alveolar pressure, it results a dynamic compression of the airways and a resulting air trapping. Moreover, the respiratory muscles are differently engaged during the expiration depending on the manoeuvre. If the slow expiration is mainly based on the relaxation of the diaphragm and external intercostal muscles, during a forced vital capacity manoeuvre, the abdominal muscles and internal intercostal muscles are actively and early engaged during the expiration. To our knowledge, no data concerning the differences between ΔFVC and ΔSVC in the context on DD are available in the literature. However, the positional changes could result in a more pronounced difference using slow rather than forced vital capacity values.

Finally, the method used to calculate ΔVC varied between the studies. All authors used relative variation (([(seated minus supine)/seated] * 100)) to quantify the change, except for Safavi et al. [17] who used absolute change and Clague et al. [15] who did not specify what method was used, and all apart one [13] failed to indicate if calculation of ΔVC% was based on changes of raw (litres) or relative values (percentage of predicted).

Only Koo et al. reported significant difference of ΔVC% between the control group and patients with UDP or BDP, whilst remaining overlap of 95% CI [4].

Contrarily, no significant difference in ΔVC% between control group and patients with UDP was reported by Brault et al, explainable by the less severe cases of unilateral disease (i.e. paresis rather than phrenic paralysis). They did not identify any significant cut-off values of ΔVC to predict the presence of unilateral DD. A ΔVC value > 15 % was associated with a high specificity (84 %) but low sensitivity (33 %) even to identify more symptomatic patients with an mMRC score ≥ -3 [11].

Both studies supported the statement of the ERS Task Force on respiratory muscle testing at rest and during exercise [7], stating that the evaluation of respiratory muscle strength frequently requires a multimodal approach, since neither maximal inspiratory pressure (MIP), the maximal inspiratory pressure/maximal inspiratory pressure (MEP/MIP) ratio, ΔVC or supine VC did not reliably identify the presence of unilateral DD.

This conclusion is also supported by Mier-Jedrzejowicz et al., who measured ΔVC% and maximum transdiaphragmatic pressure (Pdimax) in 30 patients referred for evaluation of breathlessness and diaphragm weakness [30]. They noted that ΔVC% for individuals with lesser degrees of diaphragm weakness felt within the range of normal. [30]

In this systematic review, mean or median ΔVC values were between 19 - 37% and between 7% - 23% for BDP and UDP, respectively. In case of UDP, a right-sided dysfunction had a bigger impact on diaphragmatic function as a left sided dysfunction [15]. The fall in vital capacity in the 4 patients with right-sided DD was 19% (SD +/-3,34) while that of the left-sided group was 10% (SD +/- 0,85).

A graphical representation of the mean or median ΔVC% and the corresponding SD or interquartile range (IQR) for each of the studies included in this systematic review can be found in Fig. 2.

Studies including only patients with NMD [13,14,16] reported the highest ΔVC% (ΔVC% between 23 and 40%), if we disregard results reported by Nafisa [18] who included only severe cases of DD potentially eligible for NIV. A plausible explanation could be the expected higher proportion of patients presenting BDP compared to UDP in NMD, since several NMD immediately affect the entire diaphragm.

Indeed, Türk et al. selected only patients with NMD and reported 43% of BDP [13] compared to only 25% in patients with aetiologies out of NMD reported by Koo et al. [4].

In the 4 studies measuring ΔVC% in subjects without DD (n=89), mean or median ΔVC% ranged from 3 to 6%. This range is lower than those reported by Allen et al. [22], often used as a reference for normal variability of VC with positional change in subjects without DD. For comparison, the reduction in forced standing to supine vital capacity reported by Allen (50 control, 50 with obstructive, and 47 with restrictive lung function) was 7.5% +/- 5.7, 11.2% +/- 13.4, 8.2% +/- 7.7 respectively, with no significant difference between groups. We initially suspected that this difference was caused by the variation of study design (sitting to supine vs standing (!) to supine), but Allen's results are comparable to the 8–10% decline in VC observed by other authors [15,31–34] measuring sitting to supine fall in vital capacity in healthy individuals. The 95% upper confidence limits for ΔFVC for the three groups were 18.9% for the control group, 23.6% for patients with restrictive and 38% for patients with obstructive ventilatory pattern.

The less important decrease in VC seen in patients without DD in this systematic review might be because we only included studies that confirmed diaphragmatic dysfunction using methods other than measurement of ΔVC%. Some other diagnostic methods, like ultrasound, might be more sensitive than ΔVC%, potentially allowing for the correct classification of patients with milder forms of DD who would otherwise have been considered healthy.

When using the patients without DD reported by Allen et al. [22] as a reference group, we observed a considerable overlap in the 95% CI of ΔVC% with patients reported by Koo and Brault [4,11] having UDP, but not those with BDP. This emphasises the importance of a relatively high cut-off value for ΔVC% to allow the diagnosis of UDP with a reasonable amount of specificity.

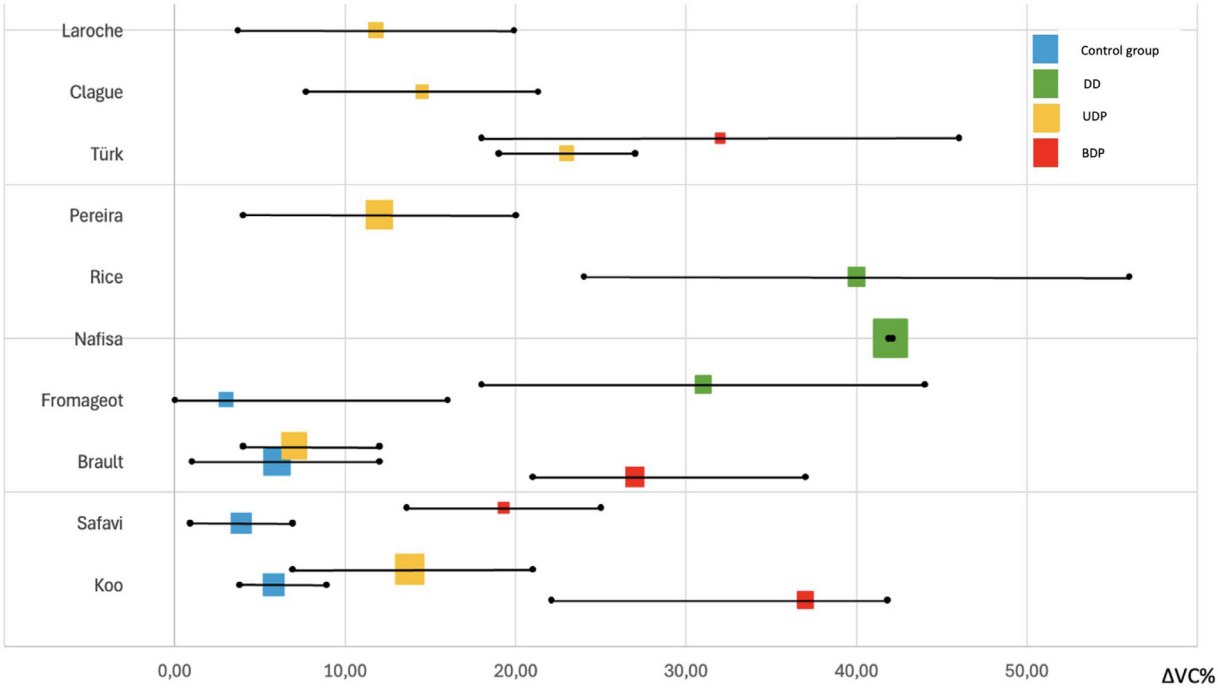

Fig. 2. Visual representation of ΔVC% for control groups, patients with UDP, BDP or DD in general
Square: mean or median ΔVC%, size proportional to sample size.
Blue square: control group; green square: diaphragmatic dysfunction without further specification (DD); yellow square: unilateral diaphragmatic dysfunction (UDP); red square: bilateral diaphragmatic dysfunction (BDP).
Horizontal line between dots: standard deviation or interquartile range.

Depending on the cut-off value, ΔVC can be used either as an initial step in a multimodal strategy to detect DD or, if the cut-off value is sufficiently high, as a diagnostic tool to confirm the presence of DD even in a monomodal approach.

In the literature, the most frequent cut-off diagnostic values of ΔVC used in a monomodal approach were either 20% [35,36] or 25% [37–40].

Among the six studies in this review that measured ΔVC% in patients with UDP, only Türk (exclusively patients with NMD) reported a mean ΔVC% above the 20% cut-off value. In addition, all the lower SD and IQR values, except for Türk's, were below the upper 95% CI of ΔVC% for a healthy population reported by Allen [22]. This suggests that most UDP patients would not have been diagnosed with DD, even when using the lower cut-off value of 20%, and that there is significant overlap in ΔVC% between healthy individuals and those with UDP.

By contrast, in 5 out of 6 studies measuring ΔVC% in patients with BDP and/or NMD, the mean or median ΔVC% exceeded the 20% cut-off. Nevertheless, in 3 of these studies, the mean minus one standard deviation values (or the corresponding "median minus one interquartile range" values) overlapped with the upper 95% CI for a healthy population reported by Allen [22] and remained below the 20% cut-off, indicating better but not optimal sensitivity and specificity of ΔVC for these populations.

When using ΔVC in a monomodal approach to identify DD, a cut-off value of 20% for ΔVC seems to be the best choice for a test with good specificity since less than 5% of healthy patients are diagnosed as false positives [22]. However, it has a low sensitivity, especially for less symptomatic patients or patients with UDP.

The ERS task force proposed in 2019 using a VC below 80% of predicted, combined with a ΔVC above 15%, as an initial step in a multimodal strategy to detect UDP. They defined the cut-off value of 15% to be twice the coefficient of variation of ΔVC in healthy individuals, representing the upper limit of normal [24]. This value is lower than the 95% upper confidence limit for ΔFVC of 18,9% for healthy patients reported by Allen [22].

Due to our study design, every case of DD was initially confirmed through independent measurements such as CT, ultrasound, or electrophysiological examinations. Subsequently, ΔVC values were compared between control groups and those with DD. In this context, patients can meet the diagnostic criteria for DD using a test that is more sensitive than ΔVC, resulting in diagnoses of DD even when ΔVC% is below the 15% normality threshold set by the ERS. Consequently, the negative predictive value of a ΔVC of 15% could appear less important in the studies included in our review compared to other studies not following the same design.

Except for Türk's study [13], which included only patients with NMD and who reported a minus one SD value for ΔVC% of 19%, all the lowest SD or IRQ values in the studies measuring UDP included in this systematic review ranged from 3.7% to 7.3% [4,10–12,15] and were below the cut-off.

This highlights the poor negative predictive value of this diagnostic threshold, despite its importance for screening purposes. Even in one of the four studies measuring ΔVC in patients with BDP [17], the minus one SD for ΔVC% overlapped with the 15% cut-off value.

For instance, patients with a ΔVC below 15% who are suspected of having DD due to a severe disease potentially causing irreversible lesions without treatment (e.g. enzyme replacement therapy for

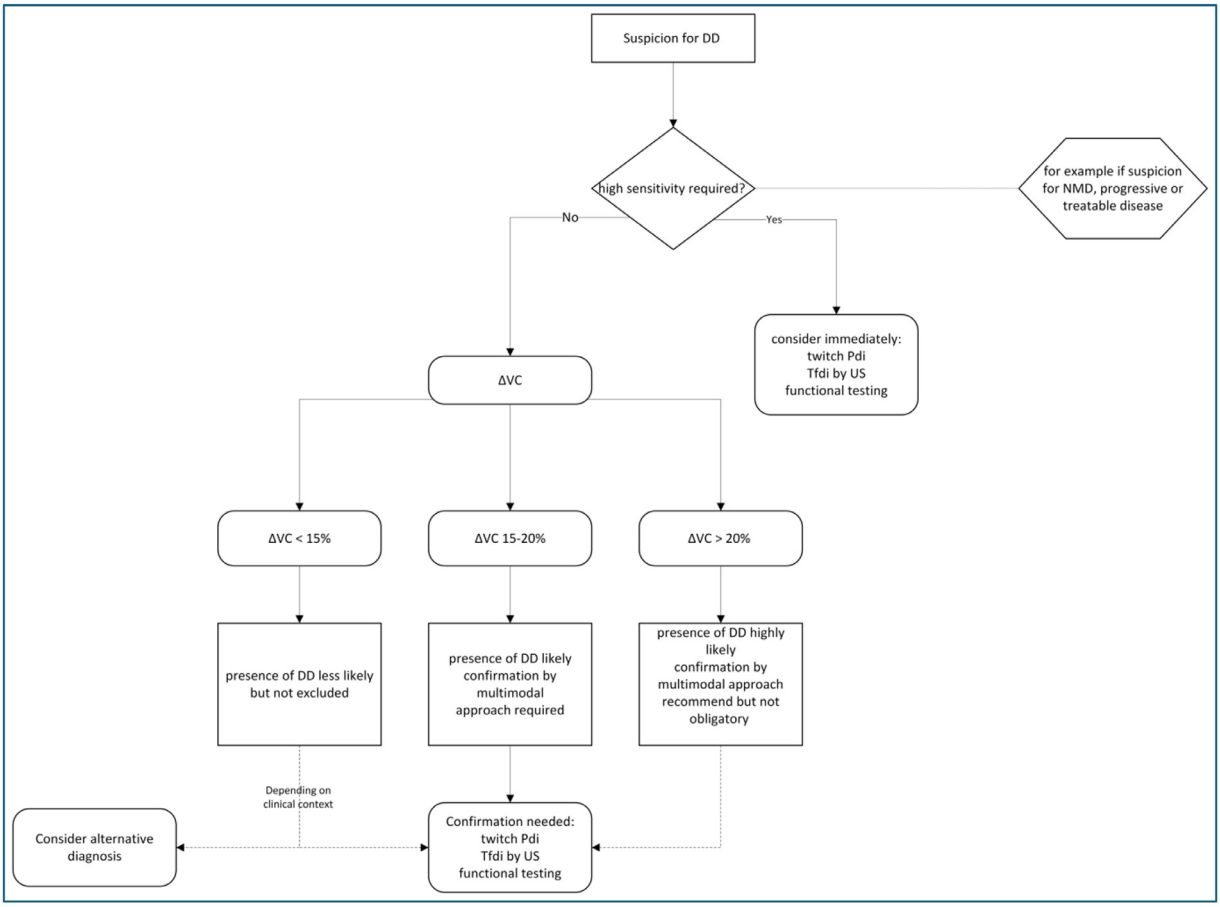

Fig. 3. Diagnostic algorithm.
Authors' proposal for the management of a patient with suspected diaphragmatic dysfunction, adapted to the clinical context, based on the fall in vital capacity.

pompe disease) should undergo further evaluation with more precise diagnostic tools no matter the value of ΔVC. Conversely, for patients presenting with dyspnoea without clear diaphragmatic aetiology and ΔVC values below 15%, alternative diagnoses could be prioritized.

A proposed management plan for patients with suspected diaphragmatic dysfunction, adapted to the clinical context and based on the decline in vital capacity, is illustrated in the flow chart in Fig. 3.

Key limitations of this systematic review include the variations in study designs, such as differences in populations analysed (due to inclusion criteria or recruitment context), diagnostic criteria used to confirm DD and statistical methods used (e.g., mean vs. median).

The aforementioned heterogeneity is partially a consequence of our review design, which included all types of aetiology of DD if the latter was independently confirmed by a criterion other than ΔVC.

Additionally, most of the authors failed to mention if slow or forced vital was used to calculate ΔVC, and the way they calculated the change.

Consequently, quantitative inter-study comparisons of ΔVC values were of limited interest and no meta-analysis were conducted.

In conclusion, in a monomodal approach, ΔVC% is a valid test to confirm the presence of DD by choosing a relatively higher cut-off value (20%) than the one suggested by ERS, but confirmation of the diagnosis by other tests is still recommended.

A multimodal approach using a lower cut-off value for ΔVC of 15% as initial test allows to obtain better sensitivity without being able to rule out presence of DD and seems to be better adapted to daily clinical practice.

Especially if ΔVC% indicates absence of DD and a high negative predictive value is important, results must be interpreted in clinical context and other diagnostic tests such as US should be prioritized.

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Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Author contributions

Hendrik Kever, Conception and realization of the study, analysis of the results, and writing of the manuscript.

Gregory Reychler, Conception and realization of the study, analysis of the results, and writing of the manuscript.

Giuseppe Liistro, Conception of the study, analysis of the results, reviewing the final draft.

Dominique Butenda Babapu, Analysis of the results, reviewing the final draft.

Appendix 1. xx

Search Strategy Documentation

Search summary

Database Name	Platform	Date Range	Date of Search	# of results
MEDLINE	Via PubMed	Beginning – December 5th 2023	05/12/2023	275
SCOPUS		Beginning - December 5th 2023	05/12/2023	144
EMBASE		Beginning - December 5th 2023	05/12/2023	338

Total Records = 757
Records by snowballing = 2
Total Records after deduplication = 497
Master search strategy
MEDLINE (PubMed)
Date of Search: 05/12/2023
Number of results: 257

#	Search string	# of results
1	((((((diaphragm palsy) OR (diaphragm paralysis)) OR (diaphragmatic palsy)) OR (diaphragmatic paralysis)) OR (diaphragm dysfunction)) OR (diaphragmatic dysfunction)) AND (supine vital capacity)	122
2	((((((diaphragm palsy) OR (diaphragm paralysis)) OR (diaphragmatic palsy)) OR (diaphragmatic paralysis)) OR (diaphragm dysfunction)) OR (diaphragmatic dysfunction)) AND (supine) AND (vital capacity)	122
3	((((((diaphragm palsy) OR (diaphragm paralysis)) OR (diaphragmatic palsy)) OR (diaphragmatic paralysis)) OR (diaphragm dysfunction)) OR (diaphragmatic dysfunction)) AND (vital capacity)	1037
4	(((diaphragm) OR (diaphragmatic)) AND (((dysfunction) OR (paralysis) OR (palsy))) AND (supine) AND (vital capacity)	111
5	((((((diaphragm palsy) OR (diaphragm paralysis)) OR (diaphragmatic palsy)) OR (diaphragmatic paralysis)) OR (diaphragm dysfunction)) OR (diaphragmatic dysfunction)) AND (supine) AND (((((vital capacity) OR (lung function)) OR (pulmonary function test)) OR (PFT)) OR (respiratory function))	275

SCOPUS
Date of Search: 05/12/2023
Number of results: 135

#	Search string	# of results
1	((diaphragmatic AND dysfunction) OR (diaphragmatic AND paralysis) OR (diaphragmatic AND palsy) OR (diaphragm AND palsy) OR (diaphragm AND paralysis) OR (diaphragm AND dysfunction)) AND (supine) AND (vital AND capacity)	97
2	((diaphragmatic AND dysfunction) OR (diaphragmatic AND paralysis) OR (diaphragmatic AND palsy) OR (diaphragm AND palsy) OR (diaphragm AND paralysis) OR (diaphragm AND dysfunction)) AND (supine AND vital AND capacity)	97
3	((((((diaphragm AND palsy) OR (diaphragm AND paralysis)) OR (diaphragmatic AND palsy)) OR (diaphragmatic AND paralysis)) OR (diaphragm AND dysfunction)) OR (diaphragmatic AND dysfunction)) AND (supine) AND ((((vital AND capacity) OR (lung AND function)) OR (pulmonary AND function AND test)) OR (pft))	135

(*continued*)

(*Continued*)

#	Search string	# of results
4	TITLE-ABS-KEY (((((((diaphragm AND palsy) OR (diaphragm AND paralysis)) OR (diaphragmatic AND palsy)) OR (diaphragmatic AND paralysis)) OR (diaphragm AND dysfunction)) OR (diaphragmatic AND dysfunction)) AND (supine) AND (((((vital AND capacity) OR (lung AND function)) OR (pulmonary AND function AND test)) OR (pft)) OR (respiratory AND function)))	144

EMBASE
Date of Search: 05/12/2023
Number of results: 272

#	Search string	# of results
1	(diaphragm AND palsy OR (diaphragm AND paralysis) OR (diaphragmatic AND palsy) OR (diaphragmatic AND paralysis) OR (diaphragm AND dysfunction) OR (diaphragmatic AND dysfunction)) AND supine AND ('vital capacity'/exp OR 'vital capacity' OR (('vital'/exp OR vital) AND ('capacity'/exp OR capacity)))	160
2	('diaphragm palsy'/exp OR 'diaphragm palsy' OR (('diaphragm'/exp OR diaphragm) AND ('palsy'/exp OR palsy)) OR 'diaphragm paralysis'/exp OR 'diaphragm paralysis' OR (('diaphragm'/exp OR diaphragm) AND ('paralysis'/exp OR paralysis)) OR 'diaphragmatic palsy' OR (diaphragmatic AND ('palsy'/exp OR palsy)) OR 'diaphragmatic paralysis'/exp OR 'diaphragmatic paralysis' OR (diaphragmatic AND ('paralysis'/exp OR paralysis)) OR 'diaphragm dysfunction'/exp OR 'diaphragm dysfunction' OR (('diaphragm'/exp OR diaphragm) AND dysfunction) OR 'diaphragmatic dysfunction'/exp OR 'diaphragmatic dysfunction' OR (diaphragmatic AND dysfunction)) AND supine AND ('vital capacity'/exp OR 'vital capacity' OR (('vital'/exp OR vital) AND ('capacity'/exp OR capacity)) OR 'lung function'/exp OR 'lung function' OR (('lung'/exp OR lung) AND ('function'/exp OR function)) OR 'pulmonary function test'/exp OR 'pulmonary function test' OR (pulmonary AND ('function'/exp OR function) AND ('test'/exp OR test)) OR pft)	272
3	('diaphragm palsy'/exp OR 'diaphragm palsy' OR (('diaphragm'/exp OR diaphragm) AND ('palsy'/exp OR palsy)) OR 'diaphragm paralysis'/exp OR 'diaphragm paralysis' OR (('diaphragm'/exp OR diaphragm) AND ('paralysis'/exp OR paralysis)) OR 'diaphragmatic palsy' OR (diaphragmatic AND ('palsy'/exp OR palsy)) OR 'diaphragmatic paralysis'/exp OR 'diaphragmatic paralysis' OR (diaphragmatic AND ('paralysis'/exp OR paralysis)) OR 'diaphragm dysfunction'/exp OR 'diaphragm dysfunction' OR (('diaphragm'/exp OR diaphragm) AND dysfunction) OR 'diaphragmatic dysfunction'/exp OR 'diaphragmatic dysfunction' OR (diaphragmatic AND dysfunction)) AND supine AND ('vital capacity'/exp OR 'vital capacity' OR (('vital'/exp OR vital) AND ('capacity'/exp OR capacity)) OR 'lung function'/exp OR 'lung function' OR (('lung'/exp OR lung) AND ('function'/exp OR function)) OR 'pulmonary function test'/exp OR 'pulmonary function test' OR (pulmonary AND ('function'/exp OR function) AND ('test'/exp OR test)) OR pft OR 'respiratory function'/exp OR 'respiratory function' OR (('respiratory'/exp OR respiratory) AND ('function'/exp OR function)))	338

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