



Original Contribution

Ultrasound imaging measurements to determine reduced diaphragm thickness and relevance to breathing pattern disorders diagnosis in females

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ARTICLE INFO

Handling Editor: Prof. MD Manjiri Dighe

Keywords:

Diaphragm
Respiration
Ultrasound
Thickness
Physiotherapy

ABSTRACT

Background: Breathing pattern disorders (BPD) are commonly managed by physiotherapists. As no gold-standard assessment diagnostic tools are currently available, diagnosis is challenging. Ultrasound imaging has become popular in physiotherapy. This research examined diaphragm thickness using ultrasound imaging in females with BPD and healthy female controls to ascertain if diaphragm thickness at different measurement points related with reduced diaphragm thickness.

Methods: Observational cross-sectional design was used. Two female groups were recruited from an outpatient setting: BPD group ($n = 19$) and control group ($n = 18$) with normal body mass index (BMI). BPD inclusion criteria assessment included: Nijmegen Questionnaire (NQ) score, respiratory rate, Hi-Lo test, and breath hold time. USI measured diaphragm thickness at the measurement points of: tidal exhalation (Tvex), tidal inhalation (Tvin), maximum inhalation (Tmax) and exhalation to residual volume (Tmin); diaphragm thickening fraction (TF) was calculated.

Results: Results indicated significant differences of diaphragm thickness between the BPD and control groups at Tvex, Tvin, Tmax and TF on the left and Tvex and Tvin on the right side ($P < 0.05$).

Conclusion: Diaphragm thickness is reduced in females with BPD when compared with healthy controls. Diaphragm measurement undertaken by USI may provide a useful assessment tool in BPD. Further research is required to validate this assessment and to broaden its use in BPD.

1. Introduction

Breathing pattern disorders (BPD) is an umbrella term that includes many specific sub-patterns of breathing such as hyperventilation, chronic mouth breathing, dominant apical breathing, forced expiratory breathing, paradoxical breathing, erratic breathing, breath holding, and inappropriate sighing and yawning [1–3]. Despite recognizable sub-patterns, no formal definition for BPD exists [1,4], leading to confusion in the diagnosis of BPD [5]. The etiology BPD is believed to be multifactorial, influenced by inter-related biochemical, psychological, and biomechanical factors [4,6]. Estimates of the prevalence of BPD range from 6% to 11% in adult populations [2,3,7], with prevalence greater in females (55%) compared to males (45%) [8].

BPD diagnosis is difficult, as no clear gold-standard tests are available [9,10], and is compounded by the multifactorial etiology [11,12]. Recent

reviews recommend a variety of diagnostic assessments for BPD, including the Nijmegen Questionnaire (NQ), manual assessment of respiration motion (MARM), Hi-Lo test, measurement of breath-hold time (BHT), oxygen saturation, and respiratory rate (RR) [4,6]. However, concerns surround the validity and reliability of many of these assessments, including the MARM [13] and NQ [9,14]. Furthermore, many of these assessments are primarily subjective, and none provide a valid or objective measurement of diaphragm muscle function, despite the diaphragm purported to being weak and dysfunctional in BPD [4,11,15].

One of the postulated causes of BPD includes increased dominant apical breathing and diaphragm muscle weakness with resultant associated reduced diaphragm thickness [4,11]. Skeletal muscle morphology (i.e., size and thickness) closely correlates to muscle strength [16,17], and diaphragm thickness correlates to inspiratory muscle strength and pulmonary function in healthy individuals [18]. Conversely, diaphragm

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atrophy and reduced diaphragm thickness has been shown in clinical populations including people with phrenic neuropathy or phrenic nerve injury [19,20], stroke (when the hemiplegic side is compared with the less affected side) [21], low-back pain [22], following mechanical ventilation in intensive care [23,24] and following a COVID19 infection [25,26]. Furthermore, a number of demographic variables exist that can also influence diaphragm thickness including age (reduced thickness if less than 18 or greater than 70 years [27,28]), gender (females having reduced thickness compared to males [27,29]), and body mass index (BMI) or body composition (lower BMI correlates to reduced diaphragm thickness compared to higher BMI [27,30]).

In recent decades, ultrasound imaging (USI) has been growing in use to assess the diaphragm, both in clinical practice and research [31,32]. Advantages of USI as a technique in point of care assessment are numerous, including simple and rapid assessment, device portability, cost-effectiveness, and enhanced patient comfort as it is non-invasive [31–33]. Reported diaphragm measurements using USI include diaphragm thickness (including at a variety of different lung volumes) [18, 27,34], diaphragm excursion or motion using B-mode and M-mode USI [35], diaphragm thickening ratio (TR) [27,34], and thickening fraction (TF) [18]. Furthermore, assessment of diaphragm morphology and function, using USI, provides quantitative measures of diaphragm dysfunction, which other assessments in BPD (i.e., NQ) do not provide.

USI is sensitive and has been able to detect differences in normal and manipulated styles of breathing [36,37], movement and exercise [37], hypertrophy [30,38], and atrophy of the diaphragm [23]. USI has been shown to have excellent levels of sensitivity (93%) and specificity (100%) for the diagnosis of neuromuscular diaphragmatic dysfunction (via morphological measures such as diaphragmatic thickness), in people with phrenic neuropathy, when compared with needle electromyography studies [19]. To date, USI investigation of diaphragm thickness has not been assessed in people with BPD and yet could provide valuable objective diagnostic assessment. An initial exploration of this measure in females would be useful, due to the higher prevalence of BPD in females compared to males [8].

This study's primary aim was to measure diaphragm thickness and diaphragm TF at different lung volume measurements of tidal exhalation (Tvex), tidal inhalation (Tvin), maximal inhalation (Tmax) and exhalation to residual volume (Tmin) in the left and right hemi-diaphragm in females with BPD compared with matched healthy females.

2. Materials and methods

An observational cross-sectional design was used. All participants were female aged over 18 years. To control for gender was considered important due to the increased prevalence of BPD in females [8] coupled with reduced diaphragm thickness in females compared to males [27, 29].

2.1. Participants and recruitment

Specific measures were used to assess participants' eligibility, specifically: the NQ, RR, BHT, and the Hi-Lo test. Inclusion criteria for participants within the BPD group were: aged 18–65 years, a NQ score ≥ 23 (a conservative cut-off point for diagnosis of BPD [10]), oxygen saturation (SpO₂) of $>96\%$ (measured with via pulse oximetry), RR > 16 breaths per minute, a BHT ≤ 30 s, and presence of an apical dominant breathing pattern during the Hi-Lo test. Inclusion criteria for healthy females (control group) were: aged 18–65 years, a NQ score < 16 (a conservative value for healthy populations [10]), SpO₂ of $>96\%$, a RR of 8–15 breaths per minute, a BHT >30 s and presence of an abdominal dominant breathing pattern during Hi-Lo assessment. Participants who did not meet all the inclusion criteria were excluded.

Exclusion criteria included factors that may affect breathing patterns. Participants were excluded if they had: a SpO₂ of $<94\%$, lung disease (e.g., asthma, bronchiectasis), smoking history, any other disease processes (e.g., renal disease), or chronic pain problems. These factors influence the

respiratory or musculoskeletal systems, and therefore controlling for these factors was important for external validity of the current study.

Participants were recruited through referrals to a private physiotherapy clinic and other public referral sources (e.g., hospitals and university respiratory physiotherapy clinics); control participants were recruited through gyms, Auckland University of Technology campuses, and other health centres. Written consent was obtained from all participants. Ethics Approval was obtained Auckland University of Technology Ethics Committee (# AUTEC 17/419).

Demographic and clinical variables (Table 1) were collected from all participants at baseline. Standardised methods were used to collect baseline data and screen for eligibility. BHT was assessed as per previously reported methods [39]. Due to variability in published cut-off values for BHT [39,40], this study used a conservative cut-off time of >30 s, used to represent normal breath hold on tidal exhalation. A RR of ≥ 16 breaths per minute was the cut-off for inclusion in the BPD group, and a rate of 8–15 was used for inclusion in the control group [4,39]. The Hi-Lo test was completed in sitting, with the inclusion criterion for the BPD group being the presence of an upper chest/apical dominant pattern of breathing, whereas for the control group it was an abdominal/diaphragmatic dominant breathing [41].

2.2. USI measures of the diaphragm

Diaphragm thickness was measured bilaterally with USI using an 8300 Chison ultrasound machine with a 10 MHz linear probe (Chison Ultrasound, China), as described in previous studies [19,27]. Measurements of diaphragm thickness was recorded by placing the USI probe in a longitudinal orientation at the level of rib space 8–9, or 9–10 (Fig. 1). All measurements were completed by the primary author, who was blinded during both data collection and analysis. Diaphragm thickness was assessed in supine, with pillows under the knees and head supporting a neutral spinal posture, and during a momentary pause at specific lung volumes, namely total lung capacity (Tmax), tidal inhalation (Tvin), at tidal exhale (Tvex), and at residual volume (Tmin) (Fig. 1). The TF was calculated using the formula: $TF = (\text{diaphragm thickness at } Tmax - \text{diaphragm thickness at } Tvex) / \text{diaphragm thickness at } Tvex$ [18].

2.3. Statistical analysis

A cohort of at least 34 participants (17 each in the BPD and control groups) was determined (G*Power software version 3.1.9.4, University Dusseldorf) to detect a difference in diaphragm thickness between groups. The power calculation was informed by both clinical notes audit

Table 1
Demographic and respiratory characteristics.

	Group	n	Mean	Standard deviation
Age (years)	BPD	19	36.32	11.56
	Control	18	29.61	11.27
Height (metres)	BPD	19	1.65	0.07
	Control	18	1.67	0.06
Weight (kilograms)	BPD	19	60.84	6.72
	Control	18	62.35	8.12
BMI (kg/m ²)	BPD	19	22.09	1.94
	Control	18	22.21	1.76
Pulse oximetry (%)	BPD	19	98	0.96
	Control	18	98	0.49
Respiratory rate (breaths/minute)	BPD	19	19.68	4.26
	Control	18	13.94	1.11
NQ (score out of 64)	BPD	19	35.16	8.59
	Control	18	6.61	3.60
Breath hold time (seconds)	BPD	19	17.47	4.98
	Control	18	32.67	3.40
Exercise hours/week	BPD	19	3.47	2.36
	Control	18	6.75	4.22

Notes: BPD = breathing pattern disorder; BMI = body mass index. NQ = Nijmegen Questionnaire.

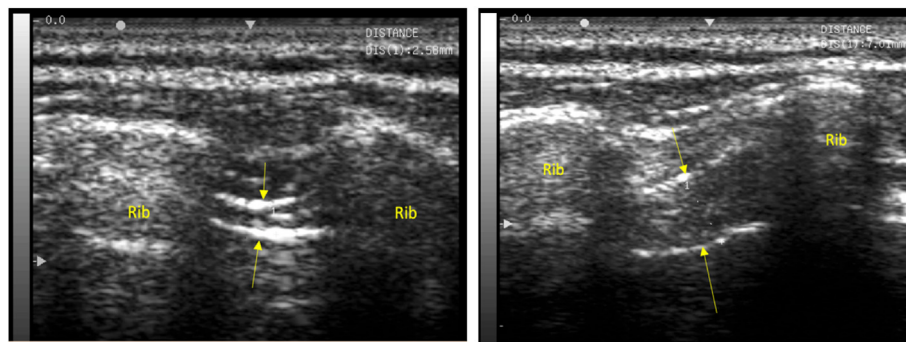


Fig. 1. Ultrasound of the diaphragm thickness measurement at Tvex or tidal exhale (left image) and at Tmax or maximum inhale (right image). Key: Yellow arrows depict the top and bottom boundaries of the diaphragm muscle (personal image, no copyright). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

of diaphragm thickness, and the published results of Boon, Harper [27]. SPSS version 25.0 (IBM Corporation, New York, USA) was used to analyse the data with a P -value of <0.05 considered significant. Normality using a Shapiro-Wilk test and Levene test was used for all outcome variables to examine the constant variance. Where data failed normality assumptions, the data were transformed to a logarithm scale, and reassessment of normality was performed. Independent t-tests were performed to investigate mean differences between the BPD and control groups for diaphragm thickness and TR.

3. Results

Recruitment took place between 29 March 2018 and 30 June 2019. In total, 74 females responded to the invitation to participate by email and phone. Of these participants, 37 were excluded and the remaining 37 participants met the inclusion criteria ($n = 19$ BPD group; $n = 18$ control group). The exclusion of participants ($n = 37$) was based on the strict inclusion and exclusion criteria, which was necessary for the design of this study, and was consistent with the current recommendations in the BPD literature [41]. Both groups were similar in baseline comparability in the age, height, weight, BMI, or pulse oximetry between the BPD and control groups (Table 1). Expected differences between BPD and control groups were found for respiratory rate, NQ, BHT, as per the eligibility criteria. A difference was noted between the groups for exercise hours per week (Table 1).

To satisfy the normality assumption, data for left Tvex, right Tvex, right Tvin, right Tmax, left Tmin and right Tmin were transformed to a natural logarithm scale. This allowed the use of independent t-tests to examine the difference between the BPD and control groups for all outcome measures.

Diaphragm thickness for the BPD participants was significantly reduced ($P < 0.05$) when compared to control participants bilaterally for Tvex and Tvin (Table 2). Whilst significant between group differences were seen on the left side for Tmax and left TF ($P < 0.05$). Furthermore, both right Tmax ($P = 0.07$) and right Tmin ($P = 0.06$) both approached the threshold for a significant difference between groups (Table 2). Finally, diaphragm thickness was not different between groups for left Tmin ($P = 0.92$) or for right TF ($P = 0.94$) (Table 2).

4. Discussion

This is the first study that has examined differences in diaphragm thickness, using USI, in females with BPD compared to healthy matched controls. The primary hypothesis was that there would be a significant difference in diaphragm thickness between females with BPD and healthy matched controls. This was proven true with findings of reduced diaphragm thickness of participants within the BPD group at Tvex (left and right); at Tvin, Tmax and for TF on the left side, and at Tvin on the right side compared to healthy control participants. This novel finding establishes a clear relationship between reduced diaphragm thickness

Table 2
Diaphragm thickness on the right and left sides (BPD $n = 19$; Control $n = 18$).

	Group	Mean (mm)	Standard deviation (mm)	Data transformed in	Mean difference with 95% CI	Statistic (t)	P-value
R Tvex	BPD	1.65	0.37	Log scale	-0.08 (-0.15, -0.01)	-2.23	0.03 *
	Control	2.01	0.62				
L Tvex	BPD	1.58	0.34	Log scale	-0.09 (-0.17, -0.1)	-2.67	0.01 *
	Control	2.00	0.58				
R Tvin	BPD	1.86	0.36	Log scale	-0.11 (-0.19, -0.04)	-3.04	0.01 *
	Control	2.48	0.77				
L Tvin	BPD	1.75	0.40	-	-0.69 (-1.04, -0.34)	-4.00	<0.01 *
	Control	2.44	0.63				
R Tmax	BPD	3.60	1.34	Log scale	-0.10 (-0.20, 0.01)	-1.85	0.07
	Control	4.49	1.81				
L Tmax	BPD	3.15	1.42	-	-1.68 (-2.66, -0.70)	-3.48	<0.01 *
	Control	4.83	1.52				
R Tmin	BPD	2.15	0.52	Log scale	0.06 (-0.00, 0.13)	1.92	0.06
	Control	1.86	0.49				
L Tmin	BPD	1.94	0.39	Log scale	-0.00 (-0.08, 0.07)	-0.11	0.92
	Control	2.01	0.66				
R Thickening Fraction	BPD	1.24	0.86	-	0.02 (-0.45, 0.48)	0.07	0.94
	Control	1.23	0.47				
L Thickening Fraction	BPD	1.00	0.76	-	-0.44 (-0.86, -0.02)	-2.16	0.04 *
	Control	1.44	0.45				

Notes: BPD = breathing pattern disorder; CI = confidence interval; TF = thickening fraction; R = right; L = left; Tvex = tidal exhale; Tvin = tidal inhale; Tmax = maximum inhale; Tmin = maximum exhale; *denotes significant differences between groups $P < 0.05$.

and BPD in females, and with further research, this may potentially influence how people with BPD are assessed and treated by physiotherapists.

The findings of this study demonstrated a link between reduced diaphragm thickness and BPD and provides evidence to support previously theorized biomechanical and pathophysiological processes in BPD [11,15]. The proposed mechanisms for reduced diaphragm thickness may be due to BPD creating increased hypertonicity in the intercostal and chest wall muscles, along with hyperinflation, leading to mechanical unloading of the diaphragm, and then subsequent diaphragm thinning due to disuse of the diaphragm [11,15]. A vicious cycle of diaphragm weakening is thereby created, which further increases reliance on the accessory muscles to generate forces required for breathing [11,15]. Furthermore, reduced diaphragm thickness found in the BPD group, may also be partially explained by the difference in exercise levels per week between the BPD group (3.47 h/week) and control groups (6.75 h/week). The reduction in exercise levels in the BPD group may be a further contributing factor of the BPD vicious cycle, where increased dyspnoea and shortness of breath at rest and with exercise [42], makes exercise more unpleasant, leading to reduced activity levels, reduced diaphragm loading, and eventually further diaphragm thinning. These findings suggest that specific treatments to strengthen the diaphragm may be useful to reduce BPD morbidity.

The results of the BPD and control group are comparable to a previous study involving a low back pain (LBP) population ($n = 20$) and healthy controls ($n = 20$) [22]. The study conducted by Calvo-Lobo, Almazan-Polo [22] found that diaphragm thickness was significantly reduced in the low back pain group, compared to controls (right Tvex 1.6 ± 0.7 mm LBP vs. 2.3 ± 0.6 mm controls; $P = 0.006$; left Tvex 1.3 ± 1.2 mm LBP vs. 2.0 ± 1.0 controls; $P = 0.015$). These results are similar to those in the present study.

The results of this study suggest that BPD is linked with reduced diaphragm thickness, and recent research suggests that BPD exist in some patients with Long COVID or Post Acute Sequelae of COVID19 [43,44]. Other authors have established that USI is useful to detect diaphragm atrophy in patient cohorts with Acute and Long COVID [25,45,46]. Therefore, further research is warranted to investigate if BPD and reduced diaphragm thickness concurrently exist in Long COVID patients, and if this can be translated into effective treatment strategies.

People with BPD may contribute significant cost and health burdens, as many of these people present to emergency departments and require expensive screening to rule out other serious pathologies. For example, one case-study of a person with BPD reported healthcare costs of \$1,853 NZD (\$1270 USD) due to emergency department visits and health testing in New Zealand [47]. Furthermore, a one-year-long retrospective study in a large tertiary hospital suggested that approximately 1.76% of all attendees to accident and emergency department may be due to BPD [8]. The findings from the current study suggest USI may be a useful tool to determine reduced diaphragm thickness which, when put alongside other diagnostic criteria, may help to identify BPD as a diagnosis and may help to reduce the cost burden of BPD.

USI has grown in its use in physiotherapy providing cost effective, safe, objective, valid and useful information to aid diagnosis and management of respiratory conditions [32,48]. This study indicates the potential value of USI as a means to quantify reduced diaphragm thickness in females with BPD. Furthermore, USI of the diaphragm is gaining popularity as an objective assessment measurement tool in populations with neurological conditions such as stroke [21,49], respiratory conditions such as chronic obstructive pulmonary disease (COPD) [50,51], and musculoskeletal conditions such as low back pain [22]. Therefore, this research further supports the use and application of USI within the context of respiratory medicine and physiotherapy.

This study had limitations. Causation cannot be inferred in an observational study, and as such is a limitation. It can be concluded that reduced diaphragm thickness was associated with BPD, but it cannot be determined that BPD causes reduced diaphragm thickness. Future

prospective research using a randomized control trial design is needed to confirm if BPD is causally linked to reduced diaphragm thickness, and whether specific physiotherapy interventions can reverse this process. Furthermore, all study participants were female. Generalisability of the results is therefore limited when considering the effect of BPD in males upon diaphragm morphology. Likewise, the participants represented a group with a BMI <25 kg/m². Future research for people with BPD should aim to control for gender, age, BMI, and exercise levels, as these variables are known to impact diaphragm thickness. Research is also warranted for treatments that include strengthening (hypertrophy) of the diaphragm in the management of BPD. The findings of this research may be a useful addition in the assessment of people with BPD, with the additional benefit of more efficient diagnosis, targeted treatment interventions and ultimately reduce treatment costs for patients with BPD.

5. Conclusion

In conclusion, diaphragm thickness was generally found to be reduced in females with BPD compared to healthy matched participants. USI of the diaphragm is a useful, non-invasive and objective measurement that may assist with diagnosis effectiveness in BPD. Further work is required to validate this assessment for a wider population, taking into account other potential linked variables, and to broaden its use in BPD.

Declaration of interest statement

The authors report there are no competing interests to declare.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Scott Peirce reports administrative support and equipment, drugs, or supplies were provided by Physiotherapy New Zealand.

Acknowledgements

Kind thanks to all the participants involved in this study.

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