

Research Article

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Ultrasound Assessment of Diaphragmatic Function: Methodology, Normative Values

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RELEVANCE Diaphragmatic dysfunction (DD) is common in critically ill patients, and is often the cause of respiratory failure requiring respiratory support. A generally accepted method for noninvasive dynamic evaluation of diaphragm function has not yet been proposed.

THE AIM OF STUDY To develop a method for ultrasound examination of diaphragm mobility and relative thickening, to propose standard parameters of diaphragm excursion and relative thickening depending on gender and age.

MATERIAL AND METHODS In 81 healthy volunteers aged 25 to 84 years (mean age 55±15 years), we used ultrasound to determine the thickness of the diaphragm on the right and left at the attachment site of the muscular part on end-expiration, tidal and forced inspiration; to calculate the fractional thickening (FT), diaphragm excursion during quiet and maximum inspiration, as well as indices of functional reserve by thickening (IFR(t)) and by diaphragm excursion (IFR(e)). We traced the dependence of the determined parameters on the age, gender, height, body mass index (BMI) and body surface area (BSA) of the subjects. To assess interobserver reproducibility, we calculated the limits of agreement and the intraclass correlation coefficient of the ultrasound parameters of the diaphragm function.

RESULTS The excursion of the diaphragm in women is smaller than in men, and statistically significantly decreases with age. A direct relationship between the thickness of the diaphragm on exhalation and the BSA was demonstrated. The FT during quiet inspiration on the left slightly but statistically significantly decreases with increasing BMI. The IFR(t) on the right slightly but statistically significantly decreases with age. The lower limits of the reference intervals for IFR(e) and IFR(t) do not depend on the factors considered and are the same for the right and left halves of the diaphragm. Inter-study reproducibility of ultrasound indices of diaphragm function is high: intra-class correlation coefficients for various parameters ranged from 0.81 to 0.96, measurement error according to the results of Bland-Altman analysis was small relative to the measured values.

CONCLUSION A method for ultrasound examination of diaphragm function is proposed. High inter-study reproducibility of the considered ultrasound parameters was confirmed, reference intervals were proposed. Functional reserve indices do not depend on age, gender and constitutional characteristics of the subjects.

Keywords: diaphragm ultrasound, diaphragm dysfunction, thickening fraction, diaphragm functional reserve index

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BMI — body mass index

BSA — body surface area

CI — confidence interval

DD — diaphragm dysfunction

IFR(e) — index of the functional reserve for excursion

IFR(t) — index of the functional reserve for thickening

TF — thickening fraction

TF_1 — thickening fraction on tidal breathing

TF_2 — thickening fraction on forced inspiration

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INTRODUCTION

Diaphragmatic dysfunction (DD) is common in critically ill patients and is often the cause of respiratory failure requiring respiratory support. Long-term mechanical ventilation leads to diaphragm atrophy, which complicates weaning patients from mechanical ventilation and reduces survival [1]. This necessitates a dynamic assessment of the functional state of the diaphragm for timely correction of respiratory support parameters. A number of proposed methods, such as measuring transdiaphragmatic pressure or electromyography of the diaphragm, despite their reliability, are characterized by high labor intensity and low availability, and are not always applicable in conditions of mechanical ventilation and depression of consciousness [2].

On the other hand, the ultrasound method allows dynamic measurement of the excursion and relative thickening of the diaphragm. It has been shown that ultrasonographic parameters of diaphragm function can be used to diagnose diaphragm paralysis, as well as to assess its dysfunction, which can influence the determination of the patient's readiness for weaning from mechanical ventilation [1,3–5].

The first ultrasound examination of the diaphragm excursion as an alternative to fluoroscopy was performed in 1975, noting the difficulties that arise when visualizing the left half of the diaphragm due to the presence of gas in the stomach; and it was proposed to conduct the examination in the Trendelenburg position after filling the stomach with water [6]. The use of M-mode simplified the measurement of excursion [7]. The first studies used a longitudinal position of the ultrasound probe along the midclavicular line.

The technique of measuring the diaphragm thickness in M-mode was first demonstrated on cadaveric material and healthy volunteers in 1989. In this case, an approach to the IX intercostal space along the anterior or middle axillary line was used with the patient in a sitting position. A high degree of agreement between the values obtained by ultrasound measurement of the diaphragm thickness and the thickness of the m.phrenicus according to pathomorphological data was demonstrated [8]. The first use of B-mode for measuring diaphragm thickness dates back to 1995: the study was performed with the patient in a sitting position, the

probe was positioned between the anterior and midaxillary lines [9].

Visualization of the diaphragm from the intercostal approach between the midclavicular and midaxillary lines allows achieving satisfactory quality of visualization for both halves of the diaphragm; and the reproducibility of the obtained indicators with a horizontal position of the body, as well as the degree of correspondence between the excursion and the respiratory volume, is higher than with a vertical position of the body [10].

Thus, a unified method for ultrasound examination of diaphragm function has not yet been proposed.

The aim of the study was to develop a technique for ultrasound examination of the excursion and relative thickening of the diaphragm in healthy volunteers, to propose standard values for different age groups.

MATERIAL AND METHODS

The study included 81 subjects who came to the N.V. Sklifosovsky Research Institute for Emergency Medicine for ultrasound examinations on an outpatient basis from August 2021 to March 2023. Of these, 39 were men (48.1%), 42 were women (51.9%); the mean age was 55±15 years. The exclusion criteria were as follows: presence of signs of acute respiratory infection at the time of the examination, functional class (FC) II and higher chronic heart failure (CHF) (the New York Heart Association (NYHA) classification), history of surgical interventions with thoracotomy access, neuromuscular diseases. All patients underwent ultrasound examination of the diaphragm using a Philips EPIQ 7 ultrasound machine (USA) with convex (C 5-1) and linear (eL 18-4) probes. The study was performed with the patients lying on their back. After obtaining informed consent for the study, the body mass index (BMI), height, and body surface area (BSA) were recorded for each subject.

In order to determine the excursion of the diaphragm, the convex probe was installed in the frontal plane between the posterior and middle axillary lines on the right and left to visualize the corresponding half of the diaphragm through the intercostal spaces. A clear image of the diaphragm was achieved through the liver parenchyma (on the right) or spleen (on the left) (Fig. 1).

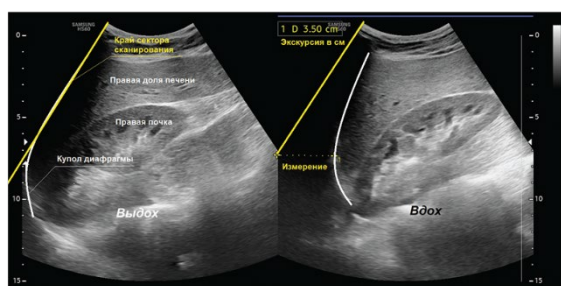


Fig. 1. Sonographic measurement of diaphragm excursion. At end-inspiration in B-mode vertical distance between hemidiaphragm and field of view left margin is measured

On tidal breathing of the patient, the probe was shifted in the cranio-caudal direction until on end-expiration the image of the hemidiaphragm approached the left margin of the field of view. Holding the probe in this position, we noted the displacement of the corresponding half of the diaphragm at end-inspiration, recorded the image, and measured the distance from the hemidiaphragm to the left margin of the field of view in the direction parallel to the scanning surface of the probe, which corresponded to the excursion of the diaphragm on tidal breathing. The measurement was repeated three times, and the average value was calculated. The excursion on forced inspiration was measured in a similar manner. The measurements were performed bilaterally. Compliance with this measurement technique allowed us to measure the true value of the diaphragm displacement in the cranio-caudal direction.

Next, the index of the functional reserve of the diaphragm for excursion (IFR(e)) was calculated:

$$\text{IFR(e)} = \frac{\text{Excursion on forced inspiration}}{\text{Excursion on tidal breathing}}$$

$$\text{IFR(e)} =$$

The diaphragm thickness was measured using a linear probe. In the scanning program settings, auxiliary visualization modes — tissue harmonic and multiplanar imaging — were disabled. The probe was positioned in the frontal plane between the posterior and middle axillary lines and moved vertically until a clear image of the m.phrenicus at the site of its attachment to the ribs was obtained. To improve the quality of visualization, the probe was allowed to rotate by 5–15 degrees counterclockwise (on the right) or clockwise (on the left) for orientation along the intercostal space (Fig. 2).

The diaphragm thickness was measured after fixing the image on the screen during end-expiration, tidal and forced inspiration. The markers of the electronic measuring device were positioned perpendicular to the muscle fiber orientation from the middle of one hyperechoic line corresponding to the diaphragmatic peritoneum to the middle of a similar in structure line corresponding to the diaphragmatic pleura. All three measurements were performed without changing the tilt of the probe or moving it. The measurements were repeated three times, then the series of measurements with the lowest values was selected, which corresponded to the probe position closest to orthogonal one relative to the diaphragm.

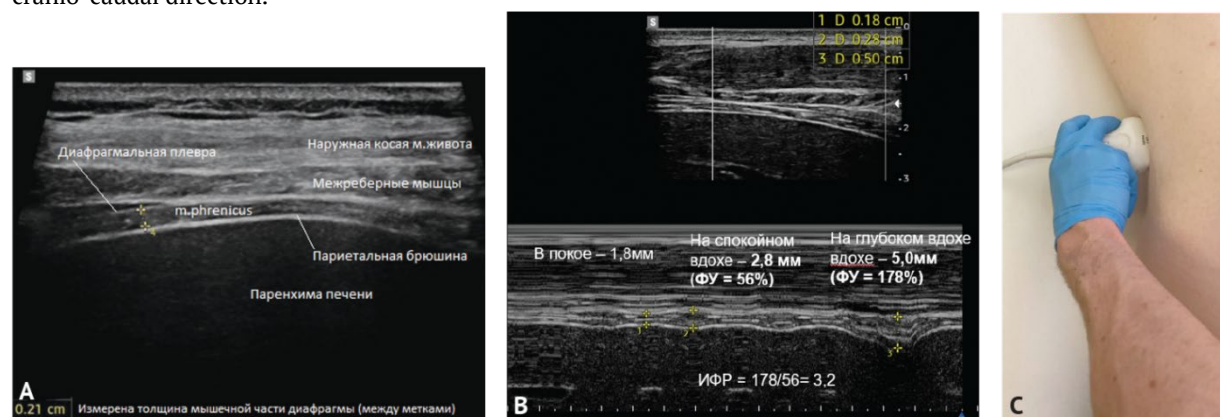


Fig. 2. Sonographic measurement of diaphragm thickness on end-expiration, tidal and forced inspiration. Calculation of TF_1, TF_2, IFR(t). A—ultrasonographic image with captions; Diaphragm thickness measurement is done perpendicular to muscle fibers orientation, between two hyperechoic lines representing diaphragmatic pleura and peritoneum. B—calculation of TF_1, TF_2, IFR(t); For the sake of clarity, all three thickness measurements are done in M-mode. B—positioning of an ultrasound probe. Scanning plane is frontal, perpendicular to diaphragm excursion direction

Notes: ИФР(т)— functional reserve index for thickening; ФУ_1— thickening fraction during tidal breathing; ФУ_2— thickening fraction during deep inhalation

Next, the fraction of diaphragm thickening (TF) on tidal breathing (TF₁) and forced inspiration (TF₂) was calculated:

$TF_1 = (\text{Thickness on tidal breathing} - \text{Thickness on end-expiration}) / \text{Thickness on end-expiration} \times 100\%$,

$TF_2 = (\text{Thickness on forced inspiration} - \text{Thickness on end-expiration}) / \text{Thickness on end-expiration} \times 100\%$

Also index of the functional reserve for thickening (IFR(t)):

$IFR(t) = TF_2 / TF_1$

$IFR(t) =$

After all measurements were performed by Operator 1 — an ultrasound specialist with 5 years of independent work experience in the specialty and 1 year of ultrasound examination of the diaphragm (at the start of recruitment of subjects), — Operator 2 — a clinical resident and later an ultrasound specialist, — measured the maximum excursion of the diaphragm on the right and on the left, the thickness of the diaphragm on end-expiration, tidal and forced inspiration, calculated TF₁, TF₂, IFR(t), IFR(e). Operator 2 was blinded to the measurements of Operator 1.

The normality of distribution was assessed using the Shapiro-Wilk test and a graphical method (the quantile-quantile plot). For distributions different from normal, the result was described as "Median (2.5th percentile; 97.5th percentile)"; and the statistical significance of intergroup differences was assessed using the nonparametric Mann-Whitney U test. The significance of intergroup differences in qualitative characteristics was assessed using the chi-square test. The presence of a linear relationship between quantitative values was assessed using the Pearson correlation coefficient and linear regression with direct stepwise selection of regressors based on the value of the Akaike information criterion with preliminary data transformation using the Box-Cox transformation. Interobserver reproducibility of ultrasonographic parameters was assessed using the Bland-Altman method and the intraclass correlation coefficient. Taking into account the limited sample size and the fact that the distribution of most indicators differs from the normal one, the reference intervals were determined nonparametrically, using percentiles. 95% confidence intervals (CI) for the lower and upper bounds of the reference intervals

were determined using bootstrapping (for measurements less than 120) or nonparametric methods (for measurements more than 120), according to generally accepted recommendations (Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline—3rd Edition (C28-A3)). Single outliers were determined using the Cook distance method among the values of all the studied variables; they were not taken into account when calculating the reference intervals. For statistical calculations, the following software was used: Microsoft Excel 2007, MedCalc 23.0.5, RStudio 2023.03.0.

RESULTS

Visualization of the diaphragm on both sides with assessment of the excursion and thickness of the diaphragm on end-inspiration and end-expiration was successfully performed in 100% of subjects. To evaluate the influence of age on the assessed parameters, all subjects were additionally divided into three subgroups:

— subgroup 1 — 18–45 years old — 24 people, of which 10 (41.7%) were women and 14 (58.3%) were men;

— subgroup 2 — 46–59 years old — 27 people, of which 15 (55.6%) were women, 12 (44.4%) were men;

— subgroup 3 — 60 years and older — 30 people, of which 17 (56.7%) were women, 13 (43.3%) were men.

In terms of gender structure, the subgroups were homogeneous ($p=0.468$).

According to the results of the Shapiro-Wilk test and graphical assessment, statistically significant deviations from the normal distribution for age, height, BMI, BSA were not revealed ($p > 0.05$). The distribution of the values of maximum excursion on the right and left, TF on forced inspiration on the right and on the left, TF on tidal breathing on the left, IFR (e) and IFR (t) on the right and on the left significantly differed from normal, namely, the distribution of values for all parameters was characterized by positive asymmetry (skewed to the right); after data transformation, the distribution of all parameters was normalized (Fig. 3). According to the correlation analysis, a number of statistically significant correlation dependencies were identified (Fig. 4)

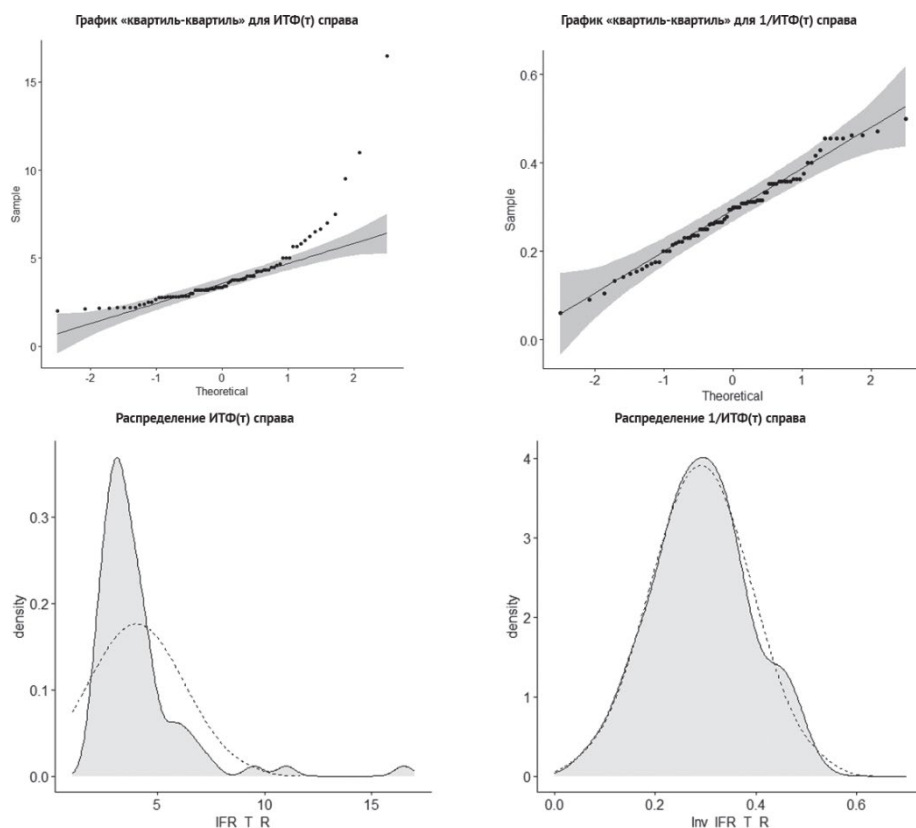


Fig. 3. Box–Cox transformation of functional reserve index for thickening (IFR(t)) values for right hemidiaphragm for normalization of the parameter distribution. Theoretical normal distribution is shown with dotted line, actual data distribution – with solid line and gray fill. After data transformation the two distributions are close to each other

Note: Inv_IFR_T – functional reserve index for thickening, transformed values

From the data of the correlation matrix (Fig. 4) it follows that there is a high degree of statistically significant multicollinearity (mutual dependence) between the parameters under study: statistically significant correlations are observed between patient characteristics (age, gender, height, BMI, BSA) and ultrasonographic parameters of diaphragm function, as well as between different ultrasonographic parameters of diaphragm function.

To determine the independent influence of each of the patient characteristics on the value of the ultrasonographic parameters of the diaphragm function, a linear regression analysis was performed (Table 1).

According to the linear regression analysis:

— the excursion of the diaphragm on forced inspiration on the right and left statistically

significantly decreases with age ($p < 0.001$) and has higher values in males ($p = 0.0147$) (Fig. 5);

— diaphragm thickness on end-expiration (at rest) increases with increasing BSA ($p < 0.001$), and does not depend on age;

— TF_1 on the left decreases with increasing BMI ($p = 0.0483$);

— IFR(t) on the right slightly but statistically significantly decreases with age ($p = 0.0295$), and the lower limit of the reference interval does not depend on age (Table 1);

— for the remaining indicators, including TF_2, IFR(t) on the left, IFR(e) on the right and on the left, no statistically significant regressors were identified ($p > 0.05$).

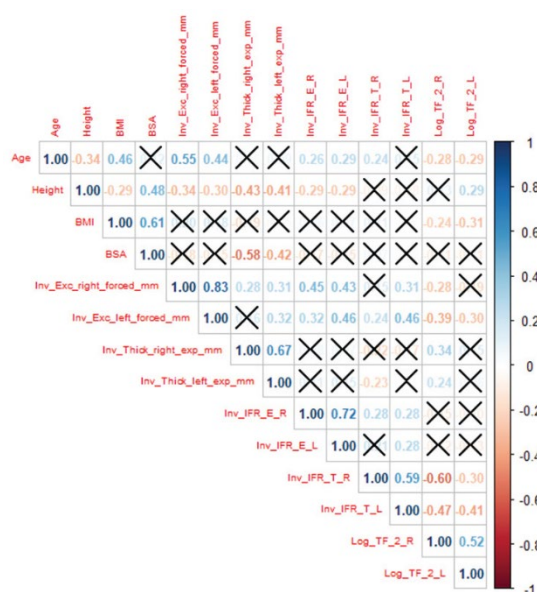


Fig. 4. Correlation matrix of main sonographic diaphragm function parameters of study subjects

Notes: The number in the cell is the value of the Pearson correlation coefficient between the parameters specified in the row and column headings, the font color corresponds to the coefficient value on the scale shown on the right. Sign "X" in a cell means no statistically significant relation between parameters in the corresponding column and line. BMI — body mass index; BSA— body surface area; Inv_Exc_right_forced_mm — maximal excursion of right hemidiaphragm (values transformed with inverse power function); Inv_Thick_right (left)_exp_mm — right (left) m. phrenicus thickness (values transformed with inverse power function); Inv_IFR_E_R(L) — functional reserve index for excursion of right (left) hemidiaphragm (values transformed with inverse power function); Inv_IFR_T_R(L) — functional reserve index for thickening of right (left) m.phrenicus (values transformed with inverse power function); Log_TF_2_R(L) — thickening fraction for deep inhalation for right (left) hemidiaphragm (values transformed with inverse log function)

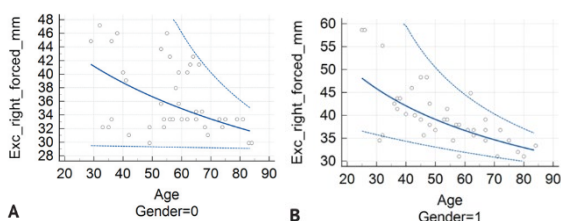


Fig. 5. Graphic representation of maximal right hemidiaphragm excursion depending on age in females (A) and males (B). Regression curves are shown by solid lines, 95% confidence bounds — by dotted lines

Table 1

Regression analysis output: diaphragm ultrasonographic parameters and subject characteristics

	Estimated value of the regression coefficient (b_1)	Standard error	Statistical significance (p)
Maximum excursion ON THE RIGHT **			
Constant (b_0)	0.0003978	0.00007552	0.00000119*
Age	0.000007093	0.000001249	0.000000223*
Male gender	0.00009339	0.00003744	0.0147*
Maximum excursion ON THE LEFT **			
Constant (b_0)	0.0004219	0.00008589	0.00000486*
Age	0.000005761	0.000001420	0.000117*
Male gender	0.001156	0.00004258	0.008134*
Diaphragm thickness on end-expiration ON THE RIGHT**			
Constant (b_0)	0.9732	0.10391	<0.00000001*
Body surface area	-0.33251	0.05288	0.0000000166*
Diaphragm thickness on end-expiration ON THE LEFT **			
Constant (b_0)	0.92039	0.09043	<0.00000001*
Body surface area	-0.18767	0.04602	0.000108*
Thickening fraction on tidal inspiration ON THE LEFT			
Constant (b_0)	3.358291	0.242678	<0.00000001*
Body mass index	-0.01758	0.008765	0.0483*
Functional reserve index for thickening ON THE RIGHT **			
Constant (b_0)	0.2067904	0.0393417	0.0000012*
Age	0.0015359	0.0006929	0.0295*

Notes: * — $p < 0.05$; ** — values of independent variable are transformed with inverse power function, hence positive regression coefficient means inverse relationship and visa versa

Taking into account the identified regressors, reference values of the considered ultrasonographic parameters by subgroups are proposed (Table 2).

As can be seen from the table, the reference intervals for the diaphragm excursion on tidal and forced inspiration differ depending on gender and age group. The thickness of the diaphragm on end-expiration increases with increasing BSA. The TF of the left half of the diaphragm on tidal inspiration decreases with increasing BMI. The lower limits of the reference intervals for IFR (e) and IFR (t) are the same for the right and left hemidiaphragms and do not depend on gender, age, BMI and BSA.

Table 2

Reference ranges for main sonographic parameters of diaphragm function

Indicator	Subgroup	2.5 percentile (95% CI)	97.5 percentile (95% CI)
Right excursion (tidal inspiration), mm	18–45 years old	16 [15–16]	26 [26–29]
	46–59 years old	15 [14–15]	23 [23–25]
	60+ years old	15 [14–15]	22 [22–23]
Left excursion (tidal inspiration), mm	18–45 years old	16 [14–16]	28 [28–30]
	46–59 years old	15 [13–15]	24 [24–28]
	60+ years old	16 [15–16]	22 [22–23]
Maximum excursion on the right, mm	Women 18–45 years old	31 [29–31]	47 [47–49]
	Women 46–59 years old	30 [26–30]	46 [46–52]
	Women 60+ years old	30 [28–30]	43 [43–45]
	Men 18–45 years old	35 [29–35]	59 [59–69]
	Men 46–59 years old	31 [25–31]	48 [48–58]
	Men 60+ years old	31 [29–31]	45 [45–53]
Maximum excursion on the left, mm	Women 18–45 years old	29 [24–29]	53 [53–58]
	Women 46–59 years old	31 [28–31]	47 [47–55]
	Women 60+ years old	30 [28–30]	43 [43–45]
	Men 18–45 years old	36 [29–36]	62 [62–74]
	Men 46–59 years old	28 [17–28]	58 [58–71]
	Men 60+ лет	31 [25–31]	47 [47–54]
Thickness at end-expiration on the right, mm	Body surface area up to 1.80 m ²	1.4 [1.3–1.4]	1.7 [1.7–1.8]
	Body surface area 1.81–1.95 m ²	1.4 [1.4–1.4]	2.3 [2.3–2.7]
	Body surface area 1.96–2.10 m ²	1.6 [1.5–1.6]	2.4 [2.4–2.5]
	Body surface area from 2.11 m ²	1.6 [1.5–1.6]	2.4 [2.4–2.5]
Thickness at end-expiration on the left, mm	Body surface area up to 1.80 m ²	1.5 [1.4–1.5]	1.9 [1.9–2.1]
	Body surface area 1.81–1.95 m ²	1.4 [1.4–1.4]	2.2 [2.2–2.4]
	Body surface area 1.96–2.10 m ²	1.6 [1.5–1.6]	2.2 [2.2–2.2]
	Body surface area from 2.11 m ²	1.6 [1.4–1.6]	2.5 [2.5–2.9]
Thickening fraction on tidal inspiration on the right, %		11 [8–11]	38 [38–40]
Thickening fraction on tidal inspiration on the left, %	Body mass index under 25.0	6 [6–6]	44 [44–54]
	Body mass index 25.0–29.9	11 [6–11]	33 [33–38]
	Body mass index 30.0–34.9	11 [6–11]	39 [39–44]
	Body mass index from 35.0	8 [2–8]	19 [19–29]
Thickening fraction on forced inspiration on the right and left, %		44 [35–52]	139 [129–144]
Index of the functional reserve for excursion on the right and on the left		1.7 [1.5–1.7]	2.4 [2.3–2.5]
Index of the functional reserve for thickening on the right and on the left		2.1 [1.7–2.2]	7.3 [6.5–7.5]

Note: CI – confidence interval

Interobserver reproducibility of sonographic parameters of diaphragm function was assessed using two methods: the intraclass correlation coefficient and Bland-Altman plot (Table 3).

High values of the intraclass correlation coefficients and narrow ranges of agreement with respect to the measured values indicate sufficient interobserver reproducibility. The difference in measurements of all parameters between the operators does not differ significantly from 0 ($p>0.05$), which allows us to conclude that there is no statistically significant systematic measurement error.

DISCUSSION

To measure the diaphragm excursion, a method was chosen with the placement of the ultrasound probe between the middle and posterior axillary lines along the intercostal spaces in the frontal plane. The method proposed by a number of authors using the M-mode along the midclavicular line does not always allow achieving orthogonal orientation of the of the field of view relative to the diaphragm. In addition, in patients with constitutional features who are not prepared for the examination, visualization of the left half of the diaphragm by this approach during the expiration phase is not always possible [11]. When assessing the excursion of the diaphragm from the subcostal approach along the midclavicular line in a standing position, measuring the excursion of the left hemidiaphragm is possible only in 21.4% of subjects [12]. When using the subcostal approach, the absolute error in determining the diaphragm excursion during forced inspiration reaches 10 mm, the relative error in determining the excursion of the left half exceeds 30% of the measured value [13]. Based on the literature data on the lower reproducibility of left-sided indicators, this study assessed interobserver reproducibility specifically for them.

A method for measuring the excursion of the diaphragm relative to the right renal hilum with the patient in a semi-sitting position (the head of the bed at an angle of 30–45 degrees to the horizontal) is described [14]. The reproducibility of measurements obtained by this method is questionable, since the kidney normally moves during breathing.

Table 3

Reproducibility of sonographic parameters of diaphragm function

Parameter	Intraclass correlation coefficient (with 95% CI)	Lower bound of 95% agreement limits	Upper bound of 95% agreement limits	Average difference in measurements between two operators (with 95% CI)
Maximum excursion on the right, mm	0.93 [0.89–0.96]	-5	+7	1 [0–2]
Maximum excursion on the left, mm	0.95 [0.91–0.96]	-6	+7	1 [0–2]
Thickness at rest on the left, mm	0.91 [0.86–0.94]	-0.3	+0.2	0 [-1–0]
Thickening fraction on tidal inspiration on the left, %	0.91 [0.86–0.94]	-11	+10	0 [-1–+1]
Index of the functional reserve for excursion on the left	0.81 [0.70–0.88]	-0.5	+0.4	-0.1 [-0.1–0]
Index of the functional reserve for thickening on the left	0.96 [0.95–0.98]	-1.3	+1.4	0 [-0.2–+0.2]

Note: CI – confidence interval

According to Skaarup et al., the diaphragm excursion values obtained by ultrasound examination in M-mode from the subcostal approach along the midclavicular line are more consistent with fluoroscopic measurements than similar data obtained using the lateral approach. However, the authors refer to the Houston method, which involves placing the probe between the midclavicular and midaxillary lines, but do not specify in what specific position the probe was located when measuring the excursion, and this could have had a significant impact on the measurement results [10, 15].

Visualization of the diaphragm from the intercostal acoustic window along the midaxillary line in the frontal plane allows for visualization in all subjects, both on the right and on the left. The value of the diaphragm excursion on forced inspiration of less than 25 can be used as a sign of its pronounced dysfunction [16]. This study proposes a lower limit for the normal maximum excursion of the right half of the diaphragm from 28 to 35 mm, depending on the side of the study, gender and age of the subjects, which does not contradict the literature.

The values obtained by measuring the diaphragm thickness in the supine position have no less high reproducibility than those obtained by measuring in the vertical position [17]. Similar data were demonstrated in our study, which allows us to recommend the use of this technique in patients in critical condition. In a vertical position of the body, the thickness of the diaphragm both at rest and on forced inspiration is on average 20% higher than in a horizontal position; however, the ratio of the thickness on end-inspiration and at rest remains

constant, which makes it appropriate to use calculated indices of relative thickening of the diaphragm on end-inspiration [18].

When measuring the thickness and thickening fraction of the diaphragm in patients on mechanical ventilation in the supine position, the values for the right hemidiaphragm are characterized by sufficient intra- and interobserver reproducibility, especially when marking the probe position for repeated measurements. The frequency of successful visualization of the left half of the diaphragm is insufficient to measure the corresponding parameters in most patients [2]. The diaphragm thickening fraction decreases with increasing respiratory support pressure and tends to zero during muscle relaxation. Moreover, it has been shown that when the inspiratory volume is less than 50% of the vital capacity of the lungs, the relative thickening of the diaphragm is almost entirely due to its contractile activity; and at values of inspiratory volume approaching the vital capacity of the lungs, passive displacement of the diaphragm makes a significant contribution to the value of TF. Therefore, the use of the diaphragm thickening fraction as a surrogate for its muscular activity during tidal breathing is justified, which further explains the appropriateness of calculating the diaphragm TF [2].

When measured in the supine position, the thickness of the diaphragm at end-expiration in men, according to published data, is statistically significantly higher than in women (0.19 ± 0.04 cm and 0.14 ± 0.03 cm, respectively). The dependence of the diaphragm thickness on the chest circumference and body mass index does not reach the level of

statistical significance [19]. When measured in the supine position, it was shown that the thickness of the diaphragm statistically significantly correlates with the height, weight and body mass index of the subjects, and in men, the diaphragm thickness is significantly greater than in women [20]. When examined in a sitting position, the diaphragm thickness in women is statistically significantly less than in men, but TF does not depend on gender [21]. According to Shabaev et al. (2023), ultrasound examination of the diaphragm in the supine position in healthy volunteers reveals gender differences in diaphragm thickness in all phases of respiration, as well as in the magnitude of the maximum excursion measured from the subcostal approach along the midclavicular line on the right [11]. The diaphragm thickness is greater in men than in women, and the diaphragm thickness increases with increasing body mass index; age and gender do not significantly affect the diaphragm thickness and TF [22]. The use of regression analysis in this study demonstrated that BSA is the only independent predictor of resting end-expiratory diaphragm thickness, and that age and gender differences are secondary to BSA values in the respective subgroups.

When measuring the thickness of the diaphragm, the reproducibility of the obtained values is higher in the M-mode, but in the hands of an experienced operator in the B-mode, the values are also characterized by sufficient reproducibility, and the visualization of the left half of the diaphragm is also satisfactory [2]. This study demonstrated sufficient interobserver reproducibility of thickness measurements for the left hemidiaphragm.

It was shown that the highest reproducibility is demonstrated by the diaphragm thickness values obtained by measuring along the midaxillary line [23]. This does not contradict the methodology described in this study.

Limitations of the study

The potential limitations of this study include, first of all, the small sample size. However, its structure was balanced by age and gender indicators, and all proposed reference values were given with confidence intervals, statistical criteria — with levels of statistical significance. The interobserver reproducibility values were determined mainly for the left hemidiaphragm, which is due to the literature data on comparable or lower interobserver reproducibility for ultrasound values of the left half of the diaphragm.

CONCLUSION

A technique for ultrasound examination of diaphragm function using intercostal bilateral acoustic access is proposed. The possibility of ultrasound visualization of the right and left hemidiaphragm in all subjects with subsequent calculation of the thickening fraction for tidal and forced inspirations has been proven. For the first time, it has been proposed to calculate ultrasound indices of the functional reserve for excursion and thickness — indicators characterizing the ratio of excursion and relative thickening indices obtained during tidal and forced inspiration. The lower limits of the reference intervals for the indices of functional reserve for thickness and excursion to the right and left are universal for all age and gender groups, and the examined constitutional characteristics of the subjects. High interobserver reproducibility of the examined ultrasonographic parameters is confirmed.

FINDINGS

1. For bilateral ultrasound examination of the diaphragm, it is proposed to use the intercostal approach between the posterior and midaxillary lines.

2. The excursion and thickness of the diaphragm measured by ultrasound examination are characterized by dependence on the age, gender and constitutional characteristics of the subjects:

- the excursion of the diaphragm during tidal inspiration statistically significantly decreases with age (on the right - from 16-26 to 15-22 mm, on the left - from 16-28 mm to 16-22 mm) ($p < 0.05$);

- maximum excursion of the diaphragm statistically significantly decreases with age, in men the maximum excursion is greater ($p < 0.05$);

- the thickness of the diaphragm at rest is statistically significantly directly dependent on the body surface area, increasing on the right from 1.4–1.7 mm (BSA less than 1.81 m²) to 1.6–2.4 mm (BSA from 2.11 m²); on the left - from 1.5–1.9 mm (BSA less than 1.81 m²) to 1.6–2.5 mm (BSA from 2.11 m²);

- the thickening fraction for tidal inspiration on the left statistically significantly decreases with increasing BMI ($p < 0.05$);

- thickening fractions for tidal inspiration on the right, for forced inspiration on the right and left do not statistically significantly depend on age and gender characteristics ($p < 0.05$).

3. The lower limit of the reference interval for IFR(e) and IFR(t) does not depend on the age, gender

and constitutional characteristics of the subjects, therefore universal lower reference limits are proposed - 1.7 and 2.1, respectively.

4. All the examined ultrasound indices of diaphragm function are characterized by sufficient interobserver reproducibility: the intraclass

correlation coefficients ranged from 0.81 for IFR (e) on the left to 0.96 for IFR(t) on the left; statistically significant systematic error in measuring all the examined indices by the two operators was not detected ($p > 0.05$).

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