The Role of Ultrasound in Assessment of Diaphragmatic Dysfunction in I.C.U Patients

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Abstract:

Background: Diaphragm dysfunction (DD) is frequently seen in critically ill patients, and ultrasound could be a useful tool to detect it and to predict extubation success or failure in mechanically ventilated patients. Besides, it would also be useful in differential diagnosis of dyspnea and respiratory failure. **Aim of work :**The aim of work is to evaluate usefulness and accuracy of ultrasound in assessment of DD in intensive care unit (ICU) patients in comparison with clinical outcome of patients.. In this prospective study, we compared the performance of ultrasound in visualization of diaphragm, detection of paradoxical movement, measurement of tidal and maximal thickness, and excursion, and calculation of thickening fraction (TF) of the diaphragm in quiet breathing. **Patients and Method:** The present study was performed on50 patients (26 males and 24 females) admitted in RICU in Benha university hospital The field study was conducted from March 2019 to September 2019. Ultrasound of the Rt, hemidiaphragm was done on the day of admission or soon after admission (1-2) days**. Results:** there was no statistical significant difference between the studied groups regarding ultrasound measurement (DTF, DE and DT) and patient outcome with p value (0.273,0.245 and 0.497)respectively .**Conclusion:** ultrasound of diaphragm in ICU patients may be a reliable, noninvasive and convenient way to assess the DD in ICU patients to predict their outcome.

Key words: Diaphragm ultrasound; Diaphragm Dysfunction; Diaphragm Excursion; Diaphragm Thickness

Introduction

The diaphragm is the principal respiratory muscle. With an excursion of 1 to 2 cm, the diaphragm provides nearly 75% of the resting pulmonary ventilation, while during the forced breathing, its amplitude is up to 7 to 11cm.(1)**.** Abnormal diaphragmatic motion is

observed in conditions such as phrenic nerve injury, neuromuscular diseases, after abdominal or cardiac surgery and in critically ill patients under mechanical ventilation**(2.3)]**, in addition the diaphragm is vulnerable to damage from hypotension, hypoxia, and sepsis, all of which are very common in critically ill patients. While in surgical patients, diaphragm dysfunction is often caused by acute insults such as trauma or surgical procedures. In addition, mechanical ventilation itself can decrease the force of the diaphragm and induce diaphragmatic dysfunction, named as ventilator-induced diaphragmatic dysfunction **(4.5).**

Diaphragm dysfunction is responsible for a number of pulmonary complications, an early diagnosis of diaphragm dysfunction (before extubation) is mandatory to avoid weaning failure **(6).**

including atelectasis and pneumonia, which are risk factors for extubation failure. Hence,

The use of tools previously available for assessment of diaphragmatic dysfunction is limited due to the associated risks of ionizing radiation (fluoroscopy, computed tomography) or due to their complex and/or highly specialized nature, requiring a skilled operator (transdiaphragmatic pressure measurement, diaphragmatic electromyography, phrenic nerve stimulation, magnetic resonance imaging **(7)** Bedside Ultrasonography US has become a valuable tool in the management of intensive care unit patients. Fig. 1,2 **(8).** This is especially true in emergency situations where an adequate imaging technique is frequently limited by a variety of factors, including difficulty of patient transportation to the radiology department due to illness severity .US is a noninvasive technique, which has proved to be an accurate, safe, easy to use bedside modality, overcoming many of the standard limitations of imaging techniques.(9)

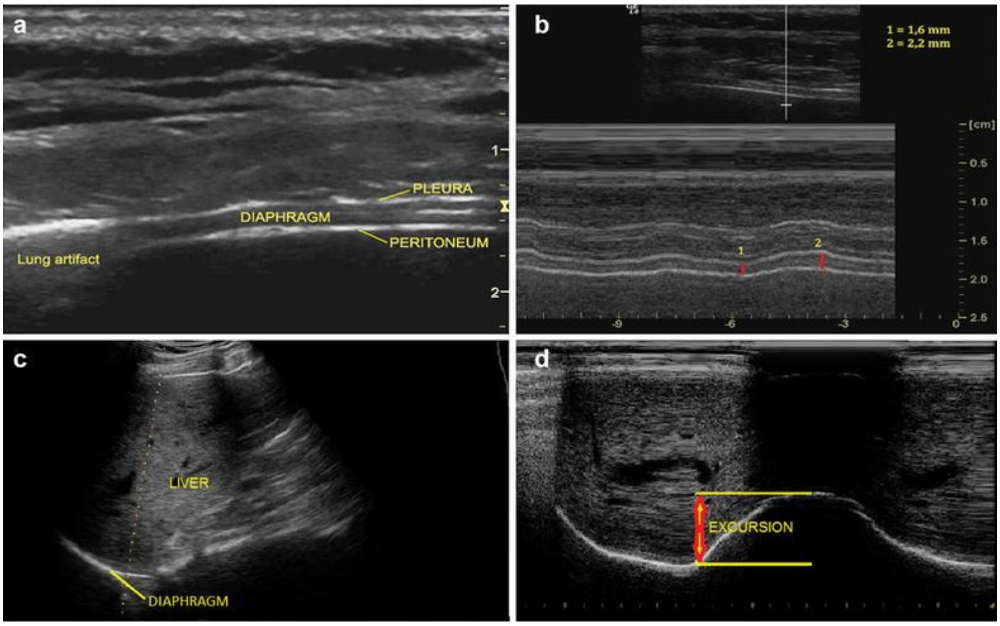
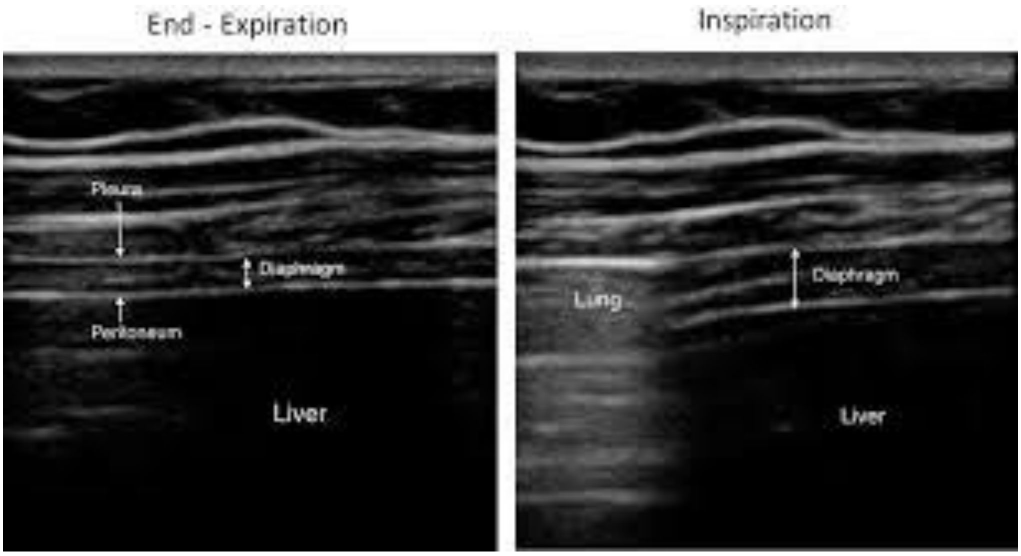


Fig.(1): Diaphragm ultrasonography (DU) at the zone of apposition in **a** B-mode, **b** M-mode. *1* Thickness at end expiration, *2* thickness at end inspiration.DU, right subcostal in **c** B-mode, **d** M-mode



(Fig.2): Ultrasound image of diaphragm showing change in thickness during inspiration and expiration(8)

Aim of The work:

The aim of this work is to evaluate the role of US in assessment of diaphragmatic dysfunction in ICU patients.

Patients and method:

This prospective study was performed aiming to determine the role of ultrasound in diagnosis of diaphragm dysfynction and prediction of patient outcome

Study population

- The study was conducted on **50** patients (26 male 52% and 24.female 48%)
- Those patients were admitted to the Respiratory intensive care unit (RICU) in chest department Benha University Hospital .during the period between March 2019 and September2019.
- The study was approved by the Ethical Clearance Committee of Benha university.
- Informed consent was obtained from all patients or their relatives
- The same investigator performed all the recordings
- Diaphragm thickness and excursion (via B-mode ultrasonography) was measured done by ultrasound machine PHILIPS HD5 on the day of admission or soon after admission (1-2) days**.**
- The whole ultrasound examination was accomplished In(20-25) min
- Only the right hemidiaphragm was studied, as the limited acoustic window offered by the spleen does not always allow obtaining clear images on the left; intestinal or gastric gas may also interfere with imaging of the left diaphragmatic dome.

Inclusion criteria:

1. Patients admitted to I.C.U. with clinical suspicion of diaphragmatic dysfunction who will undergo detailed US for diaphragm.
2. The patients will approve to participate in the study

Exclusion criteria:

1. Patients admitted to I.C.U. with no clinical suspicion of diaphragmatic dysfunction .
2. Patients admitted to I.C.U. with clinical suspicion of diaphragmatic dysfunction who will undergo detailed US for diaphragm and refuse to participate in the study
3. Hemodynamically unstable patient.

Methods:

All the following data were collected for each patient

- Complete history taking including medical and surgical history.
- Complete physical examination (General and Chest examination).
- Laboratory evaluation
- Real-time thickness of the diaphragm was recorded by B- mode ultrasonography using 10 MHz linear transducer. Diaphragmatic excursion should be measured with a lower frequency curvilinear probe (we used a 3-5 MHz probe) in anterior subcostal view.

Results:

This prospective study included 50 patients(26 males 52% and 24 female48%) who were admitted to the Respiratory intensive care unit (RICU) in chest department Benha University Hospital .during the period between March 2019 and September2019.

Data management and statistical analysis were performed using the Statistical Package for Social Sciences (SPSS) version 24. Numerical data were summarized using means and standard deviations or medians and ranges. Data were explored for normality using Kolmogrov-Smirnov test and Shapiro-Wilk test. Categorical data were summarized as percentages. Comparisons between the 2 groups with respect to normally distributed numeric variables were done using the independent t-test. Non-normally distributed numeric variables were compared by Mann-Whitney test. For categorical variables, differences were analyzed with χ^2 (Chi square) test and Fisher's exact test when appropriate. All p-values are two-sided. P-values ≤ 0.05 were considered significant Roc curve were used to detect cut off point that will determine the bad outcome.

The results of the study will be presented under the following sections:

1. Socio-Demographic characteristics of the participants.
2. vital signs and laboratory results
3. Radiological results
4. Factors affecting patients' outcome

Roc curve to detect cut off point for Radiological measures effect on patients outcome

1. **Socio-Demographic characteristics of the participant**s.

The mean age of cases was 62.1±17.8 year ranging from 17 to 85 years. Female represented the majority of cases 52%. The mean duration of ICU stay was a (13.5±9.3 day) ranging from (3 to 47). Forty four patients had comorbid diseases; 16 (32%) had DM, 14 patients 28% had COPD or ILD and 6 patients (12%) had DVT. The main cause of admission in ICU was pneumonia (24 patients; 48%).followed by ARF 14 patients 28% then COPD 11 patients 22%, the last is pulmonary embolism 4 patients 8%. The majority of cases (40 patients; 80%) discharged from ICU to chest department ward and (10 patients 20% died), table (1), fig 3,4,5.

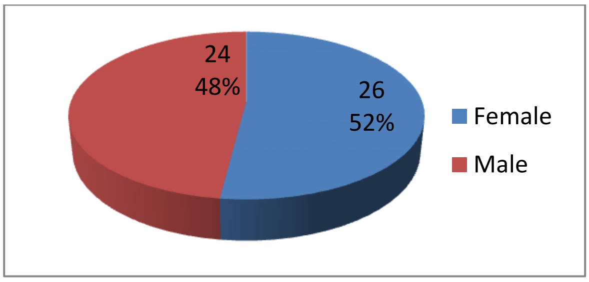


Fig.(3): pie chart representing gender distribution of the studied patients

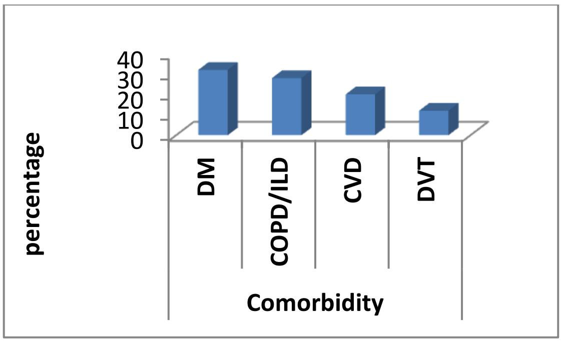


Fig.(4): Bar chart representing comorbidity distribution of the studied patients

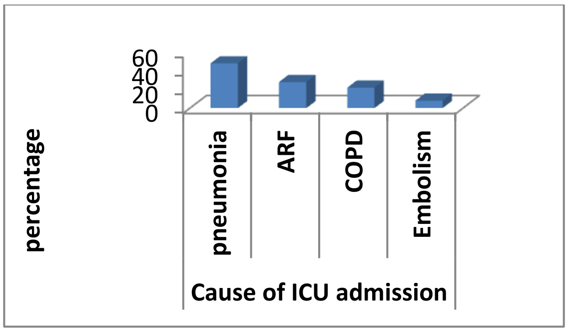


Fig.(5): Bar chart representing causes of ICU admission of the studied patients

2. vital signs and laboratory results

The mean systolic blood pressure was 116±15. with range100 to160 The mean diastolic blood pressure was 73±1 with range 60 to 100. The mean temperature was 37.4±0.9. with range 36.5 to 40.5 The mean pulse was 90±12 with range 65 to 120 The mean respiratory rate was 25±6. with range 13 to 45 (table 2,3).

3.Radiological results.

The mean DTF was 54.25±31.38 with range 9.21 to 132.5. The mean diaphragmatic US excursion was 1.05 ±0.50 with range 0.33 to 2.42. The mean Diaphragmatic US thickening was 0.193 ±0.08 with range 0.062 to 0.407 (table 4).

4. Factors affecting patients' outcome.

Demographic: All the demographic factors were comparable between the discharged and died group of patients as shown in table (5). In died patients 29.4% had no hypertension compared to none with hypertension; this was statistically significant (p=0.015).

Vital signs: All the vital signs were comparable between the discharged and died group of patients as shown in table (6).

Laboratory findings: All the lab results were comparable between the discharged and died group of patients as shown in table (7). For platelets: there was statistically significant decrease in the dead patients For pco2: there was statistically significant decrease in the dead patients For creatinine : there was statistically significant increase in the dead patients

US findings: All the US findings were comparable between the discharged and died group of patients as shown in table (8), fig 4,5.

Roc curve to detect cut off point for Radiological measures effect on patients outcome:

All the radiological findings can't discriminate the outcome of patients (p>0.05), (table 9, 10,11), (fig. 6,7,8)

Table (1): Demographic data of the studied patients (n=50)

		Count	%
Age (years)	Mean± SD	62.1±17.8	
	Range	17-85	
Gender	Female	26	52.0
	Male	24	48.0
Comorbidity*	yes	44	88.0
	DM	16	32.0
	COPD/ILD	14	28.0
	DVT	6	12.0
	CVD	10	20.0
Cause of ICU admission*	Embolism	4	8.0
	pneumonia	24	48.0
	ARF	14	28.0
	COPD	11	22.0
Outcome	Discharged	40	80.0
	Died	10	20.0
Duration of stay (days)	Mean± SD	13.5±9.3	
	Range	3-47	

SD: standard deviation, DM; diabetes mellitus, HTN: hypertension,……..*: patients may have more than one

Table (2): Vital signs in the studied patients (n=50)

	Mean	SD	Median	Minimum	Maximum
BP. Systolic	116	15	110	100	160
BP. Diastolic	73	11	70	60	100
T	37.4	0.9	37	36.5	40.5
P	90	12	90	65	120
RR	25	6	23	13	45

Table (3): laboratory results in the studied patients (n=50)

	Mean	SD	Median	Minimum	Maximum
WBC (x10^3/cc)	10.99	4.77	10.2	4.6	23.3
Hb (gm/dl)	11.9	2.3	11.8	6.9	17.2
HCT	34	6.9	33	19.7	50.8
PLT (x10^3/cc)	241	100	222	62	534
pH	7.35	0.09	7.35	7.14	7.49
PO2	66.1	14.2	66	35	92
PCO2	42.4	19.4	39	24	117
NaCH3	24.5	11.5	21	9	63
SaO2%	86.9	10.6	91	62	97
Urea (mg/dl)	74	63	41	18	285
creat. (mg/dl)	2.09	1.98	1.3	0.7	10
Ka (mEq/L)	4.4	1	4.4	3.1	7.7
Na (mEq/L)	138	5	139	129	145

Table (4): US results in the studied patients (n=50)

	Mean	SD	Median	Minimum	Maximum
DTF	54.25	31.38	43.58	9.21	132.5
Diaphragmatic US excursion (1-2cm)	1.05	0.505	1.055	0.327	2.42
Diaphragmatic US thickening(0.24+/- 0.08 cm4)	0.193	0.08	0.186	0.062	0.407

Table (5): Demographic factors, comorbidities and cause of admission effect on patients outcome (n=50)

		Discharged- Improved (n=40)		Died (n=10)		
		Count	%	Count	%	p value
Age (yrs.)	Mean ±SD	61.0±18.9		66.4±12.4		0.397
Gender	Female	20	76.9	6	23.1	0.571
	Male	20	83.3	4	16.7	
Comorbidity	No	6	100.0	0	0.0	0.327[a]
	Yes	34	77.3	10	22.7	
DM	No	26	76.5	8	23.5	0.363
	Yes	14	87.5	2	12.5	
HTN	No	24	70.6	10	29.4	**0.015**
	Yes	16	100.0	0	0.0	
COPD/ILD	No	30	83.3	6	16.7	0.345
	Yes	10	71.4	4	28.6	
DVT	No	34	77.3	10	22.7	0.327[a]
	Yes	6	100.0	0	0.0	
CVD	No	32	80.0	8	20.0	1.000
	Yes	8	80.0	2	20.0	
Embolism	No	36	78.3	10	21.7	0.571[a]
	Yes	4	100.0	0	0.0	
Pneumonia	No	22	84.6	4	15.4	0.396
	Yes	18	75.0	6	25.0	
ARF	No	28	77.8	8	22.2	0.529
	Yes	12	85.7	2	14.3	
COPD	No	32	82.1	7	17.9	0.495
	Yes	8	72.7	3	27.3	
Duration of ICU stay	Median(range)	12(3-47)		11(5-18)		0.284

SD: standard deviation, p≤0.05 is statistically significant ,analysis done by Chi square test , a: analysis done by fisher exact test

Table (6): vital signs effect on patients outcome (n=50)

	Discharged- Improved		Died		
	Mean	SD	Mean	SD	p value
BP Systolic /mm	117	17	114	5	0.645
BP Diastolic /mm	74	12	68	8	0.133
Temperature °C	37.5	0.9	37.1	0.2	0.152
Pulse /min	89	10	93	17	0.308
RR /min	24	4	26	13	0.573

Table (7): laboratory results effect on patients outcome (n=50)

	Discharged- Improved		Died		
	Mean	SD	Mean	SD	p value
WBC (x10^3/cc)	10.66	4.94	12.3	3.96	0.336
Hb (gm/L)	11.9	1.8	11.8	3.8	0.917
HCT	33.9	5.4	34.2	11.4	0.905
PLT (x10^3/cc)	256	97	182	93	0.033
pH	7.35	0.08	7.35	0.13	0.925
PO2	66.8	13.4	63.2	17.4	0.472
PCO2	44.8	20.7	32.7	6.8	0.003
NaCH3	25.8	11.9	19.3	8.2	0.114
SaO2%	88.5	8.9	80.6	14.8	0.035
Urea (mg/dL)	67	48	102	104	0.318
Creatinine (mg/dL)	1.73	1.1	3.54	3.63	0.008
Ka (mEq/L)	4.4	1	4.4	1	0.989
Na (mEq/L)	138	5	139	5	0.910

SD: standard deviation, p≤0.05 is considered statistically significant, analysis done by independent t test

Table (8): Radiological findings effect on patients outcome (n=50)

	Discharged- Improved			Died			
	Median	Min.	Max.	Median	Min.	Max.	p value
DTF	43.58	9.21	132.5	41.7	16.8	66.9	0.273
Diaphragmatic US excursion	1.055	0.327	2.02	1.325	0.462	2.42	0.245
Diaphragmatic US thickening	0.177	0.062	0.407	0.232	0.078	0.292	0.497

min: minimum, max: maximum,p≤0.05 is statistically significant analysis done by Mann Whitney test

Table (9): DTF performance of outcome of patients:

lower cases indicates deaths				95% Confidence Interval	
Test Result Variable(s)	**Area**	**SE**	**P value**	**Lower Bound**	**Upper Bound**
DTF	0.625	0.103	0.273	0.423	0.827

SE: standard error, P≤0.05 is statistically significant

Table (10): DTF performance of DE and DT outcome of patients:

higher indicate deaths				95% Confidence Interval	
Test Result Variable(s)	**Area**	**SE**	**P value**	**Lower Bound**	**Upper Bound**
Diaphragmatic US excursion	0.631	0.133	0.245	0.371	0.891
Diaphragmatic US thickening	0.700	0.097	0.077	0.509	0.891

SE: standard error, P≤0.05 is statistically significant

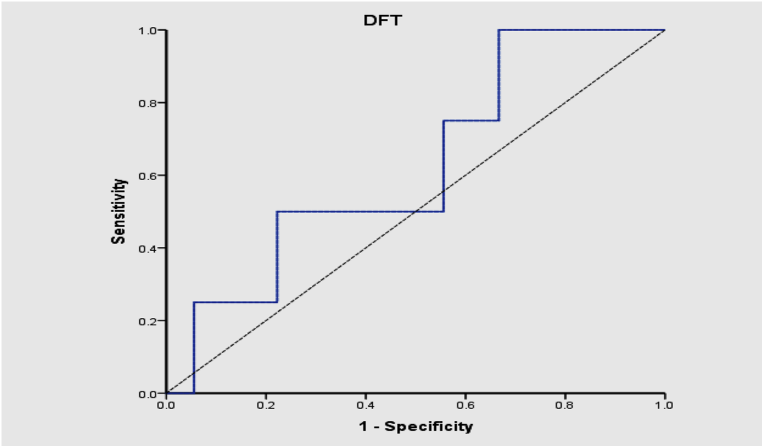


Fig.(6): ROC curve for DFT performance in detecting deaths in ICU

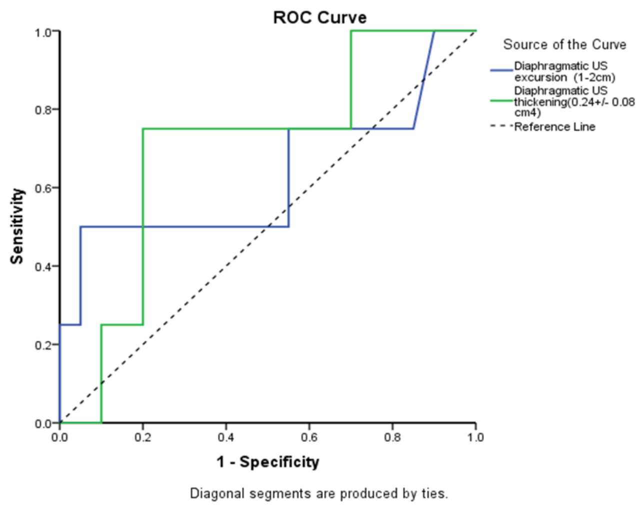


Fig.(7): ROC curve for Diaphragmatic US performance in detecting deaths in ICU

UC = 0.5	No discrimination (i.e., might as well flip a coin)
0.7 ≤ AUC < 0.8	Acceptable discrimination
0.8 ≤ AUC < 0.9	Excellent discrimination
AUC ≥ 0.9	Outstanding discrimination (but extremely rare)

Table (11): how to interpret the roc curve with significant p value

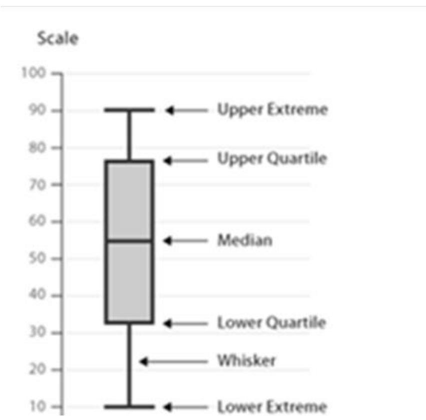


Fig.(8): Boxplot

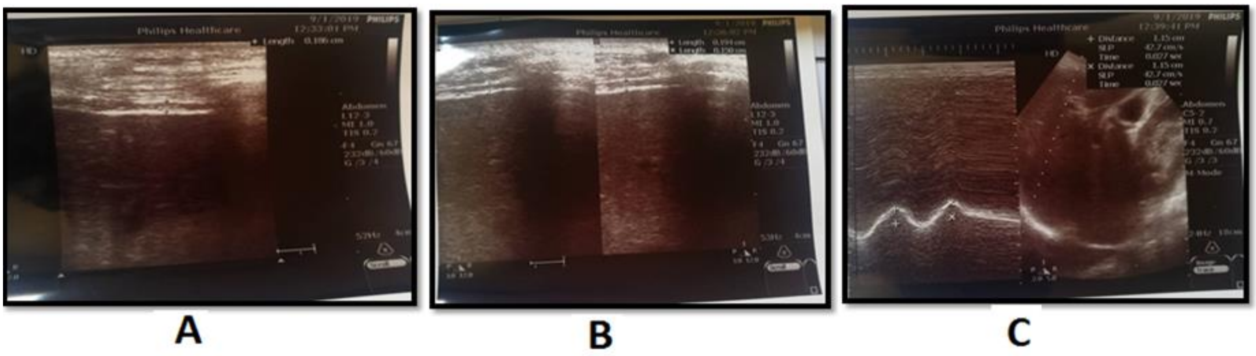


Fig.(9): A.diaphragm thickness at ZOA using superficial linear probe.B.diaphram thickness at end ispiration(+).and diaphragm thickness at end of expiration (*) C.diaphragm excursion by using convex (abdominal)probe.on the Lf.M mode trace,and on the Rt.2D image.

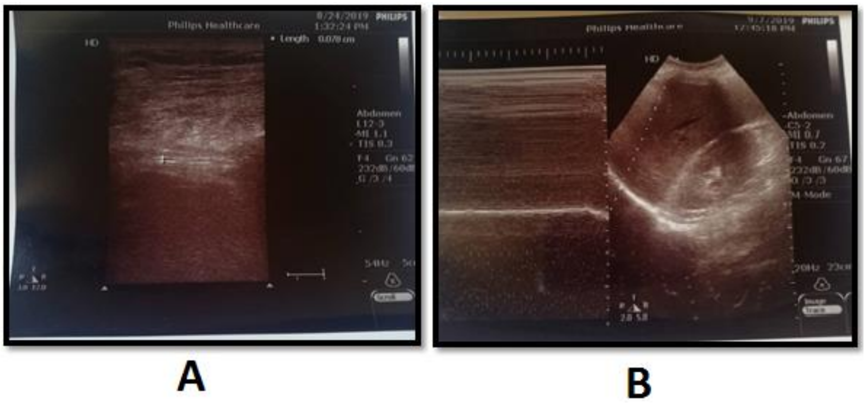


Fig.10: A. diaphragm thickness at ZOA using superficial linear probe. B. diaphragm thickness at end inspiration(+).and B. diaphragm excursion by using convex (abdominal) probe. on the Lf.M mode trace, and on the Rt.2D image.

Discussion:

In intensive care unit (ICU) patients, diaphragmatic dysfunction (DD) can occur on admission or during the subsequent stay. It has become a major concern in ICU patients and the subject of an increasing number of reports. To date, two major patterns of diaphragm dysfunction have been described in ICU patients. First, the diaphragm, like all organs, can be involved in the shock related generalized organ failure observed in many patients on admission to the ICU is determined by sepsis and the severity of the disease and is associated with higher mortality**(10)**. Second, diaphragm dysfunction in critically ill patients can occur during the ICU stay in patients without prior diaphragm dysfunction. It can be a consequence of ICU-acquired neuromuscular disorders. It can also be a negative consequence of mechanical ventilation per se, which is associated with a time-dependent decrease of diaphragm strength called ventilator-induced diaphragm dysfunction (VIDD) **(11).** In addition, diaphragm strength is also sensitive to ICU-acquired neuromuscular disorders and hypercatabolism and corticosteroid use that are frequently observed in the ICU **(12)**

However, the findings of related studies are inconsistent and lack statistical power, and the clinical significances of DE and DTF still remain controversial **(13)**demonstrated that DE correlated well with transdiaphragmatic pressure and suggested that DE could reflect diaphragmatic dysfunction. On the contrary**, it is** believed that DTF rather than DE was a reliable index of respiratory effort and diaphragmatic contractile function**. (14)** So, in our study we trying to assess role of ultrasound of the diaphragm in ICU patients and correlate the results with clinical outcome of patients.

In this study there was no statistical significant difference between the studied groups regarding the patient age. With p value 0.39, the mean ± SD for groups of study(improved and died) 61.0 ± 18.9 and 66.4 ± 12.4 respectively.

This goes on hand with **(15)** whose study was about the role of ultrasound in assessment of diaphragmatic function in chronic obstructive pulmonary disease (COPD) patients during admission to ICU which was carried on 50 patients. Patients were divided into two groups: Group A consisted of 30 COPD patients admitted to the respiratory ICU and group B consisted of 20 COPD patients during attendance at the Chest Department. found that there was no statistical significant difference between the two groups of study regarding patient's age with p value 0.18. the mean ± SD of their age was 57 ± 6 and 66.2 ± 7.1 respectively, which is nearly close to the age mean ± SD in our study.

In this work there was no statistical significant difference between the studied groups regarding ultrasound measurement (DTF, DE and DT) and patient outcome with p value (0.273,0.245 and 0.497)respectively.

This not go with **(10)** who find that there is positive correlation between ultrasound measurement (DTF, DE ,and DT).and patient outcome in term of length of stay (LOS), ICU mortality and failure of weaning from mechanical ventilation with p value (0.035, 0.041 and 0.0211) study included 43 patients divided into 2 groups.one with DD on admission (23 patients 53%) and other group with no DD on admission (20 patients 47%).

Also, these results are not going with**(16)**. *Their study aimed* to evaluate role of diaphragmatic thickening and excursion, assessed by ultrasound, in predicting patient outcome carried out on 54 patients admitted to ICU and the results of ultrasound measurements (DE,DT and DTF)show (87.5%, 77.5%, 80% and 90% sensitivity respectively and 71.5%, 86.6%, 50% and 64.3% specificity respectively.)

In our study there is no statistical significant difference between the two groups regarding diaphragmatic excursion. With (AUC =0.631, SD =0.133 and 95% Confidence Interval CI = 0.371-0.891) This agrees with**(14)** in his study on 25 patients admitted to ICU post-surgery. and found that there is no correlation between DE and patient outcome with p value 0.981.nor was between DE and DT with p value 0.450.

In other hand these results not going with**(17)** who found that there is good correlation between DE and diagnosis of DD in his study on 22 patients admitted to medical ICU . s with acute respiratory failure (ARF).and diagnose DD as follow: diaphr Gmatic paralysis defined by paradoxical movement or immobility of the hemidiaphragm during unassisted deep breathing in bidimensional mode and TM mode and diaphragmatic paresis was defined by a hemidiaphragmatic excursion of less than 10 mm during unassisted deep breathing in bidimensional mode and TM mode.

In the same way the above result is not agree with**(18)**who found that Diaphragm excursion DE seems more accurate than a change in the diaphragm thickness to predict patient outcome in his study on 60 patient admitted to ICU With (AUC =0.836, and 95% Confidence Interval CI = 0. 717-0. 919).

In our study there is no statistical significant difference between the two groups regarding diaphragmatic thickening fraction DTF and diaphragm thickness. With (AUC =0.625, SD =0.103 and 95% Confidence Interval CI = 0.423-0.827)(AUC =0.700, SD=0.097 and 95% Confidence Interval CI = 0.509-0.891) respectively.

This result is agree with (**19)** who study was designed to examine the ultrasonographic changes that occur in muscles during ICU hospitalization the study is carried out on Patients admitted to the ICU for acute respiratory failure those were enrolled prospectively and underwent serial muscle ultrasound for thickness and gray-scale assessment of the tibialis anterior, rectus femoris, abductor digiti minimi, biceps, and diaphragm muscles over 14 days. the result on diaphragm show, increased from 0.88 cm at baseline to 1.03 cm at day 14 (P = 0.024).

This result is not going with (**20)** who found that : Ultrasound measurements of diaphragm thickness (DT) and thickening fraction (DTF) may be useful to monitor diaphragm activity and detect diaphragm dysfunction (as atrophy) in ICU patients. their study was carried on 96 patients admitted to ICU and their results was right hemidiaphragm thickness was obtained on 95 % of attempts; left hemidiaphragm measurements could not be obtained consistently. Right hemidiaphragm thickness measurements were highly reproducible (mean ± SD 2.4 ± 0.8 mm, repeatability coefficient 0.2 mm, reproducibility coefficient 0.4 mm), particularly after marking the location of the probe. DTF measurements were only moderately reproducible (median 11 %, IQR 3–17 %, repeatability coefficient 17 %, reproducibility coefficient 16 %).

Conclusion:

Ultrasonography appears to be a promising tool in the evaluation of diaphragmatic function in ICU patients .It has the advantage of being fully noninvasive and is becoming widely available in an increasing number of ICUs, bypassing limitations of previously used methods for this purpose. Diaphragmatic ultrasonography provides qualitative and quantitative information regarding diaphragmatic function, as part of an overall respiratory assessment in ICU patients. Apart from clear findings, such as during diaphragmatic paralysis, ultrasonographic evaluation of diaphragmatic function may become helpful in identifying a subpopulation of ICU patients at high risk of further respiratory complications.

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