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Feasability of Diaphragmatic Speckle Tracking In Intensive Care Units

Michael Poette (poette.m@chu-toulouse.fr)

Toulouse University Hospital https://orcid.org/0000-0002-3999-9929

Laure Crognier Toulouse University Hospital

Fanny Vardon-Bounes Toulouse University Hospital

Stéphanie Ruiz Toulouse University Hospital

Bernard Georges

Toulouse University Hospital

Thierry Seguin

Toulouse University Hospital

Jean-Marie Conil

Toulouse University Hospital

Olivier Lairez

Toulouse University Hospital

Vincent Minville

Toulouse University Hospital

Research

Keywords: Diaphragm, Sonography, Speckle-tracking, Strain, Strain-rate, Intensive care, Feasibility, Reproducibility

Posted Date: November 1st, 2021

DOI: https://doi.org/10.21203/rs.3.rs-957574/v1

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Abstract

Background: Diaphragmatic dysfunction is a common condition in intensive care units (ICU). Its presence correlates with prolonged weaning from mechanical ventilation and mortality. Diaphragmatic excursion (EXdi) and thickening fraction (TFdi) are the 2 main measures currently described in diaphragmatic ultrasound, but each has its limitations. Strain and strain rate are already used cardiac sonography and could be of interest in the assessment of diaphragmatic function in ICU. The aim of this work was to evaluate the feasibility of diaphragmatic strain and strain rate in ICU and to describe their distribution, reproducibility and agreement with existing parameters.

Methods: All patients who underwent a T-tube weaning test were prospectively included. Ultrasound loops were recorded on each side of the patient during the last 30 minutes of the weaning test. Two operators measured strain, strain rate, EXdi, and TFdi blind to each other in post-treatment analysis.

Results: Thirty patients were analyzed. The median values for strain and strain rate were -6.74% and -0.23.s⁻¹ on the left side and -8.17% and -0.22.s⁻¹ on the right side. Concerning strain and strain rate, intra-class coefficients showed systematically a very good reliability between operators.

Conclusion: Diaphragmatic strain and strain rate measurements appeared feasible in an ICU environment and seemed reproducible and not strongly correlated with EXdi and TFdi. An improvement of the analysis software is needed to improve the ease of interpretation. The interest of these parameters in clinical practice should be explored in forthcoming studies.

Introduction

Diaphragmatic dysfunction (DD) is a common condition in Intensive care units (ICU) (1, 2) and has appeared to be associated with difficult weaning from mechanical ventilation, prolonged duration from mechanical ventilation and mortality (2–5). Multiple causes of DD have been described, including mechanical ventilation itself, leading to the concept of critical illness-associated diaphragm weakness (6–10).

One of the main difficulties in studying the prevalence and impact of diaphragmatic dysfunction in the ICU is a lack of suitable diagnostic tools. Indeed, the evaluation of trans-diaphragmatic pressures after bilateral transcutaneous phrenic stimulation (Twitch Pdi) is the gold-standard method for assessing diaphragmatic function in ICU but its implementation is complex and difficult to apply in daily practice (11).

Ultrasound is a rapid, non-invasive and bedside method for exploring diaphragmatic function. Diaphragmatic excursion (EXdi) and thickening fraction (TFdi) are the two mainly described sonographic parameters. EXdi is a simple measure to assess diaphragmatic function in the non-ventilated patient. In positive pressure ventilation, however, it is impossible to differentiate the patient's diaphragmatic effort from the passive movement associated with ventilator insufflation (12). Another limitation of this measurement is related to the poor echogenicity of the left subcostal window, due to the interposition of the gastric air sac. TFdi permit to assess diaphragm contraction through the zone of apposition. Despite a good correlation with the electrical activity of the diaphragm (EAdi) and trans-diaphragmatic pressure (Pdi) in the non-ventilated patient (13, 14), the reproducibility of TFdi remains moderate (15). To date, the correlation of EXdi and TFdi with clinical outcomes, such as the predictability of weaning failure when performed during a weaning test, is still debated (16–19).

Speckle tracking is an image analysis method widely used in cardiac ultrasound to assess segmental myocardial contractility (20–24). It allows the study of the strain and strain rate of a tissue by sampling groups of pixels (speckle) in a region of interest (ROI) and tracking their displacement over time. Speckle tracking would thus allow studying the contraction of the diaphragm directly in the direction of muscle fibers' contraction.

Only, few studies have looked at the contribution of speckle tracking to tissue strain out of the field of cardiovascular medicine. However, Frich et al. described a good correlation between strain and isotonic contractility of the biceps brachii and supraspinatus muscle (25). In 2015, Orde et al showed a correlation between diaphragmatic strain and the other ultrasound parameters described above (i.e. EXdi and TFdi) (26). In 2017, Oppersma et al found a correlation between diaphragmatic strain and strain rate and the evolution of Pdi and EAdi in healthy volunteers subject to a gradually increased inspiratory load (27). To the best of our knowledge, no study has assessed diaphragmatic strain and strain rate outside a population of healthy subjects. We also reported a proposition for assessing diaphragmatic strain and strain rate in a previous issue (28).

The main objective of our work is to evaluate the feasibility of speckle tracking in diaphragmatic assessment in a population of intensive care patients. It also aims to describe a first distribution of diaphragmatic strain and strain rate values among critically-ill patients and to evaluate the inter-operators' reproducibility of these measures and their agreement with EXdi and TFdi.

Materials And Methods

This observational study was conducted from May 2019 to September 2019 in the Rangueil ICU of the Teaching Hospital of Toulouse (France). The study was approved by an ethic committee. All patients were informed about their participation in this protocol and were not included if they refused to participate.

All patients undergoing a weaning test with a T-tube were prospectively included. The criteria for non-inclusion were the use of pressure support ventilation during the weaning test, the presence of a tracheostomy, failure of the weaning test within the first 30 minutes, a known pregnancy, age under 18 years, the presence of a guardianship or curatorship measure, therapeutic limitation or the absence of coverage by the French social security.

The initiation of the weaning test, its duration, the choice to perform it with a T-tube and the decision to extubate or not were made by the physician in charge of the patient. The investigator in charge of the ultrasound recordings was not involved in the patient care. At the initiation of the weaning test, the oxygen flow rate was adjusted to achieve a pulse oxygen saturation within the target range, the patient's head of bed was adjusted to a semi-seated position (between 30° and 45°), and a physiotherapist assessed limb strength using the Medical Research Council (MRC) score. If the patient was extubated after the weaning test, the quality of the cough was also assessed subjectively by the patient's physician as 'ineffective', 'partially effective' or 'effective'.

Ultrasound recordings were made using a Vivid S60N ultrasound machine (GE Healthcare) in the last 30 minutes of the weaning test by an intensivist experienced in diaphragmatic ultrasound. Patients didn't perform any breathing effort. Two ultrasound windows were defined per side, the subcostal area opposite the midclavicular line below the costal crest and the zone of apposition between the 8th and 10th intercostal spaces opposite the midclavillary line. One ultrasound loop was recorded over each subcostal area using a sector probe (1.3-4.5 MHz) and three loops over each apposition area using a linear probe (2.4-10 MHz). Each loop consisted of 3 to 4 breathing cycles. No ultrasound parameters were measured during the recording. After the diaphragmatic ultrasound was performed, the intensivist who performed the ultrasound was asked to rate the echogenicity of each window subjectively as "good", "fair" or "poor".

Analysis of the ultrasound recordings was carried out in post-processing using GE Echopacs software (GE Healthcare). Before analysis, the ultrasound loops were viewed jointly by the operators. Patients presenting at least one recording that did not allow the measurement of one of the studied parameters were excluded.

Strains and strains rate were analyzed on the apposition zone loop using the Q-analysis tool of the Echopacs software. However, as the software is designed to recognize a cardiac cycle from the ECG signal, a respiratory cycle had to be selected manually on each side. The choice of the respiratory cycle to be used and the definition of its limits were done jointly by the operators. After this step, all measurements were made separately by each operator blinded to the other. In order to measure the strain and strain rate a ROI was defined between the peritoneal and pleural sheets, visualized by 2 hyperechoic lines, trying to include the largest possible section of diaphragm within the ROI with a minimum of 5 markers. After analysis by the Q-analysis tool, the baseline was positioned on timeline at the end-expiration to measure strain and strain rate.

The thickening fraction was measured over the same breathing cycle as the strain and strain-rate using M mode by positioning the cursor perpendicular to the diaphragm. Diaphragmatic excursion was measured by positioning the cursor towards the diaphragmatic dome in M mode.

The primary objective of this study was to describe the feasibility of diaphragmatic strain and strain rate in a population of intensive care inpatients. Secondary objectives were to assess the dispersion, the inter-individual variability and the inter-operator variability of these measurements and their relationship with EXdi and TFdi.

We have first carried out a descriptive analysis with the distribution analysis using the Shapiro-Wilk test and the dispersion parameters (interquartile range, variance, standard deviation, coefficient of variation). We also analyzed the relationships between strain, strain rate, EXdi and TFdi by Spearman rank correlation. The reproducibility between the 2 operators was analyzed for the whole measurements by calculation of the Intra-Class Coefficient (ICC) and by the Bland-Altman method with a limit of concordance fixed at ± 1.96 SD. The statistical analysis was performed on MedCalc® statistical software version 15 (Mariakerke, Belgium). A p-value < 0.05 was considered statistically significant.

Results

Forty patients were included but 10 patients were excluded during post-processing analysis: 5 had at least one uninterpretable recording, 3 had a poor ultrasound window and 2 patients' data were not correctly saved. Of the 8 patients excluded for uninterpretable recordings, the left subcostal window was involved in 6 patients and the zone of apposition in the remaining 2 patients. For 7 of these patients, poor echogenicity could be directly attributed to a recent abdominal of thoracic surgery (surgical incision area or drains directly on the ultrasound window).

Thirty patients had complete ultrasound data for post-treatment analysis. The clinical and biological characteristics of the 30 patients analyzed are described in Table 1.

Table 1 Clinical and biological characteristics of analyzed patients

		Analyzed Patients (n=30)
De	mographic characteristics	
Ag	je (years)	63 (57-73) ^a
Se	x (% female)	11(36,7%)
BN	/II (kg/m²)	26,8 (23-29) ^a
SA	APS II	58,5 (52-68)
Ch	aracteristics at inclusion	
Du	ration of ventilation (days)	6,5 (3-10) ^a
Us	e of neuromuscular blockade (days)	0 (0-2) ^a
Ca	rdiac dysfunction	11 (36,7%)
MF	RC score	50 (39-58) ^a
Ab	dominal or thoracic surgery during the hospital stay	20 (66,7%)
Ple	eural effusion diagnosed during the hospital stay	12 (40%)
Pn	eumothorax diagnosed during the hospital stay	2 (6,7%)
Art	terial blood gas parameters at inclsion	
Pa	IO2 (mmHg)	82,5 (67-103) ^a
Pa	02/Fi02	281,2 (207-414) ^a
рH	1	7,5 (7,4-7,5) ^a
Pa	ICO2 (mmHg)	35 (30-40) ^a
Ext	tubated patients	26 (86,7%)
Po	st-extubation characteristics (n=26)	
Со	bugh efficiency	
- In	neffective	3 (11,5%)
- P	artially effective	8 (30,8%)
- E	ffective	15 (57,7%)
NI	V	15 (57,7%)
HF	NC	3 (11,5%)
Ex	tubation failure (at 48h)	5 (19,2%)
Но	spital mortality	3 (10%)
2		

^a : median (IQR)

BMI : Body Mass Index, SAPS: Simplfied Acute Physiology Score, MRC : Medical Research Council, NIV : Non Invasive Ventilation, HFNC : High Flow Nasal Canula

Of the 30 patients analyzed, 5 (16,7%) had poor echogenicity and 16 (53,3%) had moderate echogenicity in at least one of the windows studied. The left subcostal window was predominantly involved in both subpopulations (80% and 93,8% respectively). Concerning the zone of apposition, the echogenicity was never estimated as "poor".

Table 2 described the values measured by all investigators for each parameter studied (6 measurements per side). The median values for the left and right strains were respectively -6.74% (IQR = [-13,6; 3,3]) and -8,17% (IQR = [-11,6; -3.2]). A normal distribution of strain, left strain rate and TFdi values was found according to the Shapiro-Wilk test.

		Distril	nution descrip	Table 2	ranhic naram	otors		
	Strain (%)		Strain Rate (s ⁻¹)		EXdi (mm)		TFdi (%)	
	Left	Right	Left	Right	Left	Right	Left	Right
Lowest value	-27.45	-24.98	-1.28	-1.82	-4.67	-9.83	-15.73	1.58
Highest value	13.85	7.77	0.43	0.30	31.33	30.33	76.67	74.83
Arithmetic mean	-6.39	-7.96	-0.24	-0.25	9.93	10.56	16.65	22.3
Standard deviation	10.66	9.11	0.41	0.37	7.28	7.18	20.85	16.05
Variation coefficient	167%	114%	172%	148%	73%	68%	125%	72%
Median	-6.74	-8.17	-0.23	-0.22	8.82	9.17	14.56	20.83
Interquartile range	-13.6 to 3.3	-11.6 to -3.2	-0.36 to 0.13	-0.38 to -0.13	5.67 to 11.83	6.17 to 13.48	3.31 to 29.62	10 to 32.5
Shapiro- Wilk test	W=0.9693 (P=0.52)	W=0.9504 (P=0.17)	W=0.9342 (P=0.06)	W=0.7515 (P<0.01)	W=0.9206 (P=0.03)	W=0.9276 (P=0.04)	W=0.9527 (P=0.12)	W=0.9002 (P=0.01)

On each side, a weak correlation was found between diaphragmatic strain and TFdi. On the left side, strain rate was also weakly correlated with TFdi (Table 3). Strain and strain rate were strongly correlated on each side but this correlation was expected given the presence of a mathematical relationship between these 2 parameters.

Α	Left side		Strain	Strain Rate	EXdi	TFdi
	Strain	rho		0.940	-0.358	-0.575
		Ρ		<0.0001	0.0522	0.0009
	Strain Rate	rho	0.940		-0.335	-0.543
		Ρ	<0.0001		0.0702	0.0019
	EXdi	rho	-0.358	-0.335		0.389
		Ρ	0.0522	0.0702		0.0337
	TFdi	rho	-0.575	-0.543	0.389	
		Ρ	0.0009	0.0019	0.0337	
В	Right side		Strain	Strain Rate	EXdi	TFdi
	Strain	rho		0.851	-0.159	-0.329
		Ρ		<0.0001	0.4012	0.0758
	Strain Rate	rho	0.792		0.122	-0.346
		Ρ	<0.0001		0.5213	0.0609
	EXdi	rho	-0.159	0.122		-0.056
		Ρ	0.4012	0.5213		0.7669
	TFdi	rho	-0.329	-0.346	-0.056	
		Ρ	0.0758	0.0609	0.7669	
	n = 30 for eac	n = 30 for each parameter				
	rho: Spearman rank correlation coefficient					

Table 3 Correlation table for each sonographic paramete

The pairs of values measured by each operator for each ultrasound parameter are shown in **figure 1**. The reliability of the inter-operators' measurements according to the ICC was performed separately for each measure and on the average of the 3 measurements (Table 4). Concerning strain and strain rate, the ICC indicated systematically a very good reliability (> 0.75).

Intraclass Correlation Coefficient (ICC)			
Left strain			
Single measures ^a	0.9596 [0.9394 -0.9732]		
Average measures ^b	0.9794 [0.9687-0.9864]		
Right strain			
Single measures ^a	0.9779 [0.9666-0.9854]		
Average measures ^b	0.9880 [0.9817-0.9921]		
Left strain rate			
Single measures ^a	0.9763 [0.9641-0.9843]		
Average measures ^b	0.9880 [0.9817-0.9921]		
Right strain rate			
Single measures ^a	0.9952 [0.9927-0.9968]		
Average measures ^b	0.9976 [0.9963-0.9984]		
Left EXdi			
Single measures ^a	0.7586 [0.6524-0.8351]		
Average measures ^b	0.8627 [0.7896-0.9101]		
Right EXdi			
Single measures ^a	0.8089 [0.6911-0.8795]		
Average measures ^b	0.8944 [0.8173-0.9359]		
Left TFdi			
Single measures ^a	0.8302 [0.7496-0.8865]		
Average measures ^b	0.9072 [0.8569-0.9398]		
Right TFdi			
Single measures ^a	0.7161 [0.5941-0.8060]		
Average measures ^b	0.8346 [0.7454-0.8926]		
^a Estimation of the reliability of a single rating			
^b Estimation of the reliability of an average of 3 rating			

Then, the agreement between operators was represented according to the Bland and Altman method **(Figure 2)**. Concerning strain measurements, the mean bias value (\pm agreement interval) was evaluated as -0.217 (\pm 5.96) on the left side and as 0.00 (\pm 3.74) on the right side. For the strain rate, these values were -0.00 (\pm 0.17) and 0.00 (\pm 0.07) respectively on the left and right side.

Discussion

To our knowledge, this is the first study to evaluate diaphragmatic strain and strain rate on an inpatient population. First, our study confirms that diaphragmatic strain and strain rate can be performed at the patients' bedside despite the constraints induced by ICU environment. In patients with at least one uninterpretable sonographic loop, the left subcostal widow was mainly involved in cases of poor echogenicity. The main limit we encountered in performing diaphragmatic strain and strain rate was related to the use of an undedicated software. Indeed, the latter has been initially designed for the evaluation of myocardial speckle tracking, forcing the bypass of some functionalities that cannot be extrapolated to the evaluation of other tissues. This problem has already been raised by authors who evaluated diaphragmatic speckle tracking(26, 27).

Through this study, we also reported a first description of diaphragmatic strain and strain rate values in an ICU population with a high inter-individual variability in values distribution.

By analyzing the inter-parameters correlation on our results, the values of the diaphragmatic strain and strain rate appeared not or weakly correlated with other ultrasound parameters. The lack of correlation between strain and diaphragmatic excursion may seem consistent because the strength of diaphragmatic contraction does not necessarily correlate with the cranio-caudal displacement of the latter. However, both strain and TFdi are parameters measuring the strength of diaphragmatic contraction. The lack of a strong correlation between these two parameters might suggest additional information from strain and strain rate in the assessment of diaphragmatic function.

We analyzed the inter-operator's reliability of strain, strain rate, EXdi, and TFdi with the ICC and the inter-operator's agreement thought the method of Bland and Altman. In comparison with our study, Orde et al found a higher inter-operator variability of the right diaphragmatic strain with an ICC of 0.90 and a concordance interval of \pm 24.3 according to the method of Bland and Altman(26). However, they explored the strain in a sample of healthy subjects performing voluntary inspiratory effort and obtained a mean value of -40.3%, values for which the inter-operator variability seemed greater in our sample. As a pathological threshold of diaphragmatic strain and strain rate is not yet defined, these results should be interpreted with caution.

Our methodology permits us to analyze the variability of the measurements directly attributable to the ultrasound technique and thus without the variability related to the ultrasound recording itself or to the heterogeneity existing between the respiratory cycles of the same patient. This advantage represents one of the major limitations of our methodology because we did not evaluate the degree of intra-individual variability between 2 respiratory cycles or induced by the positioning of the ultrasound probe (especially since diaphragmatic contraction can be non-homogeneous within a single hemi-diaphragm).

The development of software dedicated to diaphragmatic speckle tracking techniques represents an essential research axis before the use of strain and strain rate in clinical practice. In addition to a consequent improvement in the ease of realization, they would also allow a better relevance of the studied parameters by proposing, as an example, a synchronization of the speckle tracking on the respiratory impedancemetry recorded by the ultrasound device.

Most of all, as diaphragmatic strain and strain rate appear to be feasible in ICU, studies analyzing its interest on clinical outcomes are needed to evaluate its contribution in patient's care.

Conclusion

Our study shows that diaphragmatic strain and strain rate are feasible in the ICU patient. It also describes a first distribution of this parameters in an ICU population with an analysis of reliability and inter-operators' agreement. An improvement of the image processing software is a prerequisite for the development of this speckle tracking technique. Our work lays the basis for the development of clinical studies about the relevance of diaphragmatic strain and strain rate in ICU.

List Of Abbreviations

- DD: Diaphragmatique dysfunction
- EXdi: Diaphragmatique excursion
- ICC: Intra-class coefficient
- ICU: Intensive care units
- MRC: Medical Research Council
- ROI: Region of interest
- TFdi: Thickening fraction

Twitch Pdi: Bilateral transcutaneous phrenic stimulation

Declarations

a. Ethics approval and consent to participate

The study was approved by an ethic committee (committee Sud-Méditérannée III, n°2019-100568-49). All patients were informed about their participation in this protocol and were not included if they refused to participate.

b. Consent for publication

Not applicable

c. Availability of data and materials

The dataset analysed during the current study is available from the corresponding author on reasonable request.

d. Conflict of interest

The authors declare that they have no competing interests

e. Funding

No funding was received for the realization of this content.

f. Authors' contribution

MP, LC and FBV realized and interpreted sonographic loops and contributed in writing the manuscript. JMC developed the statistical methodology and performed the statistical analysis. OL developed the methodology to performed speckle tracking measurements on diaphragm by using the GE Echopac software. SR, BG and TS were major contributor in writing the manuscript. VM designed the study protocol. All authors read and approved the final manuscript.

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Figures



Figure 1

Pairs of values measured by operators Each dot represents a measurement performed by an operator (n=90 per operator) A. Strain (expressed in %), B. Strain rate (expressed in s-1), C. Diaphragmatic excursion (expressed in mm), D. Thickening



Figure 2

Bland and Altman method for evaluation of inter-operator variability Each point represents the difference between the measurements made by the 2 operators according to the average of these 2 measurements (n=90 per operator and per parameter studied). The mean value of the bias (solid lines) and the agreement interval at 1.96 x standard deviation (dashed lines) are represented. A : Strain (%), B : Strain rate (s-1), C : EXdi (mm), D : TFdi (%)