UNIVERSIDAD SAN FRANCISCO DE QUITO USFQ

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A SYSTEMATIC REVIEW OF DIAPHRAGMATIC ULTRASOUND ON INTUBATED PEDIATRIC PATIENTS

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A SYSTEMATIC REVIEW OF DIAPHRAGMATIC ULTRASOUND ON INTUBATED PEDIATRIC PATIENTS

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DEDICATORIA

Dedico este trabajo a mis padres Fatima y Jorge, a mis hermanos Erika, Andres, Jorge Luis y mi sobrina Lia y a toda mi familia por ser mi fortaleza, mi guía y mi apoyo, por estar siempre presentes en este arduo camino y acompañarme a alcanzar mis metas.

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RESUMEN

ANTECEDENTES:

La atrofia del diafragma es una condición que afecta a pacientes bajo ventilación mecánica. Numerosos estudios han identificado el proceso de atrofia del diafragma a través de la ecografía, incluso antes de emprender el proceso de ventilación asistida. Conocer el estado de la atrofia del diafragma puede proporcionar una mejor visión general del diafragma y ayudar a evitar reintubaciones innecesarias.

OBJETIVOS Y MÉTODOS:

Resumir los resultados ecográficos del diafragma en pacientes intubados. Se realizó una revisión sistemática de la ecografía diafragmática de pacientes pediátricos con ventilación mecánica.

RESULTADOS:

Se incluyeron nueve artículos. A todos los pacientes se les realizó ecografía diafragmática, en algunos con varias mediciones a lo largo del tiempo y en otros con mediciones al inicio y antes de la extubación. En todos los artículos se demuestra que la ventilación mecánica prolongada conduce a la atrofia diafragmática. El DTF proporciona los datos más útiles y actúa como predictor de una extubación exitosa o fallida. Las otras medidas, sin embargo, nos proporcionan evidencia de atrofia diafragmática con el tiempo.

CONCLUSIÓN:

La ultrasonografía diafragmática es una excelente herramienta, fácil de usar y no utiliza radiación. Con pocas mediciones realizadas en el diafragma podemos predecir el éxito o el fracaso en la extubación. El tiempo también juega un factor importante, ya que se describe que cuanto más tiempo está el paciente en ventilación mecánica, mayor es la atrofia.

ABSTRACT

BACKGROUND:

Diaphragm atrophy is a condition, which affects patients under mechanical ventilation. Numerous studies have identified the process of diaphragm atrophy through echography, even before undertaking the process of assisted ventilation. Knowing the status of diaphragm atrophy can provide a better panorama of the diaphragm and help to avoid unnecessary re-intubations.

OBJECTIVE AND METHODS:

Summarize the sonographic results of the diaphragm in intubated patients. A systematic review of diaphragmatic echography of pediatric patients with mechanical ventilation were done.

RESULTS:

Nine articles were included. Diaphragmatic ultrasound was performed on all patients, in some with several measurements over time and others with measurements at the beginning and prior to extubation. In all the articles it is shown that prolonged mechanical ventilation leads to diaphragmatic atrophy. The DTF provides the most useful data and act as a predictor for a successful or failed extubation. The other measurements, however, provide us with evidence of diaphragmatic atrophy over time.

CONCLUSION:

Diaphragmatic ultrasonography is an excellent tool, easy to use and does not use radiation. With few measurements performed on the diaphragm we can predict success or failure in extubation. Time also plays an important factor, since it is described that the longer the patient is on mechanical ventilation, the greater the atrophy.

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INTRODUCTION

Diaphragm atrophy is the main cause of extubation failure in patients with mechanical ventilation. There are several causes that lead critically ill patients to diaphragm atrophy. [1] Acute diaphragm atrophy and weakness can be caused by mechanical ventilation itself. Ventilator-Induced Diaphragm Dysfunction (VIDD) was first described by Vassilakopoulos and Petrof whom presented the effects of mechanical ventilation in the diaphragm and other muscles of respiration. [2] Several mechanisms that influence diaphragm atrophy and weakness have been studied and proposed; however, insufficient inspiratory effort myotrauma is a mechanism that affects mechanical ventilation patients. These effects can lead to a prolonged ventilation and weaning failure. [1,2,3,4]

Direct diaphragm monitoring is crucial in the detection of atrophy and its long-term effects. There are rarely used techniques to measure diaphragmatic activity, e.g., electrical activity of the diaphragm (EAdi), and esophageal pressure. [5] However, expertise and specific instruments are required for the analysis. Ultrasonography is a non-invasive and pedagogic technique that offers real-time direct vision to measure and observe the movement of the diaphragm and other muscles of respiration. [1,2]

Different measurements are used in B-mode ultrasonography such as Tdi (diaphragm thickness at end-inspiration), Tde (diaphragm thickness at end-expiration), and DTF (percentage diaphragm thickness fraction). Likewise, M-mode imaging is used to observe structure movement, like heart valves, to measure the displacement of the diaphragm or diaphragmatic excursion. [5,6]

This systematic review assesses different ultrasound data in selected studies like Tdi, Tde, DTF, and the diaphragmatic excursion data as the main atrophy markers of pediatric patients with mechanical ventilation. The aim of this study is to systematically review the literature of diaphragmatic echography in pediatric patients with mechanical ventilation.

METHODS

This study followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) for systematic reviews guidelines and PICOS (Table 3) (population, Intervention, Comparator, Outcomes and Study type). The protocol research presented in was performed instead of previous research of diaphragmatic echography in pediatric patients. Research terms were developed based on other systematic reviews and adapted to SCOPUS (Table 4) and MEDLINE (Table 5) database research criteria. The screening process was performed by the author without additional secondary revisions.

Table 1. PICOS

ITEM	*DEFINITION*
***P**opulation*	Pediatric patients
***I**nterventions*	No applicable
***C**omparators*	No applicable
***O**utcomes*	Ultrasound findings
***S**tudy type*	Observational studies, prospective and retrospective studies.

The eligibility criteria included systematic reviews, meta-analysis, prospective, retrospective and case-control studies, and excluded clinical guidelines, letters to the editor and case series. Inclusion criteria consisted of pediatric patients that had been intubated for more than 24 hours, while patients with neuromuscular diseases, previous thoracic surgery or malformations (e.g. diaphragmatic hernia) were excluded. (Table 6).

RESULTS

The search provided 2626 articles from which, after title and abstract screening, 174 articles were selected. After the pediatric population filter, 11 articles were undertaken for this review; 2 articles were dupped.

Nine studies were included in this systematic review (table 2). Seven studies are prospective, one is longitudinal cohort, and one is pilot. All studies were conducted on pediatric population in a total of 687 patients. Details are summarized in the PRISMA diagram (Table 3). Sample size were small in most of the included studies. The studies selected for this systematic review were observational and conducted between 2018 and 2021. These studies where conducted in Europe (n=3), Asia (n=3), Africa (n=2), North America (n=1).

Table 2. Citation list

Author	*Title*	*Journal*	*Publication year*
1. Yang Xue et al	The predictive value of diaphragm ultrasound for weaning outcomes in critically ill children	BMC Pediatr	2019
2. Dalia A Addel Raman et al	Diaphragm and Lung Ultrasound Indices in Prediction of Outcome of Weaning from Mechanical Ventilation in Pediatric Intensive Care Unit	Indian J Pediatr	2020
3. Yang Xue, Chung Feng Yang et al	A prospective observational study on critically ill children with diaphragmatic dysfunction: clinical outcomes and risk factors	BMC Pediatr	2020
4. Eslam Bahgat et al	Sonographic evaluation of diaphragmatic thickness and excursion as a predictor for successful extubation in mechanically ventilated preterm infants	Eur J Pediatr	2021
5. Christie L. Glau et al	Progressive Diaphragm Atrophy in Pediatric Acute Respiratory Failure	Pediatr Crit Care Med	2018
6. Delia valverde montoro et al	Ultrasound assessment of ventilator-induced diaphragmatic dysfunction in mechanically ventilated pediatric patients	Paediatr Respir Rev	2021
7. Maria teresa Dionisio et al	Ultrasound Assessment of Ventilator-induced Diaphragmatic Dysfunction in Paediatrics	Acta Med Port	2019
8. Marloes M et al	The impact of critical illness on the expiratory muscles and the diaphragm assessed by ultrasound in mechanical	Ann Intensive Care	2020

	ventilated children		
9. Sabyasachi Mistri et al	Diaphragmatic atrophy and dysfunction in critically ill mechanically ventilated children	pediatric pulmonology India	2020

Medical ultrasonography was the method used for measurement. In similar techniques for diaphragm measurement including the midaxillary line of ribs 9 and 11, and patient in supine position, perpendicular to the diaphragm, M and B-mode imaging were employed [6,7] . Among these, the main types mentioned were Tdi (Diapraghm thickness), Tdi-ins (Tdi at end-inspiration), Tdi-exp (Tdi at end-expiration) and DTF (Diaphragmatic thickness fraction) that correlate in the following formula: (Tdi-ins – Tdi-exp)/Tdi-exp [5]. (Table 7).

Three articles identified DTF as the predictor of extubation success or failure rate and presented values between >21 - 36% [8,9,10]. Two studies mention DTF cut-off values as the predictors of extubation success >21% (sensibility 82% and specificity 81%), and >23% (sensibility 100% and specificity 76.2%), respectively [8,11]. Additionally, these results presented positive predictive values of 94% and 56%, and negative predictive values of 86.5% and 100%, respectively. One study showed that diaphragmatic excursion is the best indicator to predict extubation success (sensibility 94% and specificity 89%; P<0.001) [12]. Four studies mentioned a decrease in TD, Tdi-ins and Tdi-exp values during mechanical ventilation [9, 13 ,10, 14] . (Table 8, 9)

In addition to diaphragmatic ultrasound findings, one study mentioned high C-reactive protein in patients with extubation failure and higher VM time in patients with weaning failure [1,15].

DISCUSSION AND CONCLUSION

This systemic review presents several important points. Ultrasonography is the simplest, most innocuous and with good reproducibility exam for radiologists or other specialists. This technique is almost standardized in the majority of the articles reviewed in this study.

Ventilator-induced diaphragm dysfunction (VIDD) is an entity that needs to be assessed before extubation due to the morbidity that can be caused on the patient.

These results show diaphragm atrophy and dysfunction when the patient is on mechanical ventilation. The measurements mentioned in this review indicate a decrease in the diaphragm thickness independently from the demographic data of the patient. DTF is a good predictor of weaning success or failure. All the values obtained in the selected articles show changed during the ventilation process. Mechanical ventilation time is related to diaphragm atrophy: the longer time the patient is on mechanical ventilation, the higher probability of weaning failure.

Data show that serial measurement and pre-extubation is necessary in case of potential failure during the procedure. In this sense, echography provides the advantage of measuring the patient *in situ*, without the need of moving the patient or employing invasive methods.

Several systemic reviews lack focus on pediatric population, so this review represents an overlook in this area. One of the limitations of this review were no randomized studies; however, data obtained have statistical support for medical care of intubated patients.

Table 3. PRISMA Diagram

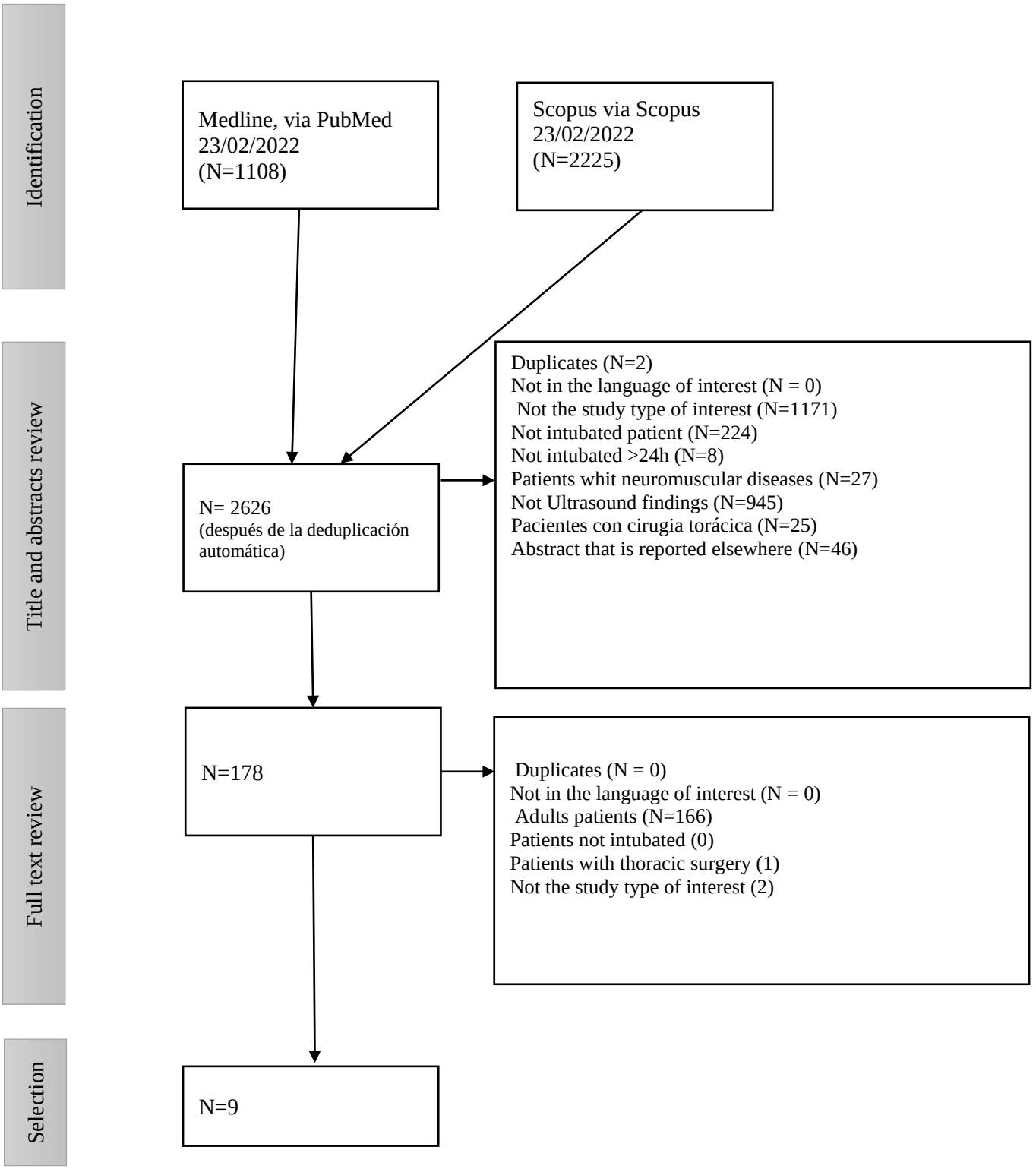

Table 4. SCOPUS Search Terms.

Items	*#*	*Search terms*	*Number of citations*
Population_rheumatoid arthritis	#1	TITLE-ABS-KEY (Intubat* OR intratrach* OR "mechanical ventilation" OR extubat*)	
Population_interstitial lung disease	#2	TITLE-ABS-KEY (ultrasoun* OR echograph*)	
Outcomes_Tomographic findings	#3	TITLE-ABS-KEY (diaphrag* OR thora* OR tors* OR chest OR chest*)	
Total	#4	#1 AND #2 AND #3	2.225

Table 5. MEDLINE Search Terms.

Items	*#*	*Search terms*	*Number of citations*
Population_Intubation	#1	"Intubation"[Mesh] OR "Airway Extubation"[Mesh] OR "Intubation, Intratracheal"[Mesh] OR "Respiration, Artificial"[Mesh]	133.931
	#2	Intubat*[TIAB] OR intratrach*[TIAB] OR "mechanical ventilation" [TIAB] OR extubat*[TIAB]	129.451
	#3	#1 OR #2	209.628
Outcome_ultrasound	#4	Ultrasound[MeSH] OR echography[MeSH] OR ultrasonography[MeSH]	491.294
	#5	ultrasoun*[TIAB] OR echograph*[TIAB]	292.970
	#6	diaphrag*[TIAB] OR thora*[TIAB] OR tors*[TIAB] OR chest[TIAB] OR chest*[TIAB]	483.900
	#7	(#4 OR #5) AND #6	30.861
Total	#8	#3 AND #7	1.108

Table 6. Eligibility criteria

Category	Exclusion criteria
0. Null entries, duplicates, not in the language of interest, abstract is reported elsewhere and not in the time period of interest	01 - Null entries
	02 - Duplicates
	03 - Abstract that is reported elsewhere
1 - Nature of study	04 - Not the study type of interest
3 - Population	05 – Adult Patients
	06 – Not intubated patients
	07 – Intubated patients les that 24 hours
	08 – Patients with toracic surgery
	09 – Patients with neuromuscular diseases
5 - Outcome	10 – Not ultrasound findings
6 - Potential	11 - Potential
7 - Cannot decide	12 - Cannot decide

Table 7. Intervention and measures.

Estudio	Diseño	tipo de estudio	Medidas tomadas
1. Yang Xue	Prospective	US	Tdi-exp, Tdi-ins, DTF y Diaphragm excursion.
2. Dalia A Addel Raman	Prospective	US	Tdi-exp, Tdi-insp, DTF y Diaphragm excursion.
3. Yang Xue, Chung Feng Yang	Prospective	US	Tdi-exp, Tdi-insp, DTF
4. Eslam Bahgat	Prospective	US	Tdi-exp, Tdi-insp, DTF y Diaphragm excursion.
5. Christie L. Glau	Prospective	US	Tdi exp, Tdi-insp, DTF
6. Delia valverde montoro	Prospective	US	Tdi-exp, Tdi-ins, DTF
7. Maria teresa Dionisio	Prospective	US	DT, Diaphragm excursion. y DTF
8. Marloes M	Longitudinal cohort	US	Tdi-ins, Tdi-exp, DTF
9. Sabyasachi Mistri	obs cohort study	US	Tdi-ins, Tdi-exp, DTF

Figure 8. DTF Values.

Estudio	DTF weaning success	DTF weaning failure	%DTF weaning success	VPP DTF	VPN DTF
1. Yang Xue	>21%	<21%	>21% S82% P81%	94	56
2. Dalia A Addel Raman	NA	NA	>23% S100% S 76.2% P< 0.001	86.5	100%
3. Yang Xue, Chung Feng Yang	NA	NA	NA	NA	NA
4. Eslam Bahgat	NA	NA	NA	NA	NA
5. Christie L. Glau	>30%/>36% Success on SBT*	NA	NA	NA	NA
6. Delia valverde montoro	NA	NA	NA	NA	NA
7. Maria teresa Dionisio	NA	NA	NA	NA	NA
8. Marloes M	>30-36%	NA	NA	NA	NA
9. Sabyasachi Mistri	NA	NA	NA	NA	NA

- SBT Spontaneous breathing trial

Figure 9. TD, Tdi, Tde values.

	Initial TD	Posterior TD	Tdi-exp Initial	Tdi-exp posterior	Tdi-ins Initial	Tdi-ins posterior
1. Yang Xue	NA	NA	NA	NA	NA	NA
2. Dalia A Addel Raman	NA	NA	NA	NA	NA	NA
3. Yang Xue, Chung Feng Yang	NA	NA	NA	NA	NA	NA
4. Eslam Bahgat	NA	NA	NA	NA	NA	NA
5. Christie L. Glau	NA	NA	2.0mm (IQR, 1.8 to 2.5)	-13.8% (IQR -27 to 0)	NA	NA
6. Delia valverde montoro	NA	NA	NA	NA	NA	NA
7. Maria teresa Dionisio	2.3mm (AIQ 2-3.5)	Reduction of 13%	NA	NA	NA	NA
8. Marloes M	NA	TD on 4 day >10% of reduction P<0.0001	NA	NA	NA	NA
9. Sabyasachi Mistri	NA	NA	1.27 (1, 1.6)	NA	1.76 (1.35, 2.10)	NA

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