ISSN 2220-3141 (online)

World Journal of *Critical Care Medicine*

World J Crit Care Med 2017 November 4; 6(4): 179-189

Published by Baishideng Publishing Group Inc

WJCCM World Journal of Critical Care Medicine

A peer-reviewed, online, open-access journal of critical care medicine

Editorial Board

2016-2019

The *World Journal of Critical Care Medicine* Editorial Board consists of 235 members, representing a team of worldwide experts in critical care medicine. They are from 44 countries, including Argentina (2), Australia (7), Austria (2), Bangladesh (1), Belgium (4), Brazil (4), Canada (6), China (23), Croatia (1), Cuba (1), Denmark (1), Egypt (4), Finland (1), France (6), Germany (9), Greece (9), Hungary (1), India (10), Iran (2), Israel (6), Italy (13), Japan (6), Jordan (1), Mexico (1), Morocco (1), Netherlands (4), New Zealand (3), Norway (1), Poland (1), Portugal (4), Russia (1), Saudi Arabia (2), Singapore (2), Slovenia (1), South Africa (1), Spain (6), Sweden (1), Switzerland (3), Thailand (1), Tunisia (1), Turkey (3), United Kingdom (7), United States (70), and Uruguay (1).

WJCCM World Journal of Critical Care Medicine

Contents

Quarterly Volume 6 Number 4 November 4, 2017

ORIGINAL ARTICLE

Retrospective Study

Prospective Study

Contents

World Journal of Critical Care Medicine
Volume 6 Number 4 November 4, 2017

NAME OF JOURNAL
World Journal of Critical Care Medicine

ISSN
ISSN 2220-3141 (online)

LAUNCH DATE
February 4, 2012

FREQUENCY
Quarterly

EDITORIAL OFFICE
Xiu-Xia Song, Director
World Journal of Critical Care Medicine
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com

PUBLISHER
Baishideng Publishing Group Inc
7901 Stoneridge Drive,
Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com

PUBLICATION DATE
November 4, 2017

INSTRUCTIONS TO AUTHORS
http://www.wjgnet.com/bpg/gerinfo/204

ONLINE SUBMISSION
http://www.f6publishing.com

World Journal of Critical Care Medicine

Submit a Manuscript: http://www.f6publishing.com

World J Crit Care Med 2017 November 4; 6(4): 179-184

DOI: 10.5492/wjccm.v6.i4.179

ISSN 2220-3141 (online)

ORIGINAL ARTICLE

Retrospective Study

Intensivist-based deep sedation using propofol for pediatric outpatient flexible bronchoscopy

Kamal Abulebda, Samer Abu-Sultaneh, Sheikh Sohail Ahmed, Elizabeth A S Moser, Renee C McKinney, Riad Lutfi

Kamal Abulebda, Samer Abu-Sultaneh, Sheikh Sohail Ahmed, Renee C McKinney, Riad Lutfi, Department of Pediatrics, Section of Critical Care, Indiana University School of Medicine, Riley Hospital for Children at Indiana University Health, Indianapolis, IN 46202, United States

Elizabeth A S Moser, Department of Biostatistics, Indiana University School of Medicine and Richard M Fairbanks School of Public Health, Indianapolis, IN 46202, United States

Author contributions: Abulebda K and Lutfi R contributed equally to this work; Abulebda K, Abu-Sultaneh S, Ahmed SS and Lutfi R designed the research; McKinney RC collected the data; Moser EAS contributed to the statistical analysis; Abulebda K drafted the first draft of the paper; the entire author group critically reviewed and approved the manuscript.

Institutional review board statement: The study was reviewed and approved by the Institutional Review Board of Indiana University.

Informed consent statement: Patients were not required to give informed consent as the study was retrospective and all clinical patient data was de-identified before data analysis.

Conflict-of-interest statement: The authors have no conflict of interest or financial relationships to disclose.

Data sharing statement: Data was not shared amongst institutions.

Manuscript source: Unsolicited manuscript

Correspondence to: Dr. Kamal Abulebda, Department of Pediatrics, Section of Critical Care, Indiana University School of Medicine, Riley Hospital for Children at Indiana University Health, Dr, Phase 2, Room 4900, Indianapolis, IN 46202, United States. kabulebd@iupui.edu
Telephone: +1-317-9449674
Fax: +1-317-9443442

Received: February 6, 2017
Peer-review started: February 12, 2017
First decision: May 17, 2017
Revised: June 30, 2017
Accepted: September 3, 2017
Article in press: September 4, 2017
Published online: November 4, 2017

Abstract

AIM

To evaluate the safety and efficacy of sedating pediatric patients for outpatient flexible bronchoscopy.

METHODS

A retrospective chart review was conducted for all children, age 17 years or under who underwent flexible bronchoscopy under deep sedation in an outpatient hospital-based setting. Two sedation regimens were used; propofol only or ketamine prior to propofol. Patients were divided into three age groups; infants (less than 12 mo), toddlers (1-3 years) and children (4-17 years). Demographics, indication for bronchoscopy, sedative dosing, sedation and recovery time and adverse events were reviewed.

RESULTS

Of the total 458 bronchoscopies performed, propofol only regimen was used in 337 (74%) while propofol and ketamine was used in 121 (26%). About 99% of the procedures were successfully completed. Children in the propofol + ketamine group tend to be younger

and have lower weight compared to the propofol only group. Adverse events including transient hypoxemia and hypotension occurred in 8% and 24% respectively. Median procedure time was 10 min while the median discharge time was 35 min. There were no differences in the indication of the procedure, propofol dose, procedure or recovery time in either sedative regimen. When compared to other age groups, infants had a higher incidence of hypoxemia.

CONCLUSION

Children can be effectively sedated for outpatient flexible bronchoscopy with high rate of success. This procedure should be performed under vigilance of highly trained providers.

Key words: Pediatric flexible bronchoscopy; Propofol; Deep sedation; Procedural sedation; Sedation time; Hypoxemia

Core tip: In this retrospective study "Intensivist-based deep sedation using propofol for pediatric outpatient flexible bronchoscopy", we are presenting our center data on pediatric patients who underwent flexible bronchoscopy under deep sedation using propofol. The study outlines our experience with intensivist-based procedural sedation as an effective strategy to facilitate successful completion of flexible bronchoscopy. This is the largest retrospective study describing the use of propofol-based procedural sedation in the outpatient settings for pediatric flexible bronchoscopy.

Abulebda K, Abu-Sultaneh S, Ahmed SS, Moser EAS, McKinney RC, Lutfi R. Intensivist-based deep sedation using propofol for pediatric outpatient flexible bronchoscopy. *World J Crit Care Med* 2017; 6(4): 179-184 Available from: URL: http://www.wjgnet.com/2220-3141/full/v6/i4/179.htm DOI: http://dx.doi.org/10.5492/wjccm.v6.i4.179

INTRODUCTION

In the last two decades, flexible bronchoscopy (FB) has become an increasingly important outpatient tool used in the evaluation of pulmonary abnormalities in children[1,2]. As FB allows direct visualization of the patient's upper and lower airway larynx[3], it has been used as a diagnostic and therapeutic tool for chronic cough, wheezing, cystic fibrosis and infection etiologies in immunocompetent and immunocompromised patients[4] to diagnose various congenital or acquired pediatric airway anomalies/abnormalities.

While the need for appropriate sedation for FB is controversial in adults[5], deep sedation is generally needed in children due to their developmental capabilities and airway anatomy in order to blunt the airway protective reflexes and suppress the cough stimulus. Using deep sedation not only decreases a child's distress and discomfort but also significantly increases the chance of a successful completion of the procedure[1,6]. Multiple sedation regimens and route had been evaluation including nasal, oral, intravenous and topical anesthetic[7]. Commonly used drugs for sedation for FB include a benzodiazepine and opioids combination or ketamine with or without benzodiazepine[6,8,9].

Propofol is an *iv* sedative-hypnotic agent that is used for induction and maintenance of deep sedation and general anesthesia[10]. Propofol has many properties, including a rapid onset, short duration of action with rapid recovery time and minimal adverse events, which makes it an ideal agent for pediatric sedation in the outpatient setting[11]. Emerging data support the safety and efficacy of using propofol outside the operating room for pediatric outpatient procedures by qualified physicians trained in sedation with advanced airway management[1,12]. Additionally, with increasing numbers of pediatric patients undergoing diagnostic and therapeutic FB and the relative shortage of anesthesiologists and operating room availability, other pediatric subspecialists, such as pediatric critical care physicians, have stepped in to provide pediatric procedural sedation[13-15].

Ketamine is a dissociative agent that has analgesic, sedative and amnestic properties. It has been frequently used to facilitate painful procedures in children and has proven to be safe and effective in numerous studies[16]. However, despite the reported safety of ketamine in these studies, it had been reported that high dose ketamine could result in respiratory depression and excessive salivary secretions leading to adverse respiratory events[17].

The combination of propofol and ketamine for pediatric sedation had been reported to provide optimal hemodynamic stability and reduced adverse effects when compared to propofol alone[18-20]. Additionally, the combination of propofol and ketamine had been shown to be beneficial in other medical fields because of allowing lower doses of propofol resulting in the reduction of the undesirable adverse effects[20]. Many authors reported the advantages of propofol-ketamine combination in terms of hemodynamic profile and pain control in cancer patients undergoing painful procedures[19].

The purpose of this study is to review the author institution's experiences using propofol-based deep, procedural sedation regimens for pediatric flexible bronchoscopy in an outpatient setting.

MATERIALS AND METHODS

This retrospective study was approved by the institutional review board of the Indiana University. All pediatric patients between the ages of two months to seventeen years of age undergoing deep sedation for flexible bronchoscopy from March 2007 to August 2012 were included. Patients were divided into three age groups; infants (less than 12 mo), toddlers (1-3

years) and children (4-17 years). Patients in whom flexible bronchoscopy evaluation was performed in the Pediatric Intensive Care Unit through tracheostomy or endotracheal tube were excluded. All bronchoscopies were performed at the Riley Hospital for Children at Indiana University Health System by a pediatric pulmonologist with the assistance of a respiratory therapist at our dedicated outpatient sedation room.

History and physical exam were performed and documented according to the American Academic of Pediatrics (AAP) guidelines for sedation[21]. Written consent was obtained from the parents or guardian prior to the procedure. Sedation was performed by a sedation team consisting of a pediatric intensivist and two sedation nurses with a pediatric critical care background who monitored the patient during and after each procedure. Guidelines have been laid down by the AAP regarding monitoring, management and discharging children during procedural sedation[21]. All patients were either classified as ASA-PS Ⅱ or Ⅰ per American Society of Anesthesiologists-Physical Status classification system. Patients were without any oral intake for at least 6 h prior to the procedure and had an intravenous catheter placed by sedation team. Physiologic parameters such as heart rate, respiratory rate, oxygen saturation and noninvasive blood pressure were measured every 5 min throughout the procedure and every 15 min after its completion until the patient was fully awake. Supplemental oxygen (2 L per min) was administered *via* nasal cannula to the majority of the patients (92%) before and during the procedure. Prior to sedation, each patient received viscous lidocaine to the nare, a transnasal approach was used for all procedures. Additional doses of lidocaine were applied to the vocal cords, trachea and major bronchi as required per pulmonologist.

Two sedation strategies were used; intravenous (*iv*) propofol only (P-O) and *iv* ketamine prior to *iv* propofol (K-P), solely based on the intensivist preference. When ketamine was used, it was administered as an initial bolus of 0.5 mg/kg for patients who weigh less than 20 kg and 0.25 mg/kg for patient's weight more than 20 kg. Propofol was administered as an initial bolus of 1-2 mg/kg with additional boluses of 1 mg/kg as needed to achieve deep sedation (level 3) based on University of Michigan sedation scale[22].

Adverse events were recorded including development of hypoxemia (oxygen saturation of less than 90% for more than 30 s), hypotension (drop in systolic blood pressure below expected for age or a drop of 20% from baseline), worsening stridor from baseline, and bleeding (hemoptysis or epistaxis). Serious adverse events such endotracheal intubation, respiratory or cardiac arrest or failure to complete the procedure were also recorded.

Procedure time was defined as the time between the first bolus of sedation until the bronchoscopy procedure completed. Recovery time (RT) was defined as the interval between the completions of the procedure until the patient's level of conscious was back to baseline. Discharge time (DT) was defined as the interval between the start of sedation until the patient was discharged home.

Outcomes analyzed included: Propofol dose, hypoxemia, hypotension, procedure and recovery times, and time to discharge. For the two sedation strategies, bivariate analyses were conducted using χ^2 and Wilcoxon Sum Rank Tests. For the three age groups, bivariate analyses were conducted using χ^2 and Kruskal-Wallis Tests.

RESULTS

During the study period, a total of 458 bronchoscopies were performed, of which 454 (99.1%) were successfully completed. Patients' demographics and indications for bronchoscopy are summarized in (Table 1). Of the 458 flexible bronchoscopies performed, 337 patients (73.6%) were sedated using propofol only strategy and 121 patients (26.4%) using propofol and ketamine. Children in the (K-P) group tend to be younger and have lower weight compared to the (P-O) group. Four cases (< 1%) (3 in the P-O group, 1 in the K-P group) were terminated early. Two patients (< 0.5%) were admitted to the pediatric intensive care unit; one toddler in the P-O group and one child in the K-P group. One of the four patients required endotracheal intubation; two other patients required fluid resuscitation and one patient had a brief bradycardic episode. Both admitted patients were discharged home in the first 24 h of admission. Transient hypoxemia occurred in 8.3% of patients while hypotension in 23.6%. Prolonged hypoxemia necessitating the need for bag/mask ventilation happened in 5.1% of all patients (Table 2). There was no significant difference in propofol dosage, adverse effects or sedation times using the two sedation strategies (P-O or K-P) (Table 2). Analysis of the three age groups showed significantly higher hypoxemia in infants compared to toddlers and children (Table 3). A logistic regression of age groups predicting hypoxemia showed that infants have significantly higher odds of hypoxemia compared to toddlers ($P < 0.0001$, OR: 13.56, 95%CI: 3.92, 46.91), and compared to children ($P < 0.0001$, OR: 10.96, 95%CI: 3.65, 32.91). However, children and toddlers do not have significantly different odds of hypoxemia ($P = 0.62$).

DISCUSSION

FB is an essential diagnostic and therapeutic modality commonly used in various congenital and acquired pediatric pulmonary disorders[9,23].

To the best of our knowledge, this is the largest retrospective study describing the use of propofol with or without ketamine for procedural sedation in the outpatient settings for pediatric FB.

Between 2007 and 2012, we have used propofol as the main intravenous sedative agent for pediatric outpatient for FB. Propofol was well tolerated in the majority of pediatric patients undergoing the FB. Compared with the study of

Table 1 Demographics and indications of bronchoscopy in patients

Variable	Overall (*n* = 458)	Propofol only (*n* = 337)	Propofol ketamine (*n* = 121)	*P* value
Age, yr	5.0 (2.5, 9.1)	5.6 (2.8, 9.8)	3.4 (1.9, 6.6)	< 0.0001
Age group, *n* (%)				
Infant (< 12 mo)	15 (3.3)	6 (1.8)	9 (7.4)	< 0.0001
Toddler (1-3 yr)	132 (28.8)	84 (24.9)	48 (39.7)	
Child (4-17 yr)	311 (67.9)	247 (73.3)	64 (52.9)	
Weight (kg)	18.1 (13.1, 31.8)	20.0 (14.4, 33.0)	14.7 (11.2, 26.0)	< 0.0001
Female gender, *n* (%)	198 (43.2)	143 (42.4)	55 (45.5)	0.57
Diagnosis, *n* (%)				
Cystic fibrosis	38 (8.3)	29 (8.6)	9 (7.4)	
Cough	93 (20.3)	62 (18.4)	31 (25.6)	0.38
Wheezing	108 (23.6)	87 (25.8)	21 (17.4)	
Stridor	56 (12.2)	41 (12.2)	15 (12.4)	
Pneumonia	57 (12.4)	42 (12.5)	15 (12.4)	
Tachypnea	106 (23.1)	76 (22.6)	30 (24.8)	

Table 2 Average doses, sedation times and adverse events

Variable	Overall (*n* = 458)	Propofol only (*n* = 337)	Propofol ketamine (*n* = 121)	*P* value
Propofol dose (mg/kg)	4.1 (2.7, 5.6)	4.2 (2.7, 5.6)	3.7 (2.8, 5.2)	0.3
Procedure time (min)	10 (6, 15)	10 (7, 12)	10 (5, 15)	0.3
Recovery time (min)	25 (20, 30)	25 (20, 30)	25 (20, 35)	0.63
Time to discharge (min)	35 (30, 43)	35 (30, 40)	35 (30, 45)	0.31
Respiratory events				
Prophylactic use of O_2 supplementation prior to bronchoscopy, *n* (%)	423 (92.4)	311 (92.3)	112 (92.6)	0.92
Hypoxemia, *n* (%)	38 (8.3)	29 (8.6)	9 (7.4)	0.69
BMV/significant desaturation[1], *n* (%)				0.58
Neither	413 (91.2)	302 (90.7)	111 (92.5)	
BMV + significant desaturation	23 (5.1)	16 (4.8)	7 (5.8)	
Significant desaturation only	16 (3.5)	14 (4.2)	2 (1.7)	
BMV use only	1 (0.2)	1 (0.3)	0 (0)	
Cardiac events				
Start MBP	77.7 (70.3, 86.7)	78.3 (71.3, 86.3)	76.3 (68.0, 88.7)	0.58
End MBP	70.3 (63.0, 78.7)	71.0 (64.0, 79.3)	68.7 (61.7, 76.3)	0.04
Difference in MBP	-7.5 (-17.0, 2.0)	-6.7 (-16.0, 2.7)	-8.7 (-19.0, 0.7)	0.12
% Change MBP from start of procedure	-9.8 (-20.0, 3.0)	-9.2 (-18.8, 4.3)	-10.5 (-22.8, 0.7)	0.12
Blood pressure drop more than 20% from the baseline (hypotension)	108 (23.6%)	76 (22.6%)	32 (26.4%)	0.4

[1]Significant desaturation defined as oxygen saturation of less than 90% for more than 30 s. BMV: Bag mask ventilation; MBP: Mean arterial blood pressure.

Hasan and Reddy, our RT and discharge time DT were significantly shorter (26.7 ± 14.3 min *vs* 40 ± 18 min) and (37.6 ± 16.1 min *vs* 80 ± 44 min) respectively[24]. These findings can be due to the variability in indications and the practice of FB in pediatrics. Additionally, our propofol dose used is in line with the findings in another study to evaluate the use of propofol in pediatric FB[1] with no significant difference between three age groups or sedation regimens.

The routine administration of small dose ketamine prior to propofol has been shown in some studies to be beneficial in maintaining hemodynamic stability and decreasing side effect profile of propofol[18,19]. We used ketamine prior to propofol in only one fourth of our patient population but we did not observe significant difference in the adverse events between two groups. Also, we observed no difference in the average propofol dose between the groups. Additionally, RT and DT were similar in both groups. It is unclear whether there is truly no difference when adding ketamine to propofol or if it was due to small sample size or could be related to the fact that ketamine dose is too low to achieve anesthetic effect.

In term of adverse events and comparing to the data from the Pediatric Sedation Research Consortium on propofol sedation, we observed higher incidence of transient hypoxemia, hypoxemia required bag/mask ventilation and unexpected hospital admission in our study (8% *vs* 1.4%, 5% *vs* 1%, 0.4% *vs* 0.07% respectively)[14]. The higher incidence of these adverse events could be related to the nature of the procedure. Additionally, the pediatric research consortium data did not include pediatric patients who undergo this category of procedures. However, our findings are consistent with other reported data of complications of FB in children[3,25]. Our infants group had a significantly higher incidence of transient hypoxemia in infants compared to toddlers

Table 3 Analysis of adverse events, propofol dose and sedation times in three age groups

Variable	Infants (n = 15)	Toddlers (n = 132)	Children (n = 311)	P value
Hypoxemia, n (%)	7 (46.7)	8 (6.1)	23 (7.4)	< 0.0001
Hypotension, n (%)	2 (13.3)	35 (26.5)	71 (22.9)	0.45
Propofol only regimen, n (%)	6 (40.0)	84 (63.6)	247 (79.4)	< 0.0001
Propofol dose (mg/kg)	4.3 (2.4, 5.4)	4.34 (3.3, 5.3)	3.7 (2.5, 5.7)	0.06
Recovery time (min)	25 (15, 30)	25 (20, 35)	25 (20, 30)	0.39
Procedure time (min)	10 (7, 15)	10 (5, 11.5)	10 (8, 15)	0.16
Time to discharge (min)	35 (25, 40)	35 (30, 45)	35 (30, 40)	0.56

and children (46.7%, 6% and 7% respectively). While infants are only 3% of our study population. This could be due to some difficulty in delivering O_2 by nasal prongs to younger children or due to their low functional residual capacity. Given the high incidence of transient hypoxemia, infants might benefit from having their bronchoscopies performed under general anesthesia with a secure airway. Two children in our study had major unexpected complications requiring hospital admission (0.4%). Both were discharged home in the next day.

Our study has a number of limitations, including its retrospective nature and the fact that it was conducted at a single institution. As a retrospective report, there are many variables that are impossible to control and any comparison of our techniques is really made impossible by the possible bias that is introduced by how our sedation providers may have chosen to deliver sedation to one patient *vs* another. In regards to the sedation regimen used or the need for oxygen supplementation, it was chosen by the attending physician based on personal preference and experience. However, statistical analysis showed no difference between the two sedation regimens. Lastly, we did not compare the efficacy, adverse events and the cost of performing these procedures as an outpatient setting to the operation room setting under general anesthesia, future study comparing both settings with tightly controlled protocols and well defined outcomes would provide important information. The purpose of this study was not to compare between these two approaches, rather to describe our experience using propofol based sedation regimen for pediatric outpatient flexible bronchoscopy as an alternative approach that might be applied in certain institutions.

In conclusion, children can be sedated using propofol based sedation regimen for flexible bronchoscopy *vs* a pediatric intensivist-based team in an outpatient setting with expediency and high rate of success. Given the nature of the procedure, we observed a higher incidence of transient hypoxemia especially in infants and an overall higher incidence of hypoxemia compared to other procedures done under the same setting. This approach can be appealing since it provides an alternative valuable option to general anesthesia with a short recovery and discharge time. Given the higher incidence of anticipated adverse events, the use of this sedation strategy should be restricted to practitioners highly trained in pediatric airway and cardiorespiratory monitoring and management. Future study comparing this strategy to general anesthesia to determine any economical and workflow advantages and monitor adverse events is warranted.

COMMENTS

Background

Flexible bronchoscopy (FB) has become an increasingly important outpatient tool used in the evaluation of pulmonary abnormalities in children. FB is often considered to be invasive procedure, therefore, deep sedation is usually required. Multiple sedation regimens and route had been evaluation including nasal, oral, intravenous and topical anesthetic with variable efficacy and safety profiles.

Research frontiers

Evaluating the safety and efficacy of sedating pediatric patients for flexible bronchoscopy using propofol based sedation regimens in an outpatient setting.

Innovations and breakthroughs

This is the largest retrospective study describing the use of propofol with or without ketamine for deep sedation in the outpatient settings for pediatric flexible bronchoscopy.

Applications

Although the approach was efficacious and safe, they did not compare the efficacy, adverse events and the cost of performing this approach as an outpatient setting to the operation room setting under general anesthesia, future study comparing both settings with tightly controlled protocols and well defined outcomes would provide important information.

Peer-review

The paper is good, nicely framed and written.

REFERENCES

1 **Godfrey S**, Avital A, Maayan C, Rotschild M, Springer C. Yield from flexible bronchoscopy in children. *Pediatr Pulmonol* 1997; **23**: 261-269 [PMID: 9141111 DOI: 10.1002/ (SICI) 1099-0496(199704)23:4<261: AID-PPUL3>3.0.CO; 2-P]

2 **Barbato A**, Magarotto M, Crivellaro M, Novello A Jr, Cracco A, de Blic J, Scheinmann P, Warner JO, Zach M. Use of the paediatric bronchoscope, flexible and rigid, in 51 European centres. *Eur Respir J* 1997; **10**: 1761-1766 [PMID: 9272916 DOI: 10.1183/09031936.97.10081761]

3 **de Blic J**, Marchac V, Scheinmann P. Complications of flexible bronchoscopy in children: prospective study of 1,328 procedures. *Eur Respir J* 2002; **20**: 1271-1276 [PMID: 12449184 DOI: 10.1183/09031936.02.02072001]

4 **Wood RE**. The diagnostic effectiveness of the flexible bronchoscope in children. *Pediatr Pulmonol* 1985; **1**: 188-192 [PMID: 4069807 DOI: 10.1002/ppul.1950010404]

5 **José RJ**, Shaefi S, Navani N. Sedation for flexible bronchoscopy: current and emerging evidence. *Eur Respir Rev* 2013; **22**: 106-116 [PMID: 23728864 DOI: 10.1183/09059180.00006412]

6 **Tobias JD**. Sedation and anesthesia for pediatric bronchoscopy. *Curr Opin Pediatr* 1997; **9**: 198-206 [PMID: 9229156 DOI: 10.1097/00008480-199706000-00002]

7 **Somu N**, Vijayasekaran D, Ashok TP, Balachandran A, Subramanyam L. Flexible fibreoptic bronchoscopy in 582 children--value of route, sedation and local anesthetic. *Indian Pediatr* 1995; **32**: 543-547 [PMID: 8613312]

8 **Slonim AD**, Ognibene FP. Amnestic agents in pediatric bronchoscopy. *Chest* 1999; **116**: 1802-1808 [PMID: 10593809 DOI: 10.1378/chest.116.6.1802]

9 **Berkenbosch JW**, Graff GR, Stark JM. Safety and efficacy of ketamine sedation for infant flexible fiberoptic bronchoscopy. *Chest* 2004; **125**: 1132-1137 [PMID: 15006978 DOI: 10.1378/chest.125.3.1132]

10 **Steinbacher DM**. Propofol: a sedative-hypnotic anesthetic agent for use in ambulatory procedures. *Anesth Prog* 2001; **48**: 66-71 [PMID: 11515950]

11 **Vardi A**, Salem Y, Padeh S, Paret G, Barzilay Z. Is propofol safe for procedural sedation in children? A prospective evaluation of propofol versus ketamine in pediatric critical care. *Crit Care Med* 2002; **30**: 1231-1236 [PMID: 12072673 DOI: 10.1097/00003246-200206000-00010]

12 **Larsen R**, Galloway D, Wadera S, Kjar D, Hardy D, Mirkes C, Wick L, Pohl JF. Safety of propofol sedation for pediatric outpatient procedures. *Clin Pediatr* (Phila) 2009; **48**: 819-823 [PMID: 19483136 DOI: 10.1177/0009922809337529]

13 **Havidich JE**, Cravero JP. The current status of procedural sedation for pediatric patients in out-of-operating room locations. *Curr Opin Anaesthesiol* 2012; **25**: 453-460 [PMID: 22732423 DOI: 10.1097/ACO.0b013e32835562d8]

14 **Kamat PP**, McCracken CE, Gillespie SE, Fortenberry JD, Stockwell JA, Cravero JP, Hebbar KB. Pediatric critical care physician-administered procedural sedation using propofol: a report from the Pediatric Sedation Research Consortium Database. *Pediatr Crit Care Med* 2015; **16**: 11-20 [PMID: 25340297 DOI: 10.1097/PCC.0000000000000273]

15 **Cravero JP**, Beach ML, Blike GT, Gallagher SM, Hertzog JH. Pediatric sedation research consortium. The incidence and nature of adverse events during pediatric sedation/anesthesia with propofol for procedures outside the operating room: a report from the Pediatric Sedation Research Consortium. *Anesth Analg* 2009; **108**: 795-804 [PMID: 19224786 DOI: 10.1213/ane.0b013e31818fc334]

16 **Grunwell JR**, Travers C, McCracken CE, Scherrer PD, Stormorken AG, Chumpitazi CE, Roback MG, Stockwell JA, Kamat PP. Procedural Sedation Outside of the Operating Room Using Ketamine in 22,645 Children: A Report From the Pediatric Sedation Research Consortium. *Pediatr Crit Care Med* 2016; **17**: 1109-1116 [PMID: 27505716 DOI: 10.1097/PCC.0000000000000920]

17 **Morton NS**. Ketamine for procedural sedation and analgesia in pediatric emergency medicine: a UK perspective. *Paediatr Anaesth* 2008; **18**: 25-29 [PMID: 18095962 DOI: 10.1111/j.1460-9592.2007.02395.x]

18 **Alletag MJ**, Auerbach MA, Baum CR. Ketamine, propofol, and ketofol use for pediatric sedation. *Pediatr Emerg Care* 2012; **28**: 1391-1395; quiz 1396-1398 [PMID: 23222112 DOI: 10.1097/PEC.0b013e318276fde2]

19 **Chiaretti A**, Benini F, Pierri F, Vecchiato K, Ronfani L, Agosto C, Ventura A, Genovese O, Barbi E. Safety and efficacy of propofol administered by paediatricians during procedural sedation in children. *Acta Paediatr* 2014; **103**: 182-187 [PMID: 24138461 DOI: 10.1111/apa.12472]

20 **David H**, Shipp J. A randomized controlled trial of ketamine/propofol versus propofol alone for emergency department procedural sedation. *Ann Emerg Med* 2011; **57**: 435-441 [PMID: 21256626 DOI: 10.1016/j.annemergmed.2010.11.025]

21 **Coté CJ**, Wilson S. American academy of pediatrics; american academy of pediatric dentistry. Guidelines for Monitoring and Management of Pediatric Patients Before, During, and After Sedation for Diagnostic and Therapeutic Procedures: Update 2016. *Pediatrics* 2016; **138**: e20161212 [PMID: 27354454]

22 **Malviya S**, Voepel-Lewis T, Tait AR, Merkel S, Tremper K, Naughton N. Depth of sedation in children undergoing computed tomography: validity and reliability of the University of Michigan Sedation Scale (UMSS). *Br J Anaesth* 2002; **88**: 241-245 [PMID: 11878656 DOI: 10.1093/bja/88.2.241]

23 **Field-Ridley A**, Sethi V, Murthi S, Nandalike K, Li ST. Utility of flexible fiberoptic bronchoscopy for critically ill pediatric patients: A systematic review. *World J Crit Care Med* 2015; **4**: 77-88 [PMID: 25685726 DOI: 10.5492/wjccm.v4.i1.77]

24 **Hasan RA**, Reddy R. Sedation with propofol for flexible bronchoscopy in children. *Pediatr Pulmonol* 2009; **44**: 373-378 [PMID: 19274622 DOI: 10.1002/ppul.21013]

25 **Schnapf BM**. Oxygen desaturation during fiberoptic bronchoscopy in pediatric patients. *Chest* 1991; **99**: 591-594 [PMID: 1995213 DOI: 10.1378/chest.99.3.591]

P- Reviewer: Nenna R, Aggarwal D **S- Editor**: Cui LJ **L- Editor**: A **E- Editor**: Lu YJ

World Journal of Critical Care Medicine

Submit a Manuscript: http://www.f6publishing.com

World J Crit Care Med 2017 November 4; 6(4): 185-189

DOI: 10.5492/wjccm.v6.i4.185

ISSN 2220-3141 (online)

ORIGINAL ARTICLE

Prospective Study

Reproducibility of diaphragm thickness measurements by ultrasonography in patients on mechanical ventilation

Ashesh Dhungana, Gopi Khilnani, Vijay Hadda, Randeep Guleria

Ashesh Dhungana, Department of Medicine, National Academy of Medical Sciences, Pulmonary Medicine, Kantipath, Kathmandu 44600, Nepal

Gopi Khilnani, Vijay Hadda, Randeep Guleria, Department of Pulmonary Medicine and Sleep Disorders, All India Institute of Medical Sciences, New Delhi 110029, India

ORCID number: Ashesh Dhungana (0000-0003-2656-4405); Gopi Khilnani (0000-0003-0820-0624); Vijay Hadda (0000-0001-5820-3685); Randeep Guleria (0000-0002-9234-602X).

Author contributions: Dhungana A, Khilnani G and Hadda V are guarantors of the paper, be responsibility for the integrity of the work; Khilnani G and Hadda V conceived the idea; Dhungana A was involved in performing ultrasonography, data collection, manuscript drafting and revision; Hadda V contributed to performing ultrasonography, manuscript drafting and revision; Guleria R was involved in drafting and revising the manuscript.

Institutional review board statement: This study was reviewed and approved by institutional review board of All India Institute of Medical Sciences.

Informed consent statement: All study participants, or their legal guardian, provided written consent prior to enrollment into the study.

Conflict-of-interest statement: None of the authors have any conflict of interest.

Data sharing statement: There is no additional data available.

Manuscript source: Unsolicited manuscript

Correspondence to: Dr. Ashesh Dhungana, MD, DM, Assistant Professor, Department of Medicine, National Academy of Medical Sciences, Pulmonary Medicine, Kantipath, Kathmandu 44600, Nepal. nams@healthnet.org.np
Telephone: +977-98-41860457

Received: April 20, 2017
Peer-review started: April 21, 2017
First decision: July 18, 2017
Revised: July 26, 2017
Accepted: September 3, 2017
Article in press: September 4, 2017
Published online: November 4, 2017

Abstract

AIM

To prospectively evaluate the reproducibility of diaphragm thickness measurement by ultrasonography at the bed-side by critical care physicians in patients on invasive mechanical ventilation.

METHODS

In a prospective observational study of 64 invasively ventilated patients, diaphragmatic thickness measurement was taken by 2 different observers at the same site. Three measurements were taken by each observer and averaged. The intraobserver and interobserver variability was assessed by estimation of intraclass correlation coefficient. The limits of agreement were plotted as the difference between two observations against the average of the two observations in Bland and Altman analysis.

RESULTS

The mean diaphragm thickness at the functional residual capacity was 2.29 ± 0.4 mm and the lower limit of the normal, *i.e.*, the 5th percentile was 1.7 mm (95%CI: 1.6-1.8). The intraclass correlation coefficient for intra-observer variability was 0.986 (95%CI: 0.979-0.991)

with a *P* value of < 0.001. The intraclass correlation coefficient for interobserver variability was 0.987 (95%CI: 0.949-0.997) with a *P* value of < 0.001. In Bland and Altman analysis, both intraobserver and interobserver measurements showed high limits of agreement.

CONCLUSION

Our study demonstrates that the measurement of diaphragm thickness by ultrasound can be accurately performed by critical care physicians with high degree of reproducibility in patients on mechanical ventilation.

Key words: Diaphragm; Ultrasonography; Mechanical ventilation

Core tip: Ultrasonography (USG) is a cheap, cost effective and non-invasive bedside tool for evaluation of diaphragm thickness during mechanical ventilation. Measurement of diaphragm thickness by USG can be accurately performed by critical care physicians with high degree of reproducibility. USG should be used more often by the physicians in the intensive care unit for the assessment of the diaphragm.

Dhungana A, Khilnani G, Hadda V, Guleria R. Reproducibility of diaphragm thickness measurements by ultrasonography in patients on mechanical ventilation. *World J Crit Care Med* 2017; 6(4): 185-189 Available from: URL: http://www.wjgnet.com/2220-3141/full/v6/i4/185.htm DOI: http://dx.doi.org/10.5492/wjccm.v6.i4.185

INTRODUCTION

Invasive mechanical ventilation causes progressive decline in diaphragm bulk and strength in a phenomenon called ventilator induced diaphragm dysfunction[1]. Diaphragm movement and function can be assessed by various methods which include chest X-ray, supine vital capacity, maximum inspiratory pressure, electromyography and magnetic phrenic nerve stimulation. Ultrasonography (USG) is a cheap, cost effective and non-invasive bedside tool for evaluation of diaphragm thickness. It has been used successfully to measure diaphragm thickness and movement in ambulatoryin dividuals[2,3]. Diaphragm thickness is a surrogate of its strength and helps to predict the outcome of extubation in patients on mechanical ventilation[4,5]. However, localization and measurement may be more difficult in critically ill ventilated patients in the intensive care unit (ICU) due to significant subcutaneous edema and supine position. The variability may also be due to variation in image acquisition and interpretation.

MATERIALS AND METHODS

This was a prospective observational study done in mechanically ventilated patients admitted to the Pulmoanry Medicine ICU, All India Institute of Medical Sciences, New Delhi. Ethical clearance was obtained from the Institute Ethics Committee and written informed consent was obtained in all patients. Diaphragm measurements were taken within the 1st 24 h of ICU admission.

Inclusion criteria

The inclusion criteria including: (1) patients aged > 18 years and requiring endotracheal intubation and mechanical ventilation; and (2) admitted to the ICU within 72 h of initiation of mechanical ventilation.

Exclusion criteria

The exclusion criteria including: (1) mechanical ventilation for more than 72 h before admission; (2) any form of mechanical ventilation in the preceding 3 mo or those who are on home non-invasive or invasive ventilation; (3) surgical dressings over the right lower rib cage; and (4) surrogates of the patient not willing for consent.

Observer training

Both observers who conducted the ultrasonography were provided training in ultrasonographic measurement of diaphragm thickness by a radiologist in 3 sessions, each session lasting 30 min.

Measurement of diaphragm thickness

All ultrasound examinations were done with Sonosite Micromaxx Portable Ultrasound Machine (Sonosite, Inc. United States) using the B-mode and a 5-10 MHz linear transducer. Patients were put in a supine position at 0 ℃ of incline. The same incline was used for all subsequent measurements for a given patient. Diaphragm thickness was measured in right hemi diaphragm in the zone of apposition. USG probe was positioned at the 8th or 9th right intercostal space with vertical orientation in the mid-axillary line and adjusted until the diaphragm was properly visualised. The distal end of the transducer was marked with permanent ink. The diaphragm was identified as the last set of parallel lines, the pleural and peritoneal membranes overlying the less echogenic muscle. Figure 1 shows an USG sample image of a patient taken at end expiration. Three measurements of the diaphragm thickness were taken and averaged to report the mean. In 10 randomly selected patients, diaphragm thickness was re-measured on the same day by 2nd observer who was blinded to the results of the 1st observer. The results of diaphragm measurements were not revealed to the treating physician nor it was taken into consideration in any clinical decision-making or management of the patients.

Statistical analysis

The primary outcome was intraobserver and interobserver variability of the measurements. The intraobserver variability was assessed by estimation of intraclass correlation coefficient using the three observations in the same patient by the 1st observer. Interobserver variability

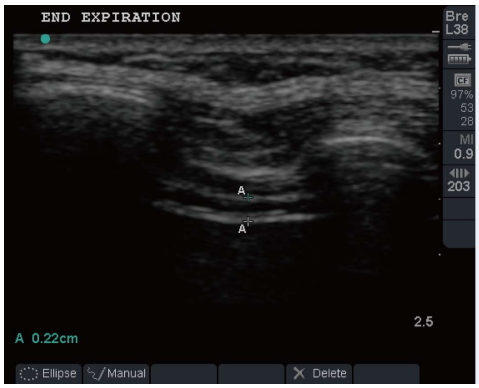

Figure 1 Ultrasonography image of a patient taken at end expiration. Diaphragm identified as the last set of parallel line, pleural and peritoneal membranes overlying the less echogenic muscle.

was tested between observations made by the 1st and the 2nd observers in the same subjects. The limits of agreement were plotted as the difference between two observations against the average of the two observations in Bland and Altman analysis. Data was analysed using International Business Machine (IBM) SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.

RESULTS

Baseline characters

A total of 106 patients admitted to the ICU were assessed for eligibility and inclusion into the study. Forty two of the 106 were excluded as they did not meet the eligibility criteria. Right hemidiaphragm localisation for measurement of thickness was successful in 64 out of 66 (97%) subjects. The flow of the patients enrolled into the study is shown in Figure 2.

The mean age of the study population was 54.5 ± 15.3 years. The mean diaphragm thickness at the functional residual capacity was 2.29 ± 0.4 mm and the lower limit of the normal, *i.e.*, the 5th percentile was 1.7 mm (95%CI: 1.6-1.8).The baseline characteristic of the study population is depicted in Table 1.

Intraobserver variability

The intraclass correlation coefficient was 0.986 (95%CI: 0.979-0.991) with a *P* value of < 0.001. In Bland and Altman plots, 2 out of 64 observations were outside the limits of agreement when first and second measurements were compared. Similarly 1 out of 64 observations was outside the 95% limit of agreement when the second and third or first and third measurements were compared.

Interobserver variability

The intraclass correlation coefficient of interobserver variability was 0.987 (95%CI: 0.949-0.997) with a *P* value of < 0.001. In Bland and Altman analysis, no measurements were outside the limit of agreement. Bland and Altman plots of intraobserver and interobserver agreement are shown in Figure 3.

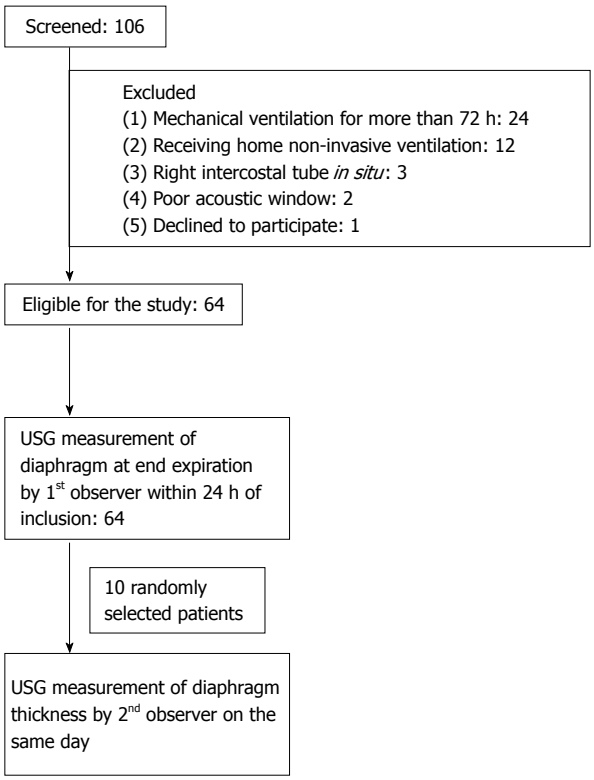

Figure 2 Flow of the patient enrolled into the study. USG: Ultrasonography.

Table 1 Baseline characters of the study population

Classification	Quantity, *n* (%)
Mean age, yr	54.5 ± 15.3
Male sex	45 (70)
Diagnoses	
COPD	20 (31)
Post tuberculosis sequelae	11 (17)
Interstitial lung disease	8 (13)
Asthma	5 (8)
Lung cancer	5 (8)
Others[1]	15 (23)
Mean apache Ⅱ score at admission	15.5 ± 5.3
Mean diaphragm thickness at FRC (mm)	2.29 ± 0.4

[1]Other diagnoses included chronic obstructive pulmonary disease, obstructive sleep apnea overlap syndrome, aspiration pneumonia, diabetic ketoacidosis and acute respiratory distress syndrome. COPD: Chronic obstructive pulmonary disease; FRC: Functional residual capacity.

DISCUSSION

Diaphragm is the principal muscle of respiration and its proper functioning is the critical determinant of the ability of a patient to be successfully weaned from mechanical ventilation. Assessment of diaphragm thickness and function is relevant to clinical practice because diaphragm dysfunction is an important cause of complications in mechanically ventilated patients[1,4]. We were able to successfully measure diaphragm thickness in 64 of the 66 (97%) patients who were eligible to participate in the study. This finding is important as

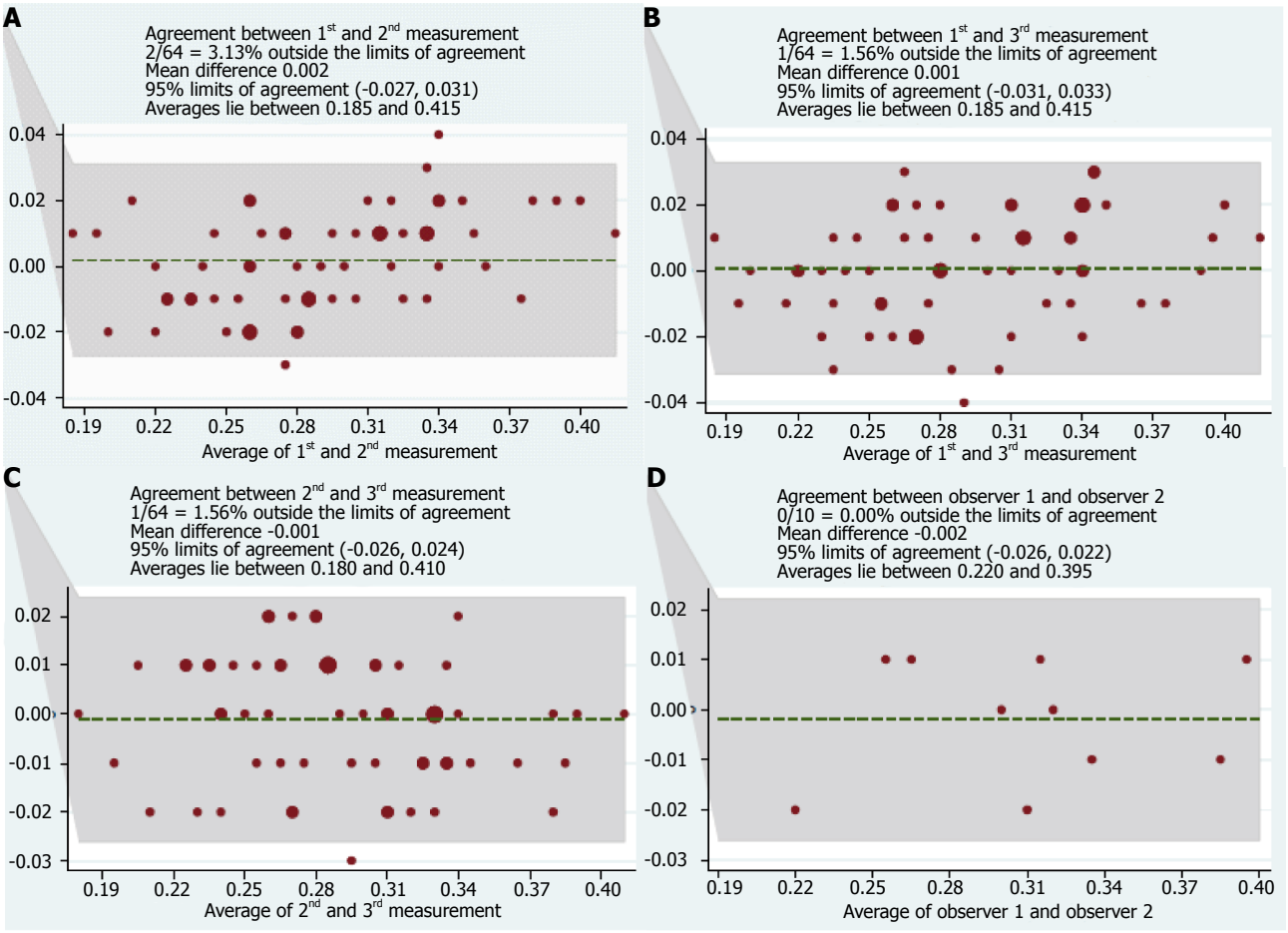

Figure 3 Bland and Altman plots of intraobserver agreement in diaphragm measurement. The result of three occasions (A-C) and between two observers (D).

measurement of diaphragm thickness by USG is an easy to learn, non-invasive bedside tool and is hazard free. It also avoids the hassle of shifting the patients out of the ICU and the associated complications.

Previous studies have shown that USG measurements of diaphragm thickness and movement have high degree of reproducibility in both spontaneously breathing and mechanically ventilated patients[6-8]. In the study by DiNino *et al*[5] diaphragm thickness was measured by an intensivist after an initial training of three to five sessions lasting ten to 15 min each. The intra-observer variability after such training was less than 10%. Similarly, in the study by Schepens *et al*[9] the coefficient of reproducibility was high (0.945 for intra-observer and 0.971 for inter-observer variability). Francis *et al*[10] also demonstrated both to be greater than 0.95. The intraclass correlation coefficients of both intra and inter observer variability in our study was high. Our study demonstrates that the measurement of diaphragm thickness by ultrasound can be accurately performed by critical care physicians after a short training with high degree of reproducibility.

The mean diaphragm thickness in our cohort was 2.29 ± 0.4 mm and the lower limit of normal was 1.7 mm (95%CI: 1.6-1.8). Prior studies have reported a diaphragm thickness in the range of 1.5 to 3.2 mm in normal healthy population[6,11,12]. The diaphragm thickness and contractility are minimally affected by age, body habitus and smoking history and may differ in different population. Majority of the patients in our study had underlying chronic respiratory disorder, as the most common diagnoses were chronic obstructive pulmonary disease (COPD), post tuberculosis sequelae, interstitial lung disease, asthma and lung cancer. The mean diaphragm thickness in COPD patients, as reported by Baria *et al*[12] was 2.8 mm and the lower limit of normal was 1.4 mm. The diaphragm thickness in COPD population was lesser than the normal controls. There was also a wider deviations of diaphragm thickness from the mean in those with COPD as compared to the controls (SD = 1.6 *vs* 1.3 mm for COPD and controls respectively).

Our study also has some limitations. Though we analysed the intraobserver variability of diaphragm thickness measurements in all included patients, inter-observer variability was only evaluated in 10 randomly selected patients in the study cohort. This was due to technical difficulties in performing ultrasonography twice in all patients. Hence, the results of interobserver agreements may need to be replicated in a larger cohort. All the measurements were taken by physicians trained in critical care ultrasonography and the radiologist was only involved in the initial training of the observers. Another limitation of the study is that we only used B mode for the measurement of diaphragm thickness. M

mode USG has also been suggested by some authors as an alternative modality to assess diaphragmatic excursions[2,8]. Reproducibility compared to a radiologist derived measurement would have added more value to the results.

In conclusion, the results of our study indicate that the measurement of diaphragm thickness by ultrasound can be accurately performed by critical care physicians with high degree of reproducibility. Hence, USG should be used more often by the physicians in the ICU for the assessment of the diaphragm.

COMMENTS

Background

Ultrasonography (USG) is a cheap, cost effective and non-invasive bedside tool for evaluation of diaphragm thickness and function during mechanical ventilation. However, there may be variability in the measurement of diaphragm thickness by USG due to variation in image acquisition and interpretation.

Research frontiers

The reproducibility of diaphragm thickness measurement by critical care physicians at bedside needs to be further explored. The results from this study suggest that the intraobserver and interobserver agreements of the measurements by critical care physicians after adequate training is high.

Innovations and breakthroughs

This study adds to the current literature of evidence that USG can be used at the bedside to measure diaphragm thickness during mechanical ventilation even by critical care physicians, and can be used as a guide to assess weaning outcomes.

Applications

USG should be used more often by the physicians in the intensive care unit for the assessment of the diaphragm.

Terminology

USG: A technique using echoes of ultrasound pulses to delineate objects or areas of different density in the body. Diaphragm: The principal muscle of inspiration muscle that separates the chest (thoracic) cavity from the abdomen. Mechanical ventilation: The technique through which gas is moved toward and from the lungs through an external device connected directly to the patient.

Peer-review

The authors describe a study to evaluate the interobserver agreement of sonographic measurement of the diaphragm thickness in 64 ventilated patients.

REFERENCES

1 **Vassilakopoulos T**, Petrof BJ. A Stimulating Approach to Ventilator-induced Diaphragmatic Dysfunction. *Am J Respir Crit Care Med* 2017; **195**: 281-282 [PMID: 28145756 DOI: 10.1164/rccm.200304-489CP]

2 **Gerscovich EO**, Cronan M, McGahan JP, Jain K, Jones CD, McDonald C. Ultrasonographic evaluation of diaphragmatic motion. *J Ultrasound Med* 2001; **20**: 597-604 [PMID: 11400933 DOI: 10.7863/jum.2001.20.6.597]

3 **Wait JL**, Nahormek PA, Yost WT, Rochester DP. Diaphragmatic thickness-lung volume relationship in vivo. *J Appl Physiol* 1989; **67**: 1560-1568 [PMID: 2676955]

4 **Kim WY**, Suh HJ, Hong SB, Koh Y, Lim CM. Diaphragm dysfunction assessed by ultrasonography: influence on weaning from mechanical ventilation. *Crit Care Med* 2011; **39**: 2627-2630 [PMID: 21705883 DOI: 10.1097/CCM.0b013e3182266408]

5 **DiNino E**, Gartman EJ, Sethi JM, McCool FD. Diaphragm ultrasound as a predictor of successfulextubation from mechanical ventilation. *Thora* 2014; **69**: 423-427 [PMID: 24365607 DOI: 10.1136/thoraxjnl-2013-204111]

6 **Cohn D**, Benditt JO, Eveloff S, McCool FD. Diaphragm thickening during inspiration. *J Appl Physiol* 1997; **83**: 291-296 [PMID: 9216975]

7 **Vivier E**, Mekontso Dessap A, Dimassi S, Vargas F, Lyazidi A, Thille AW, Brochard L. Diaphragm ultrasonography to estimate the work of breathing during non-invasive ventilation. *Intensive Care Med* 2012; **38**: 796-803 [PMID: 22476448 DOI: 10.1007/s00134-012-2547-7]

8 **Boussuges A**, Gole Y, Blanc P. Diaphragmatic motion studied by m-mode ultrasonography: methods, reproducibility, and normal values. *Chest* 2009; **135**: 391-400 [PMID: 19017880 DOI: 10.1378/chest.08-1541]

9 **Schepens T**, Verbrugghe W, Dams K, Corthouts B, Parizel PM, Jorens PG. The course of diaphragm atrophy in ventilated patients assessed with ultrasound: a longitudinal cohort study. *Crit Care* 2015; **19**: 422 [PMID: 26639081 DOI: 10.1186/s13054-015-1141-0]

10 **Francis CA**, Hoffer JA, Reynolds S. Ultrasonographic Evaluation of Diaphragm Thickness During Mechanical Ventilation in Intensive Care Patients. *Am J Crit Care* 2016; **25**: e1-e8 [PMID: 26724302 DOI: 10.4037/ajcc2016563]

11 **Boon AJ**, Harper CJ, Ghahfarokhi LS, Strommen JA, Watson JC, Sorenson EJ. Two-dimensional ultrasound imaging of the diaphragm: quantitative values in normal subjects. *Muscle Nerve* 2013; **47**: 884-889 [PMID: 23625789 DOI: 10.1002/mus.23702]

12 **Baria MR**, Shahgholi L, Sorenson EJ, Harper CJ, Lim KG, Strommen JA, Mottram CD, Boon AJ. B-mode ultrasound assessment of diaphragm structure and function in patients with COPD. *Chest* 2014; **146**: 680-685 [PMID: 24700122 DOI: 10.1378/chest.13-2306]

P- Reviewer: He HW, Muensterer OH, Zhang ZH **S- Editor**: Cui LJ
L- Editor: A **E- Editor**: Lu YJ

Published by **Baishideng Publishing Group Inc**
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com