ANESTHESIOLOGY

Diagnostic Accuracy of Diaphragm Ultrasound in Detecting and Characterizing Patient–Ventilator Asynchronies during Noninvasive Ventilation

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- Use of noninvasive ventilation in patients with acute respiratory failure is often associated with asynchronies like autotriggering or delayed cycling. These asynchronies are likely to impair efficacy of noninvasive patient ventilation.
- Surface diaphragm electromyography is the current reference for detecting synchronies in noninvasive ventilation. However this detection technique is not always effective and cannot be used routinely at the bedside. Therefore there is a clinical need for other techniques for monitoring for asynchronies in noninvasive ventilation.

What This Article Tells Us That Is New

- In 15 healthy volunteers, ultrasound assessment of diaphragm excursion and thickening detected noninvasive ventilator asynchronies with high sensitivity and specificity when compared with assessment of respiratory flow/pressure tracings.
- Surface diaphragm electromyography also had significantly higher sensitivity and specificity for detecting noninvasive ventilator asynchronies, but was only able to be successfully implemented in 60% of the study patients, suggesting that ultrasound assessment of diaphragm excursion and thickening is a more feasible technique for detecting ventilator asynchrony.

ABSTRACT

Background: Management of acute respiratory failure by noninvasive ventilation is often associated with asynchronies, like autotriggering or delayed cycling, incurred by leaks from the interface. These events are likely to impair patient's tolerance and to compromise noninvasive ventilation. The development of methods for easy detection and monitoring of asynchronies is therefore necessary. The authors describe two new methods to detect patient–ventilator asynchronies, based on ultrasound analysis of diaphragm excursion or thickening combined with airway pressure. The authors tested these methods in a diagnostic accuracy study.

Methods: Fifteen healthy subjects were placed under noninvasive ventilation and subjected to artificially induced leaks in order to generate the main asynchronies (autotriggering or delayed cycling) at event-appropriate times of the respiratory cycle. Asynchronies were identified and characterized by conjoint assessment of ultrasound records and airway pressure waveforms; both were visualized on the ultrasound screen. The performance and accuracy of diaphragm excursion and thickening to detect each asynchrony were compared with a "control method" of flow/pressure tracings alone, and a "working standard method" combining flow, airway pressure, and diaphragm electromyography signals analyses.

Results: Ultrasound recordings were performed for the 15 volunteers, unlike electromyography recordings which could be collected in only 9 of 15 patients (60%). Autotriggering was correctly identified by continuous recording of electromyography, excursion, thickening, and flow/pressure tracings with sensitivity of 93% (95% CI, 89–97%), 94% (95% CI, 91–98%), 91% (95% CI, 87–96%), and 79% (95% CI, 75–84%), respectively. Delayed cycling was detected by electromyography, excursion, thickening, and flow/pressure tracings with sensitivity of 84% (95% CI, 77–90%), 86% (95% CI, 80–93%), 89% (95% CI, 83–94%), and 67% (95% CI, 61–73%), respectively.

Conclusions: Ultrasound is a simple, bedside adjustable, clinical tool to detect the majority of patient–ventilator asynchronies associated with noninvasive ventilation leaks, provided that it is possible to visualize the airway pressure curve on the ultrasound machine screen. Ultrasound detection of autotriggering and delayed cycling is more accurate than isolated observation of pressure and flow tracings, and more feasible than electromyogram.

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Noninvasive ventilation is one of the main management tools of acute respiratory failure.[1] Its usefulness is often compromised by patient's discomfort or refusal[2] brought about by asynchronies.[3,4] The unavoidable leaks around the mask interfere with ventilator performance and generate desynchronization between the respiratory demands pattern of the patient and the ventilator pressurizations.[5] Expiratory leaks can erroneously be detected by the ventilator as inspiratory effort, leading to autotriggering;[3] similarly, inspiratory leaks can be interpreted as sustained inspiration, leading to delayed cycling.[3] Autotriggering is defined as a cycle delivered

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by the ventilator without previous inspiratory demand of the patient.[4] Delayed cycling is a cycle with mechanical inspiratory time of more than two-fold the patient inspiratory time.[4] The recognition and monitoring of these asynchronies are of clinical importance as they could be a major determinant of patient's tolerance, a cornerstone of successful noninvasive ventilation that could spare patient intubation.[2] Recent studies showed that the incidence of asynchronies during noninvasive ventilation amount to 40%,[4] which remains high despite implementation of algorithm with air leak detection and compensation.[3,6,7] The concurrent inspection of airway and flow tracings on the ventilator screen is not sensitive enough, even with training or expertise,[6] hence the need to monitor inspiratory effort in order to detect asynchronies during noninvasive ventilation.[6] Surface diaphragm electromyography (EMG) is the current reference technique, though not always effective and cannot be routinely used at bedside.[3,4,7]

Patient's inspiratory effort under noninvasive ventilation can be assessed using diaphragm ultrasound.[8] Monitoring the diaphragm dome excursion or its muscle thickening in the apposition zone, in time-motion mode, helps detect the start and end of diaphragm contraction.[9] If coupled with airway pressure monitoring, diaphragm ultrasound could theoretically help identify major asynchronies incurred by noninvasive ventilation leaks. This study was performed on healthy volunteers. Its objective was to evaluate the sensitivity and specificity of three different diagnostic strategies to detect the main ventilator asynchronies: (1) the simple analysis of flow and pressure waveform (control method); (2) an analysis combining diaphragm EMG signal and flow/pressure tracings (working standard method); and (3) the conjoint assessment of ultrasound and airway pressure tracings (diaphragm ultrasound method). Our main hypothesis was that diaphragm ultrasound method was as accurate as diaphragm EMG method and outperformed the control method.

Materials and Methods

This study was designed and centered at Henri Mondor University Hospital, approved by the French Ethics Committee CPP (comité de protection des personnes) Ile-de-France VIII (identification No. RCB 2017-A00346-47) and was registered (NCT03114384) online on ClinicalTrials.gov. It respected the Standards for the Reporting of Diagnostic Accuracy Studies (STARD) 2015 guidelines for diagnostic accuracy study (Supplemental Digital Content 1, http://links.lww.com/ALN/C299). Subjects were included in the study if they were healthy, with no respiratory comorbidity, and aged more than 18 yr. Pregnancy, lack of social care, and legal immaturity were the exclusion criteria. Each study participant was directly recruited after having provided a written informed consent.

Experimental Design and Sequence of Interventions

Healthy volunteers were consecutively subjected to a 45-min noninvasive ventilation session. Noninvasive ventilation was administered *via* an oronasal mask mounted on an intensive care unit ventilator (Engstrom Carestation; GE Healthcare, USA). The noninvasive ventilation algorithm was intentionally turned off in order to allow leaking and generate planned subject–ventilator asynchronies. In an attempt to reproduce the most common asynchronies occurring under noninvasive ventilation, a T-piece plug was inserted on the inspiratory limb of the ventilator circuit (fig. 1). A plug-opening/closing sequential series reproduced the main asynchronous leaks, depending on the time of the event as follows: autotriggering if the plug was manually opened during expiration, and delayed cycling if the plug was manually opened at the end of inspiration. The investigator and the ventilator were both positioned behind the participant receiving noninvasive ventilation in a way that the latter cannot see the manipulations performed on the T-piece. Each leak was reported in real time by a time mark on the data acquisition software, AcqKnowledge 4.0 (Biopac Systems, USA). These marks were used in association with flow/pressure tracings for the subsequent identification of asynchronies by the reference standard method.

Before recording, each subject was equipped with an EMG recording device and an ultrasound probe was fixed using a shape memory arm. A preliminary 15-min noninvasive ventilation sequence was run to accustom the participant to the interface and to test whether the leaks could induce the desired asynchrony. Given that it was impossible to simultaneously record excursion and thickening, each subject underwent two successive series of autotriggering and delayed cycling asynchronies to separately assess the continuous monitoring of diaphragmatic excursion and then diaphragmatic thickening. The aim was to generate an asynchrony at random about a dozen times per session and per asynchrony type. The time interval between each asynchrony and the following was about 10 s, the total duration of each recording was 5 to 10 min.

Monitoring of Flow Rate, Airway Pressure, and Diaphragm EMG

Airway flow was recorded using a heated pneumotachograph RX137G (Biopac Systems) inserted between the mask and the Y-piece of the ventilator circuit and connected to a differential pressure transducer TSD160A (Biopac Systems). Airway pressure was measured with a differential

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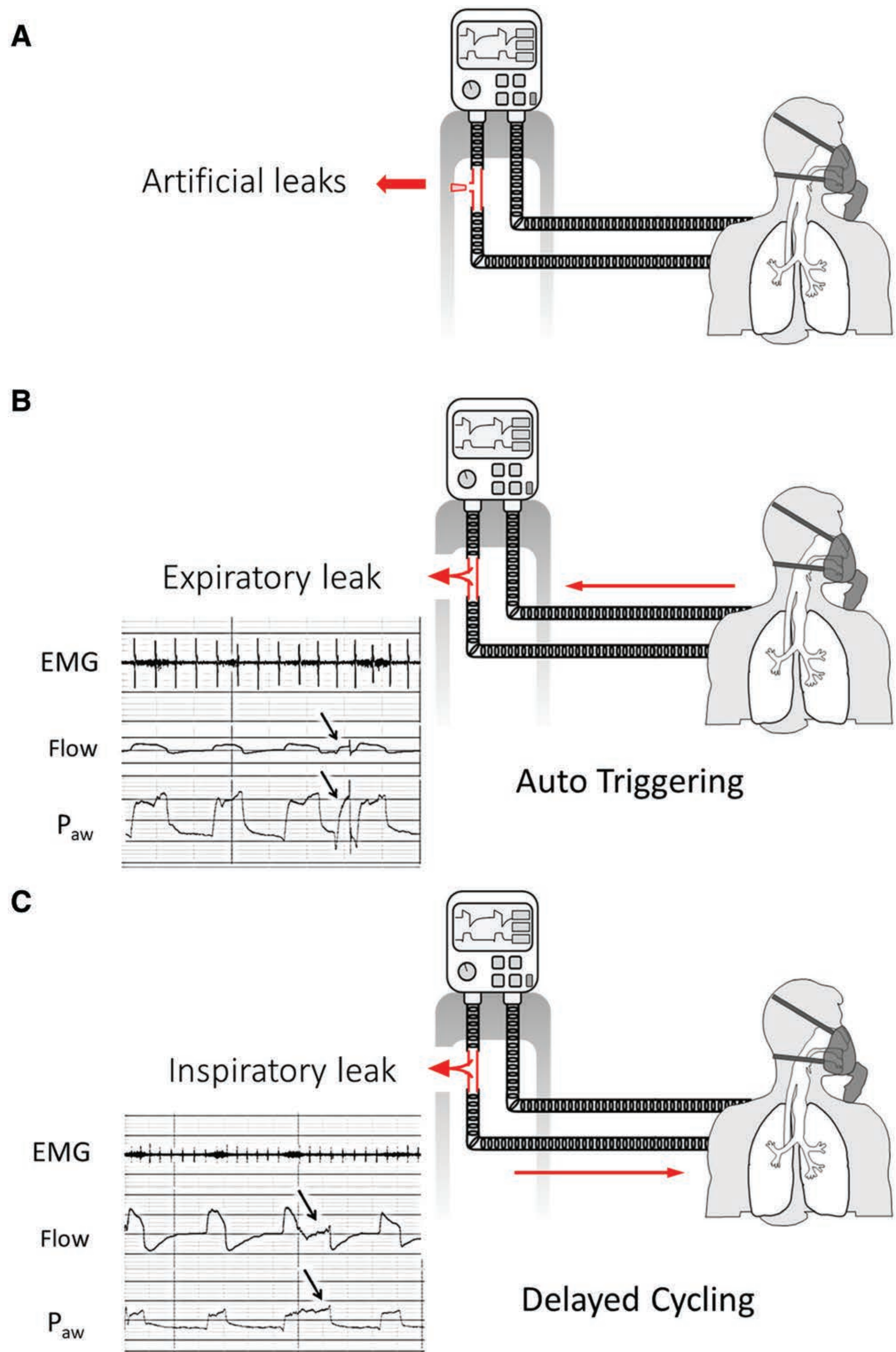

Fig. 1. Experimental setup. The ventilator was positioned behind the healthy participant. A T-piece was inserted on the inspiratory limb of the ventilator (*A*, in *red*) and was suddenly opened to generate specific asynchronies linked to the precise timing of the leaks: autotriggering during expiration (*B*) or prolonged insufflation during inspiration (*C*). Schematic patterns of concomitant diaphragm electromyogram (EMG), airway pressure (P_{aw}), and respiratory flow tracings are displayed on the *left* for each asynchrony.

pressure transducer TSD160D (Biopac Systems) inserted between the mask and the pneumotachograph. The signals were obtained online using an analog-to-digital converter (MP 150; Biopac Systems) sampled at 1000 Hz, and stored on a laptop for subsequent analysis with AcqKnowledge 4.0 software.

The diaphragm EMG was recorded with two surface electrodes placed bilaterally on the floating ribs, and a reference electrode placed on the sternum. Neck muscles electromyogram was recorded with two surface electrodes placed on the posterior neck triangle (to record scalene EMG activity) or on the sternocleidomastoid muscle (to record sternocleidomastoid EMG activity), with a reference electrode placed on the sternum. EMG signals were recorded using a BioNomadix module (Biopac Systems) and then stored on a laptop for subsequent analysis (AcqKnowledge 4.0).

Ultrasound Recordings

The airway pressure curve was displayed on the ultrasound screen using a barometric pressure gauge (sensor type: XFMP-050KPGP3; Fujikura, Japan) connected to an analog converter. This device allowed implementing pressure signal on the screen as a time-dependent curve which was coupled with ultrasound images. Ultrasound recordings of diaphragmatic excursion and thickening were performed using an ultrasound machine (Vivid S5; GE Healthcare) with either high definition probe (12 MHz) for thickening of the apposition zone or a high penetration probe (4 MHz) for the excursion of the dome. Images were acquired on a laptop with a video capture device (USB 3.0 HD Video Capture Device - 1080p; StarTech, Canada) and recorded during a 10-min period. An articulated, shape-memory arm held the ultrasound probe in the same position during the entire recording session. The diaphragm was located *via* the right subcostal route for the excursion or *via* the right anterior axillary line for the thickening, as previously described. Diaphragmatic thickening and excursion were recorded in time-motion mode. Scrolling speed was set as slow as possible to get a minimum of three cycles on the same image. Ultrasound video loops were recorded and stored for subsequent offline analysis.

Analysis of the Events

Asynchronies were analyzed cycle by cycle with four different approaches:

1. "Reference standard method" used the marked events and the flow/pressure tracings to detect and characterize each asynchrony. If the ventilator cycle was delivered immediately after an expiratory leak, the event was classified as autotriggering. If the inspiratory time was prolonged by an inspiratory leak, the event was delayed cycling.
2. "Working standard method" used diaphragm EMG with flow/pressure tracings, irrespective of the marked events. This analysis was restricted to patients in whom a sufficient-quality signal helped determine the start and end of the inspiratory effort. Autotriggering was a ventilator cycle delivered in the absence of diaphragm EMG activity. Delayed cycling was deemed present if the pressurization continued beyond the cessation of diaphragm EMG activity.
3. "Diaphragm ultrasound method" used ultrasound video loops with airway pressure tracings, irrespective of the marked events. Variations of diaphragm thickness and its excursion were used to detect each inspiratory effort. Autotriggering was a ventilator cycle delivered in the absence of diaphragmatic displacement or thickening. Delayed cycling was flagged if the pressurization continued beyond the end of diaphragmatic excursion or thickening.
4. "Control method" used the flow/pressure tracings alone, without the marked events. Autotriggering was suspected if the insufflation appeared premature, shortened, or altered. Delayed cycling was considered in long insufflations with prolonged pressurization and irregular concurrent flow.

Each of the four analyses was performed blindly from the three others.

Statistics

The diagnostic accuracy of the working standard method, the diaphragm ultrasound method using excursion, the diaphragm ultrasound method using thickening, and the control method were assessed *versus* the reference standard method. Each ventilatory cycle was evaluated as true positive, false positive, true negative, or false negative. Detecting an asynchrony by the working standard method, the diaphragm ultrasound method, or the control method was flagged true positive if consistent with the reference standard method. The erroneous detection of an asynchrony was classified as false positive. The lack of detection of an asynchrony was classified as false negative. The correct diagnosis of a synchronous cycle was considered as true negative. Standard formulas were used to calculate the sensitivity (true positive / [true positive + false negative]), specificity (true negative / [true negative + false positive]), accuracy ([true positive + true negative] / [true positive + true negative + false positive + false negative]), likelihood ratio of positive test (sensitivity / [1 − specificity]), likelihood ratio of negative test ([1 − sensitivity] / specificity), and Youden index (sensitivity + specificity − 1). Sensitivities and specificities were compared using the method advised by Newcombe *et al.*[10] and using an Excel spreadsheet provided by Prof. Newcombe.[11] A two-tailed testing was used by convention and P value < 0.05 was considered as statistically significant. We also compared the different methods using net classification methods,[12] including net reclassification index[13] and weighted comparison.[14] These three comparative analyses (Newcombe, net reclassification index and weighted comparison) were pairwise.

The sample size was calculated based on the total number of ventilatory cycles required to estimate sensitivity and specificity of the diaphragm ultrasound technique with a reasonable marginal error. Thus, to estimate an expected sensitivity of 90% with the diaphragm ultrasound method with a marginal error of 5%, 553 ventilatory cycles were needed by anticipating a prevalence of provoked asynchronies of 25%.[15] These conditions allowed the estimation of a specificity of 90% for the diaphragm ultrasound method with a marginal error of 3%. As we estimated that each type of asynchrony should be randomly generated 6 to 12 times per participant, it was planned to include 15 adults in the study to be sure to reach a sufficient number of ventilatory cycles, considering a respiratory rate of 10 to 15 cycles per min.

Continuous variables are expressed in median (interquartile, 25th and 75th percentiles). Statistical analyses were performed using SPSS software (version 16.0; SPS Inc, USA). No outliers were detected in the analyses, and the data presented here are comprehensive.

Results

The 15 participants' baseline characteristics are listed in table 1. A total of 1,925 cycles were recorded and were all included in the analysis. The experimental setup made it possible to observe 962 respiratory cycles during diaphragm ultrasound excursion recordings and 963 cycles during diaphragm ultrasound thickening recordings. Interestingly, each leak yielded its expected event. Of the whole 1,925 analyzed cycles, 537 (28%) asynchronies were identified by the reference standard method as autotriggering (n = 312 [16%]) and delayed cycling (n = 225 [12%]). All subjects exhibited a consistent incidence of autotriggering and delayed cycling (Supplemental Digital Content, table S1, http://links.lww.com/ALN/C300).

Table 1. Characteristics of the Participants (n = 15)

Age, yr	30 [28–33]
Male, n (%)	9 (60)
Body mass index, kg/m^2	23 [21–25]
Respiratory	
Spo_2 (%)	99 [97–100]
RR, breaths/min	15 [11–16]
V_T, ml	800 [665–939]
Leaks rate, %	24 [7–38]
Hemodynamic	
HR, beats/min	63 [56–73]
Systolic blood pressure, mmHg	111 [110–124]
Diastolic blood pressure, mmHg	69 [61–76]
Diaphragm ultrasound	
Diaphragm excursion, mm	22 [18–28]
End expiratory thickness, mm	3.2 [2–4.3]
Diaphragm thickening fraction (%)	21 [14–39]

Continuous variables are expressed in median [IQR]. Categorical variables are expressed in absolute value (%).

HR, heart rate; RR, respiratory rate; Spo_2, peripheral oxygen saturation; V_T, tidal volume.

The control method enabled the detection of autotriggering and delayed cycling with sensitivities of 79% (95% CI, 75–84%) and 67% (95% CI, 61–73%), and specificities of 98% (95% CI, 97–99%) and 96% (95% CI, 96–97%), respectively (table 2). Diaphragm EMG method had a sufficient quality signal to discern the start and end of the inspiratory effort in only nine participants (60%), allowing the analysis of 995 of the 1,925 recorded respiratory cycles. It enabled the detection of autotriggering and delayed cycling with sensitivities of 93% (95% CI, 89–97%) and 84% (95% CI, 77–90%), and specificities of 98% (95% CI, 97–99%) and 99% (95% CI, 98–100%), respectively. Diaphragm ultrasound was possible in all 15 subjects in whom asynchronies were detected at sensitivities above 90 and 85%, and specificities above 97 and 98%, for autotriggering and delayed cycling, respectively (table 2, fig. 2; Supplemental Digital Content, video 1 http://links.lww.com/ALN/C301 and video 2 http://links.lww.com/ALN/C302). Overall, diaphragm ultrasound and diaphragm EMG had similar sensitivities and specificities which were statistically significantly higher than those of the control method (table 2; Supplemental Digital Content, tables S2 and S3, http://links.lww.com/ALN/C300) when compared as proposed by Newcombe *et al.*[10] (Supplemental Digital Content, fig. S1, http://links.lww.com/ALN/C303). Net reclassification measures suggested that the presence and absence of asynchronies were better classified with diaphragm EMG and diaphragm ultrasound than with the control method (table 3).

Discussion

Herein, we describe a technique relying on conjoint assessment of diaphragm ultrasound signals (excursion or thickening) and airway pressure waveform displayed on the ultrasound screen to detect the main asynchronies occurring during noninvasive ventilation in healthy volunteers. This method (especially diaphragm thickening) was definitively more accurate than isolated analysis of flow and pressure waveform, and had better feasibility than diaphragm EMG.

Asynchrony Detection

Detection and mitigation of asynchronies in ventilated patients remain a great challenge for intensivists since mismatch between ventilator pressurization and patient's demand has been recognized as an outstanding clinical issue for years.[16,17] In terms of pathophysiology, the main underlying mechanisms of asynchronies differ significantly between invasive and noninvasive ventilation. In patients under invasive mechanical ventilation, ineffective triggering is the most common asynchrony during pressure support[17–19] and its occurrence is vastly enhanced by overassistance.[17,20–23] During assist-control ventilation, premature cycling and double triggering often occur as a consequence of the low insufflation time.[17,24] Asynchronies are common

Table 2. Performance of Diaphragm Ultrasound and Electromyogram to Detect Autotriggering and Delayed Cycling, in Comparison with Airway Pressure and Flow Waveform Observation Alone

Asynchrony Detection	Control Method (Pressure and Flow Tracings Observation Alone) (n = 1,925 cycles)	Working Standard Method (Pressure and Flow Tracings Coupled with Electromyogram) (n = 995 cycles)	Diaphragm Ultrasound Method (Pressure Waveform Coupled with Ultrasound)	
			Excursion (n = 962 cycles)	Thickening (n = 963 cycles)
Autotriggering				
Sensitivity (%)	79	93	94	91
Specificity (%)	98	98	98	98
Positive predictive value (%)	89	91	91	91
Negative predictive value (%)	96	99	99	98
Likelihood ratio of positive test	40	51.3	50.4	53
Likelihood ratio of negative test	0.21	0.07	0.06	0.09
Diagnostic accuracy (%)	95	97	98	97
Youden index	0.77	0.91	0.93	0.90
Delayed cycling				
Sensitivity (%)	67	84	86	89
Specificity (%)	96	99	99	99
Positive predictive value (%)	72	92	90	93
Negative predictive value (%)	96	98	98	98
Likelihood ratio of positive test	19	81	66.9	94
Likelihood ratio of negative test	0.34	0.16	0.14	0.11
Diagnostic accuracy (%)	93	97	97	98
Youden index	0.64	0.83	0.85	0.88
Any asynchrony				
Sensitivity (%)	75	89*	91*	90*
Specificity (%)	93	97*	96*	97*
Positive predictive value (%)	81	91	90	92
Negative predictive value (%)	91	96	97	96
Likelihood ratio of positive test	11.5	26.2	24.2	28.6
Likelihood ratio of negative test	0.27	0.11	0.09	0.10
Diagnostic accuracy (%)	89	94	95	95
Youden index	0.69	0.86	0.87	0.87

*P value < 0.05 for differences in sensitivity or specificity to detect any asynchrony as compared with the control method.

in invasively ventilated patients[17,18] and associated with bad prognosis, including discomfort, sleep disorders,[25] increased need for sedatives,[26] prolonged mechanical ventilation,[17,19] and higher intensive care unit and hospital mortality,[18] although a causal relationship cannot be established.

In patients under noninvasive ventilation, asynchronies have also been reported albeit with a higher incidence than with invasive mechanical ventilation (up to 40 to 50% of patients),[4] mostly in the form of autotriggering (20%) and delayed cycling (23%), and are mainly incurred by leaks present around the mask.[3,4] These asynchronies interfere with patient's tolerance, which may compromise noninvasive ventilation efficiency and feasibility.[2] Although the role of asynchronies in precipitating noninvasive ventilation failure has not been demonstrated to date, robust and simple methods to detect and reduce their incidence are required.[6]

New Method

The detection method we herein describe is robust, simple and could be an interesting alternative to the usual methods used in clinical settings to detect asynchronies. The simple analysis of flow and pressure waveform (named "control method" in our study) could be easily conducted but its accuracy is questioned due to its poor sensitivity as previously documented.[6,27] On the other hand, a rigorous analysis comparing diaphragm EMG signal and flow/pressure tracings (named "working standard method" in our study) has a much better diagnostic value[3,4,7] but poor feasibility because it is difficult to get a stable electrical signal. From a physiologic point of view, excursion and thickening are not equivalent. The diaphragm displacement could be passively induced by pressurization of the ventilator, whereas diaphragm thickening can more reliably depict an active muscle contraction.[8] However, their performance seemed to be equivalent for the detection of asynchronies in the present study. Our results encourage the innovative use of diaphragm ultrasound to detect, characterize, and quantify asynchrony under noninvasive ventilation at the bedside in intensive care units. Future studies in patients under invasive and noninvasive ventilation are needed to validate the technique. We also hope that the technological development of

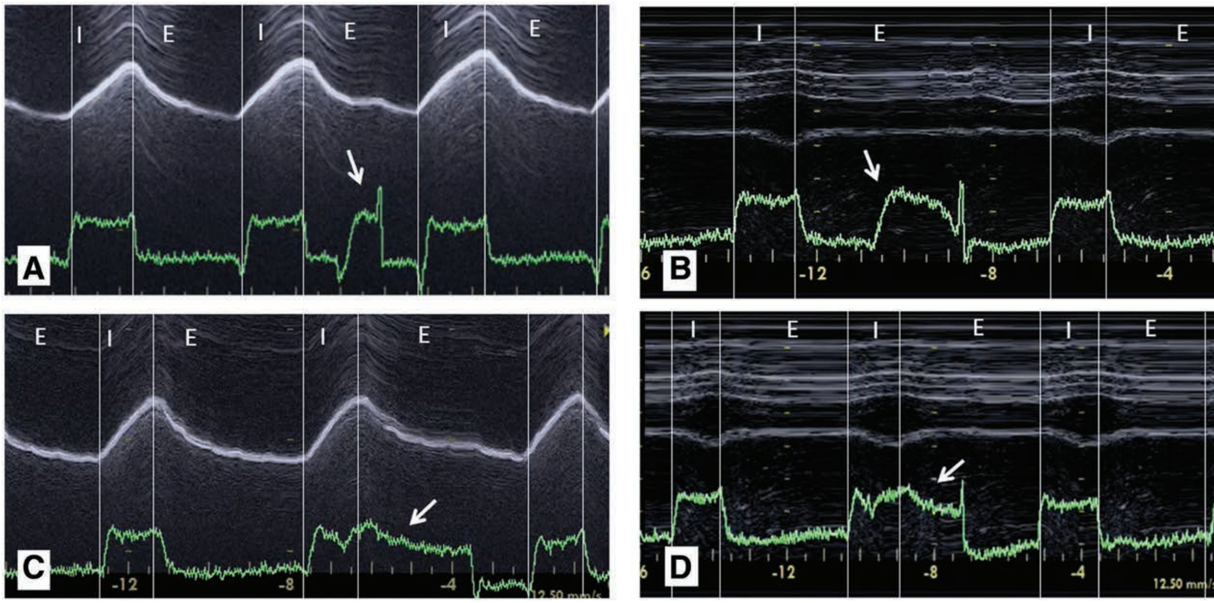

Fig. 2. Autotriggering and delayed cycling detected by monitoring of diaphragmatic excursion or thickening in time motion mode. Diaphragmatic dome movement (*A*, *B*) and diaphragm cyclic thickening (*C, D*) help detect the different respiratory phases. The diaphragmatic dome moves closer to the probe (upwards) during inspiration and moves away from it during expiration. An autotriggered cycle caused by the ventilator is defined as a pressurization that is not associated with any excursion of the diaphragm (*A*). Prolonged insufflation is characterized by a prolonged ventilator pressurization, far beyond the end of diaphragm excursion (*B*). The diaphragm thickens in inspiration and thins out in expiration. An autotriggered cycle initiated by the respirator is recognized as pressurization that is not associated with any diaphragm thickening (*C*). Prolonged insufflation is characterized by a respirator pressurization prolonged far beyond the end of diaphragm thickening (*D*). E, expiration; I, inspiration.

Table 3. Comparison of Diagnostic Accuracy of Electromyogram, Ultrasound and Control Technique Using Net Benefit Methods

	EMG *vs.* Control	Excursion *vs.* Control	Thickening *vs.* Control	Excursion *vs.* EMG	Thickening *vs.* EMG
NRI_{event}	0.12	0.11	0.11	0.01	0.05
$NRI_{nonevent}$	0.03	0.03	0.04	−0.02	0
NRI*	0.15	0.15	0.15	−0.01	0.05
WC†	0.22	0.2	0.21	−0.04	0.05

*Net reclassification improvement (NRI) is an index that attempts to quantify how well a new model reclassifies respiratory cycles. Cycles without (with) asynchronies who were correctly reclassified without (with) asynchronies are assigned a +1. Cycles without (with) asynchronies who were incorrectly classified as with (without) are assigned a −1. Cycles not reassigned are assigned a 0.

NRI is composed of two components: NRI_{event} (the sum of scores in cycles with asynchronies divided by the number of cycles in that group) and $NRI_{nonevent}$ (the sum of scores in cycles without asynchronies divided by the number of cycles in that group). The sum of these two values is the NRI.

Theoretical ranges are −1 to 1 for NRI_{event} and $NRI_{nonevent}$, and −2 to 2 for NRI.

NRI is interpreted as follows: NRI = 0: no benefit for the new test; NRI > 0 with NRI_{event} > 0 and $NRI_{nonevent}$ > 0: the new test is more efficient, with events and nonevents being better classified; NRI > 0 with NRI_{event} > 0 and $NRI_{nonevent}$ < 0: the new test is more efficient, with events being better classified but nonevents being less well classified; NRI > 0 with NRI_{event} < 0 and $NRI_{nonevent}$ > 0: the new test is more efficient, with events being less well classified but nonevents being better classified; NRI < 0: the new test is less efficient.

†Weighted comparison (WC) measure is an index weighting the difference in sensitivity and difference in specificity of two tests, taking into account the relative clinical cost (misclassification costs) of a false positive compared with a false negative diagnosis and disease prevalence.

WC is interpreted as follows: positive WC values indicate a net benefit; zero WC values show no net benefit; negative WC values show a net loss.

EMG, electromyogram.

ultrasound devices will make diaphragm ultrasound assessment even more reliable through time.[28]

Limits

The clinical application should however be counterbalanced by some limitations. First, we generated replicable and characteristic asynchronies, occurring at fairly regular intervals, thus relatively easy to detect and classify. Second, the experimental design reproduced only the most frequent asynchronies occurring during noninvasive ventilation and related to mask leaks (autotriggering and delayed cycling). Future studies should evaluate the usefulness of diaphragm ultrasound in detecting and characterizing others typical asynchronies, though less common but are much more difficult to experimentally induce. Of the latter, three are clinically meaningful: (1) ineffective triggering happens when an inspiratory effort is not met with inspiratory pressurization, and could reflect dynamic hyperinflation; (2) premature cycling is a cycle with mechanical insufflation shorter than the patient's inspiratory time and often occurs in the presence of restrictive respiratory mechanics[4]; and (3) double or reverse triggering is defined as two cycles separated by very short expiratory time and could be related to an insufficient level of assistance.[12] Third, our work needs to be conducted on intensive care unit patients. Our healthy participants were young and slender, with good echogenicity and cooperation allowing a good stability of diaphragm ultrasound signal. They also had a quite slow respiratory rate (which may not be the case for intensive care unit dyspneic patient) and big tidal volumes which probably augmented the diaphragmatic excursion[29] and facilitated the detection of inspiratory efforts with diaphragm ultrasound. A wider use of this method in patients could be hindered by the vast variability of respiratory profiles, instability of the ultrasound signal, and the expected poor tolerance of patients. Last, the study design required an *a posteriori* analysis of curves and video recordings. An online analysis should be considered for future developments.

In conclusion, diaphragm ultrasound accurately detected asynchronies during noninvasive ventilation in healthy volunteers. This technique is promising and should be evaluated in clinical settings, and compared with emerging automated techniques based on diaphragm EMG signal or respiratory flow signal.[30]

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Competing Interests

Dr. Dessap reports technical support from Phillips Healthcare (Amsterdam, The Netherlands) and General Electric Medical Systems (Chicago, Illinois). The other authors declare no competing interests.

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