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Early detection of deteriorating ventilation by monitoring bilateral chest wall dynamics in the rabbit

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Introduction

Mechanically ventilated patients are at risk of mechanical complications that can lead to inappropriate ventilation. Mechanical complication can evolve due to worsening lung disease, developing pulmonary complications (e.g., pneumothorax, atelectasis) or problems in airway management (e.g., tube displacement, obstruction

Abstract *Purpose:* Mechanical complications during assisted ventilation can evolve due to worsening lung disease or problems in airway management. These complications affect lung compliance or airway resistance, which in turn affect the chest wall dynamics. The objective of this study was to explore the utility of continuous monitoring of the symmetry and dynamics of chest wall motion in the early detection of complications during mechanical ventilation. *Methods:* The local tidal displacement (TDi) values of each side of the chest and epigastrium were measured by three miniature motion sensors in 18 rabbits. The TDi responses to changes in peak inspiratory pressure ($n = 7$), induction of one-lung intubation ($n = 7$), and slowly progressing pneumothorax (PTX) ($n = 6$) were monitored in parallel with conventional respiratory (SpO_2 , EtCO_2 , pressure and flow) and hemodynamic (HR and BP) indices. PTX was induced by injecting air into the pleural space at a rate of

1 mL/min. *Results:* A strong correlation ($R^2 = 0.99$) with a slope close to unity (0.94) was observed between percent change in tidal volume and in TDi. One-lung ventilation was identified by conspicuous asymmetry development between left and right TDIs. These indices provided significantly early detection of uneven ventilation during slowly developing PTX (within 12.9 ± 6.6 min of onset, $p = 0.02$) almost 1 h before the SpO_2 dropped (77.3 ± 27.4 min, $p = 0.02$). Decreases in TDi of the affected side paralleled the progression of PTX. *Conclusions:* Monitoring the local TDi is a sensitive method for detecting changes in tidal volume and enables early detection of developing asymmetric ventilation.

Keywords Chest wall dynamics · Ventilation symmetry · Early detection · One-lung ventilation · Pneumothorax

by secretions). Premature infants are especially prone to develop respiratory complications while mechanically ventilated. The narrow endotracheal tube can be easily obstructed by secretions, and the risk of tube displacement and one-lung ventilation is high. The incidence of pneumothorax (PTX) in very low birth weight infants (below 1,500 g) is between 3 and 9% [1, 2]. Deteriorating ventilation and hypoxia in premature infants can lead to

hemodynamic instability and intracranial hemorrhage [3, 4].

Interestingly, 25–44% of the life-threatening respiratory events in neonatal and pediatric intensive care units (NICU, PICU) are detected by attending staff inspections and not by monitoring equipment [5, 6]. In the particular case of PTX, McIntosh [7, 8] reported that the time to diagnosis in a NICU ranged from 45 to 660 min from the initial onset, with a median of 127 min. Therefore, the currently monitored modalities have two main limitations, due to physiological shortcomings in the monitored parameters. The first is a prolonged delay from the onset of a significant mechanical problem in ventilation to the appearance of detectable changes. The second is their poor ability to characterize the nature and location of the underlying problem out of the various plausible causes.

The working hypothesis of this study is that bilateral, continuous monitoring of the symmetry and dynamics of chest wall motion provides additional crucial information that can expedite the detection of deteriorating ventilation. This method was recently tested in premature newborn infants during high frequency oscillatory ventilation (HFOV) [9]. The present study aimed at exploring the utility of bilateral monitoring of chest wall dynamics in three simulated, relatively common situations during conventional mechanical ventilation: decrease in peak inspiratory pressure (PIP), one-lung intubation, and slowly progressing PTX.

Methods

The experiments were carried in 18 adult male New Zealand rabbits weighing 2.1 ± 0.35 kg. The study was approved by the Institutional Ethics Committee for the Care and Use of Animals. Rabbits were anesthetized by intramuscular injection of xylazine (5 mg/kg), ketamine (35 mg/kg), and acepromazine (1 mL/kg). Additional doses of one-third of the aforementioned amounts were added every 20 min. A 3-mm endotracheal tube was placed by direct laryngoscopy or tracheostomy and conventional intermittent mandatory ventilation (CMV) was instituted (SLE 2000, SLE, Surrey, UK). The ventilatory parameters were adjusted to maintain normal arterial blood gas tensions utilizing a blood gas and electrolyte analyzer (Roche OPTI CCA, Mannheim, Germany). A percutaneous catheter was placed in the ear artery for blood sampling and recording blood pressure (BP). A pulse oximeter was attached to the ear or legs. BP, heart rate (HR), and end-tidal expiratory carbon dioxide concentration (EtCO₂) were acquired by a standard system (Datex Ohmeda Inc., Wisconsin, USA). Endotracheal tube pressure (TP) was measured by a pressure transducer (Millar Instruments Inc., Houston, Texas, USA), and tidal volume (V_T) by a flow-meter (TSD137, Fleish Pneumotachograph, Harvard

Apparatus, Holliston, MA). The experimental setup is described schematically in Fig. 1 in the online supplementary material.

Two miniature (<1 g, 5 mm diameter) motion sensors were attached to both sides of the chest, at the mid-clavicular lines and the fifth or sixth intercostal space, and a third sensor was attached to the epigastrium (Figs. 2 and 3 in the supplementary material). These accelerometers enable one to measure the local subsonic (below 20 Hz) wall motion, as well as the vibrations from the breath and heart sounds, as presented in Fig. 4 in the supplementary material. The data were acquired at a sampling rate of 5 kHz (Pneumedicare system, Pneumedicare, Yokneam, Israel). The sounds' contributions were filtered. The signals were used to measure the amplitude of the local tidal angular displacement at each site, denoted as the local tidal displacement index (TDi), of the right (TDiR) and left (TDiL) sides of the chest and the epigastrium (TDiE). The ratio of the right to left chest wall displacement (R/L) characterized the ventilation symmetry.

The sensitivity of each sensor was calibrated by utilizing a high resolution (1 μ M) computerized lever arm system (Model 310C, Aurora Scientific Inc., ON, Canada). The system imposed oscillations at various known frequencies and amplitudes that were measured by the motion sensors. A linear relationship ($R^2 = 0.99$) between imposed oscillation amplitudes and measured tidal displacement was found, with small (3.7%) variability in sensitivity between the sensors (Fig. 5 in the supplementary material).

Study protocols

Three types of complications were simulated: (1) reduction in PIP (7 rabbits, 50 events), (2) one-lung intubation (7 rabbits, 20 events), and (3) slowly progressing right PTX (6 rabbits).

The PIP was reduced by 11, 22, 33, and 66%. These reductions were imposed in random order, with every event repeated at least twice per rabbit. One-lung intubation was induced by advancing the endotracheal tube until significant asymmetric ventilation was confirmed by auscultation. Slowly progressing PTX was created by inserting a chest tube (10 Fr) into the right pleural space, in the tenth intercostal space at the mid-axillary line. The incision was sutured, and the tube was connected to a syringe pump (Graseby 3100, SIMS Graseby Ltd., UK) which injected air at a constant rate of 1 mL/min.

Drops in PIP and one-lung intubations were imposed for at least 100 s, or until severe hemodynamic deterioration or hypoxemia ($SpO_2 < 90\%$) was observed, before restoring normal ventilation. For PTX, baseline recordings were made for at least 5 min before starting air injection into the pleural space. Injection continued until a persistent decrease in SpO_2 ($SpO_2 < 90\%$) developed.

At this point, the air in the pleural cavity was aspirated in order to measure its volume. The chest was transilluminated and photographed for qualitative control at baseline and twice during the perturbation. Arterial blood gas tensions were measured at baseline and after injecting 40, 60, and 80 mL of air.

Data analysis

Deviation was defined as a 20% change from baseline in TDiR, TDiL, or TDiE, whereas desaturation was defined as a decrease of SpO₂ below 90%.

Statistical analysis

Results are presented as mean \pm SD, and median and range. Differences between specific data means were compared using the Wilcoxon signed-rank test. Statistical significance was defined as $p < 0.05$. The linear correlation between TDi, PIP, and V_T was evaluated using the Pearson coefficient of mean-square contingency (R^2).

Results

The rabbits ($n = 18$) were ventilated at a respiratory rate of 19.9 ± 3.2 mL/min, PIP of 16.7 ± 2.0 cmH₂O, with a positive end-expiratory pressure (PEEP) of 3.0 cmH₂O. Measured V_T was 10.91 ± 0.69 mL/kg. Similar respiratory rates and V_T were used by other authors [10]. No spontaneous breaths were detected during baseline measurements, as presented in Fig. 7 in the supplementary material.

Changes in PIP

The relative decreases in ΔP , where $\Delta P = PIP - PEEP$, were larger than the relative decreases in PIP, because PEEP was equal to 3 cmH₂O. The PIP reductions by 11, 22, 33, and 66% were associated with measured decreases in ΔP of 17.4 ± 2.2 , 27.6 ± 0.8 , 46.6 ± 3.0 , and $82.2 \pm 1.9\%$, respectively.

Typical responses to 33 and 11% decreases in the PIP are displayed in Fig. 6 in the supplementary material. Clear decreases in the TDi were observed within the first or second ventilation following the perturbations, even in the smallest imposed decreases in the PIP.

Figure 1 compiles all the results and presents detection success rates for four reductions in PIP. All the 66% decreases in PIP (13 events) were detected by the TDi as well as by changes in SpO₂ and EtCO₂. The 33% decreases in the PIP (14 events) were easily detected in all cases solely by the TDi. EtCO₂ and SpO₂ sensitivities were 78.6 ± 39.3 and $52.4 \pm 41.3\%$, respectively. The 22% (17 events) and 11% (16 events) reductions in PIP were clearly detected in all events only by changes in the TDi (100% sensitivity), and hardly detected by other parameters. The TDi decreased within one or two breaths (after 1.8 ± 4.65 and 2.1 ± 2.71 s for 22 and 11% reductions, respectively). There were significant differences in the time to detection between the various indices. For simplicity, only the times to detection in response to the largest PIP reductions (-66%) are presented (Fig. 1e). Detectable changes in TDi occurred immediately in the first ventilation, followed by detectable decreases in EtCO₂ (5.7 ± 6.8 s) and in SpO₂ (22.4 ± 5.4 s).

Most importantly, changes in the TDi (ΔTDi) were proportional to changes in PIP ($R^2 = 0.99$) and the resulting reductions in V_T . A strong correlation with a

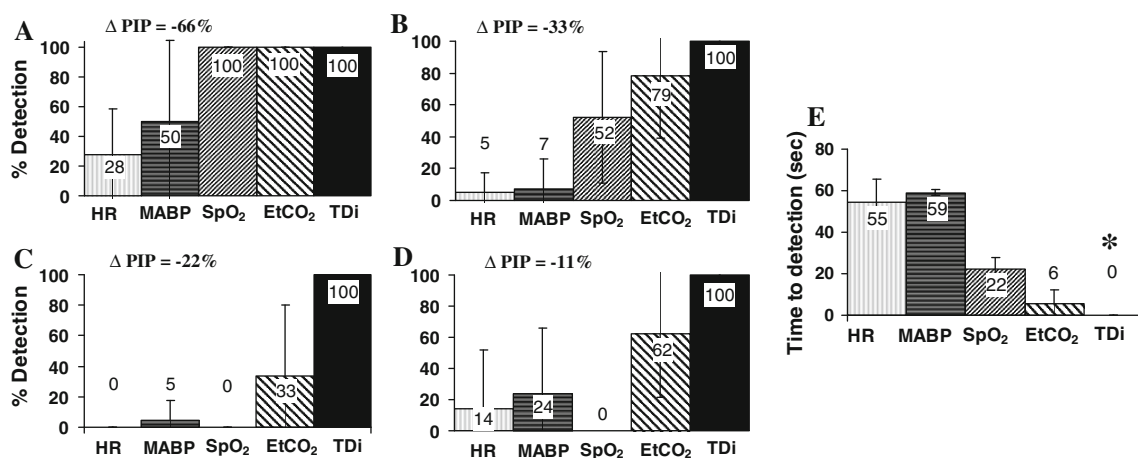


Fig. 1 Tidal displacement index (TDi) provided fast response to reduction in the peak inspiratory pressure (PIP). The figure compiles the rate of successful detection of an imposed **a** 66%, **b** 33%, **c** 22%, and **d** 11% decrease in PIP, as well as **e** the time to

detection of the event by each monitored parameter in the imposed 66% reduction of PIP. Detectable changes in TDi always occurred within one to two breath cycles

Fig. 2 a Strong correlation was observed between the changes in the tidal displacement index (ΔTDi), and the ΔP (PIP – PEEP). **b** Strong correlation was obtained between the changes in TDi (ΔTDi) and in tidal volume (ΔV_T)

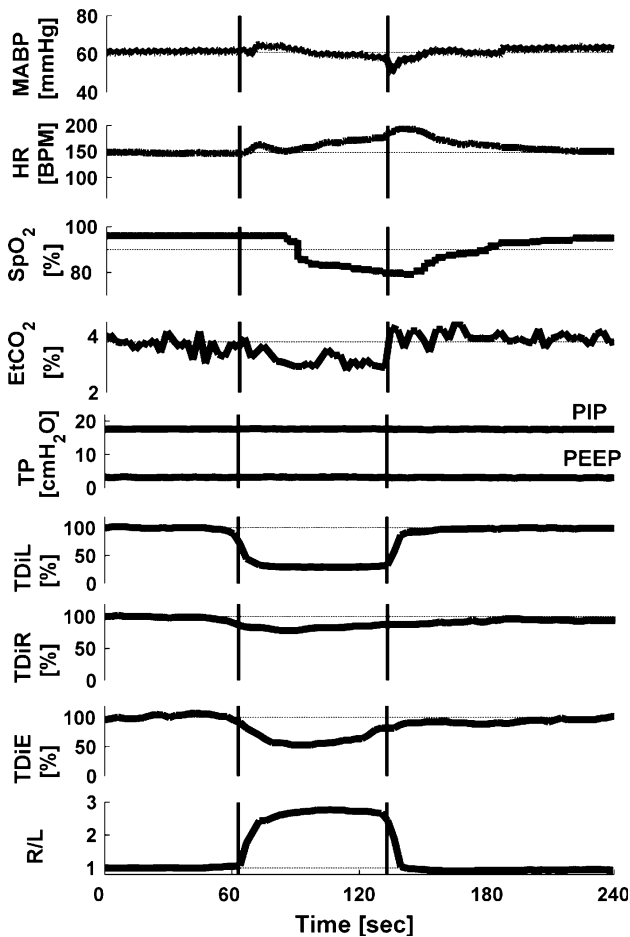
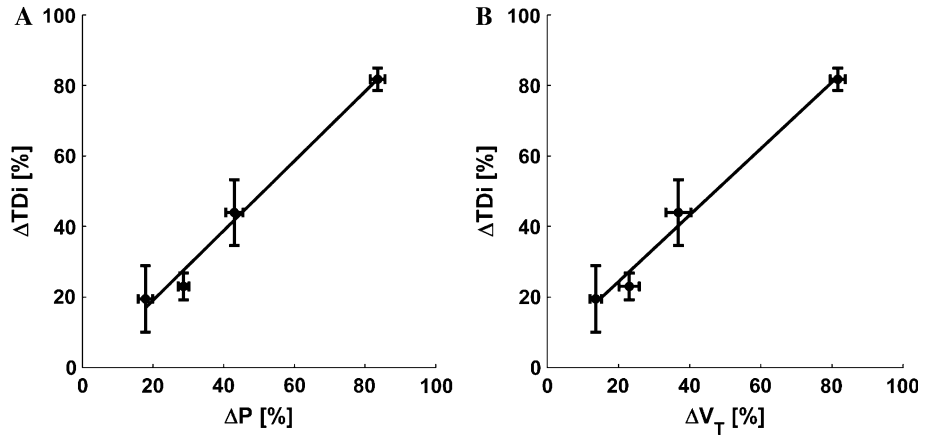


Fig. 3 Changes in the local tidal displacement indices (TDi) immediately revealed the uneven asymmetric ventilation during (*right*) one-lung ventilation. Note the decrease in the *left* TDi (TDiL) and the change in the ratio (R/L) of the *right* to *left* chest wall displacement

slope close to unity (0.99) was observed between the relative changes in ΔP and ΔTDi , as shown in Fig. 2a. A strong correlation with a slope close to unity (0.94) was

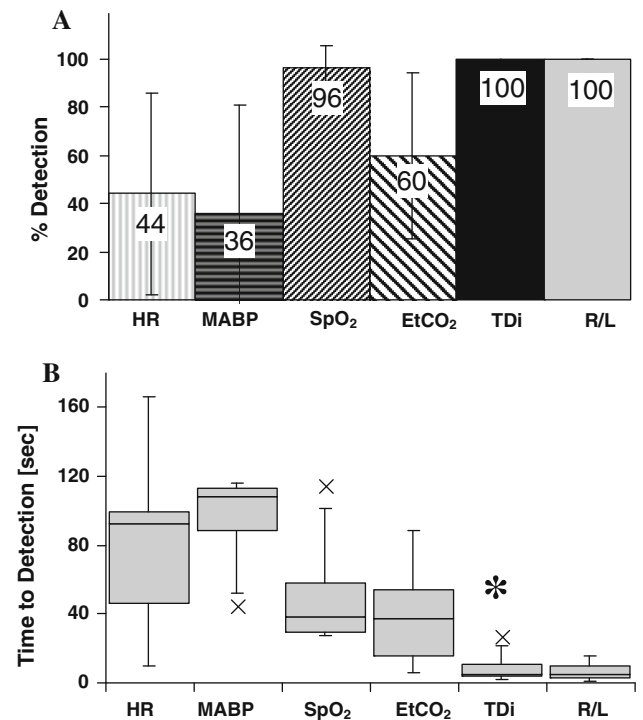


Fig. 4 Tidal displacement index (TDi) provided 100% sensitivity (a) and the fastest response (b) to the development of one-lung ventilation ($N = 7$) when compared to other studied indices ($*p = 0.01$)

also obtained between the changes in the tidal volume (ΔV_T) and the changes in ΔTDi (Fig. 2b). A decrease of 33% in PIP yielded a $46.6 \pm 3.0\%$ decrease in ΔP , a $36.8 \pm 3.5\%$ decrease in V_T and a $43.9 \pm 9.3\%$ decrease in TDi.

One-lung intubation

Figure 3 displays typically observed responses, characterized by a marked and rapid decrease in TDiL and an

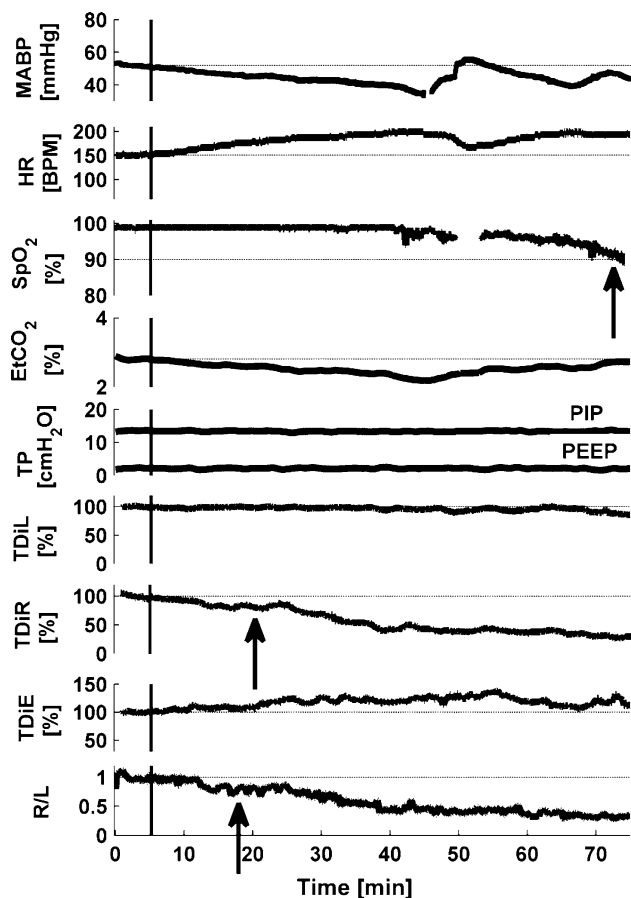


Fig. 5 Gradual decrease in the right tidal displacement index (TDiR) revealed the development of progressing right PTX with asymmetric lung ventilation significantly before desaturation evolved. PTX was induced by a 1 mL/min air injection into the right pleural space

increase in R/L. Thereafter, the EtCO₂ and SpO₂ decreased, later followed by mild changes in HR and BP. Figure 4 compiles the results of one-lung intubation (7 rabbits). Sensitivity in detecting asymmetric ventilation (R/L) and decrease in the left lung ventilation (TDiL) by the motion sensors was 100%. The perturbations were detected within 8.8 ± 9.16 s by the changes in TDi and R/L indices. The time to detection using TDi was significantly shorter than for the other indices ($P < 0.01$).

Right-side PTX

Figure 5 represents one experiment of slowly progressing right PTX. A progressive decrease in TDiR was observed with the onset of PTX. TDiR decreased by 20% within 15.6 min of initiating the slow air injection into the right pleural space, and a prominent (20%) change in asymmetric ventilation was observed, as reflected by the R/L index after 13.1 min. Mean arterial blood pressure

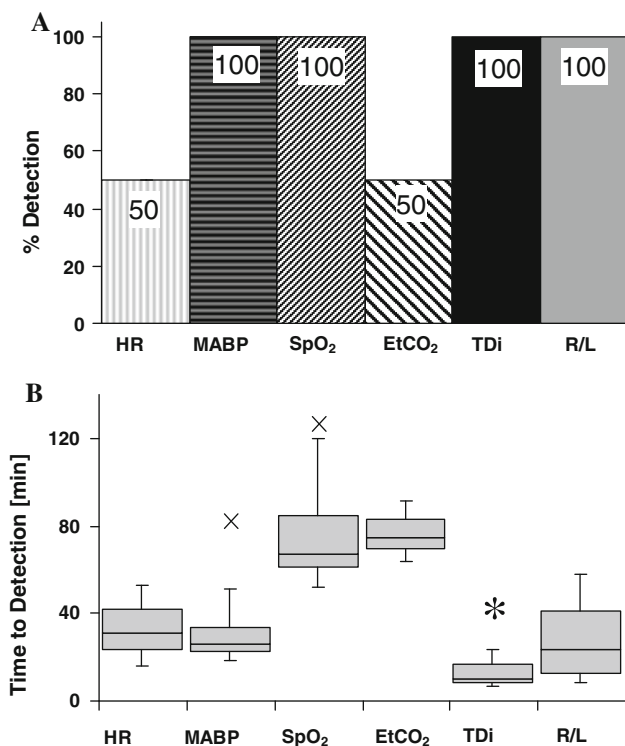


Fig. 6 Tidal displacement index (TDi) provided high sensitivity (a) and faster response (b) to the development of progressing right-side PTX ($n = 6$). Note that PTX was detected within 12.9 ± 6.6 min by the TDi and only after 77.3 ± 27.4 min by the pulse oximetry (SpO₂) ($*p = 0.01$)

(MABP) decreased after 21.2 min. Interestingly, a decline in the SpO₂ appeared at a very late stage: only after 69.0 min.

Figure 6 summarizes the sensitivity and the time to detection by the various indices (6 rabbits). The motion sensors easily detected all PTXs (100% sensitivity) as early as 12.9 ± 6.6 min after the onset of the slow (1 mL/min) air injection, and provided the first sign for deteriorating ventilation in all cases. Deteriorating ventilation was detected by both the decrease in TDiR on the affected right side and by the development of asymmetric ventilation. The significant (20%) decrease in BP was also very sensitive (100%), but appeared later (after 35.0 ± 23.9 min). The mean time until desaturation occurred was very long, after 77.3 ± 27.4 min. Hemodynamic changes preceded the changes in gas-exchange indices, i.e., EtCO₂ and SpO₂ and arterial blood gas tensions. The blood gas analyses are shown in Table 1.

Discussion

Continuous monitoring of chest wall dynamics presents the following three clinical advantages: (a) high sensitivity

Table 1 Arterial blood gas tensions were measured at baseline and after injecting 40, 60, and 80 mL of air ($n = 6$)

	Baseline	40 mL	60 mL	80 mL
pH	7.52 ± 0.06	7.54 ± 0.05	7.49 ± 0.04	7.45 ± 0.04
PaO ₂	91.2 ± 14.3	90.2 ± 11.3	70.1 ± 10.4	61.5 ± 17.7
PaCO ₂	36.1 ± 6.7	31.7 ± 5.9	34.3 ± 4.8	40.5 ± 3.5
Bic	27.9 ± 2.9	25.9 ± 1.1	25.3 ± 1.5	25.3 ± 0.8
BE	4.9 ± 2.5	3.9 ± 0.8	2.1 ± 0.6	0.6 ± 0.4
SpO ₂	96.2 ± 3.2	97.3 ± 1.2	94.2 ± 3.1	92.6 ± 4.9

Bic bicarbonate

to changes in the tidal volume and precise quantification of the severity of these changes, as demonstrated by the strong correlation between the decrease in TDi and tidal volume; (b) assessment of ventilation symmetry, as demonstrated with one-lung intubation and PTX; and (c) early detection of deteriorating ventilation, as demonstrated by the early response to the induction of slowly progressing PTX.

The sensitivity of the TDi to changes in the ventilation was tested by the imposed reductions in PIP. All events, including mild decreases in PIP, were detected. The changes in TDi also detected all one-lung intubations and PTX events. PTX was detected when a relatively small amount of air (12.9 ± 6.6 mL) was injected into the pleural space. Changes in TDi preceded the changes in all other monitored parameters because the motion sensors, which are attached to the chest wall, directly monitor the changes in lung ventilation. The other physiological indices are consequential measures of changes in ventilation, which are influenced by various compensatory mechanisms.

The TDi also allows one to assess the severity of the ventilation changes. Decreases in TDi were proportional to decreases in inspiratory pressure and in the tidal volume. Furthermore, there was a progressive decrease in TDi with time during slowly progressive PTX as the amount of intrapleural air increased.

Assessment of ventilation symmetry is of particular importance. This crucial parameter can facilitate the diagnosis and localization of the underlying cause. The information can be used to differentiate between mechanical problems in the central airways, and problems below the bifurcation of the two main bronchi. The former yields symmetrical changes in the monitored TDiR and TDiL, whereas the latter produces asymmetrical changes. Tension PTX is usually detected in the NICU by a decrease in SpO₂ and blood pH, and increase in PaCO₂. However, these changes appear after a prolonged delay, after PTX reaches a critical mass [7, 8, 11]. It is instructive to note that changes in SpO₂ were the last to occur in our study, whereas the TDI and R/L indices were able to identify the gradual development of the PTX even in its initial phase.

Numerous studies have explored the use of auscultation for ventilation monitoring, based on the characterization of

breath sound patterns in various diseases [12–14]. However, the analysis of breath sounds and comparison with sounds in databanks have inherent limitations because human breath sounds vary among different individuals [14–17]. The method described here detects changes in ventilation dynamics relative to the individual's baseline measurements. Furthermore, it characterizes the subsonic chest wall dynamics and does not use the breath sounds.

Simultaneous auscultation at multiple sites by large arrays of sensors over the chest has been suggested as a method for creating three-dimensional images of air flow through the lungs [18]. However, the use of large arrays of microphones for prolonged monitoring is cumbersome and inconvenient in the NICU setting.

Endotracheal tube air flow and pressure can be continuously measured in new ventilators [19, 20]. There are several explanations for the prolonged delay in the detection of complications [5–8] despite the close monitoring of the endotracheal tube flow and pressure. Monitoring air flows with sensors at the endotracheal tube inlet is a method insensitive to small differences between the inhaled and exhaled volumes, which gradually accumulate into large intrathoracic lesions, such as in PTX. A 1% decrease in the exhaled volume due to a leak into the pleural space cannot be detected today. However, this small air leak can develop into a tension PTX within 30 min. Measurements of endotracheal tube flow and pressure are unable to assess the symmetry of ventilation—an early sign of PTX. Moreover, the high resistance to air flow in the narrow endotracheal tube, used in pediatric patients, limits the ability to sense progressive changes in lung compliance and resistance.

Several noninvasive modalities have been developed for assessing respiratory mechanics in infants, such as respiratory inductance plethysmography [21–24], elastomeric plethysmography, optic respiratory plethysmography [25], and electrical impedance tomography (EIT) [26, 27]. The plethysmographic modalities are not easy to use for continuous monitoring in the setting of a NICU because they utilize belts that must be tight and encircle the chest and abdomen, and are bulky [22]. These plethysmographic techniques may chafe the skin, especially in the more immature of patients. None of these modalities are presently used routinely in the clinical NICU setup. The suggested continuous TDi monitoring was recently tested in premature infants during high frequency oscillatory ventilation [9]. Monitoring the deviations in TDi enabled the detection of deteriorating ventilation 22.4 ± 18.7 min before the obstruction by secretions evolved into hypoxemia requiring treatment [9].

Limitations

Measurement of TDi cannot accurately assess the absolute tidal volume. A strong correlation between the

changes in the TDi and V_T was presented. However, assessing the absolute V_T from the TDi requires complex calibration. The aim of this new method is to monitor changes in the symmetry and dynamics of lung ventilation, rather than assessing the absolute V_T .

The recorded chest wall dynamics in patients is more complex because the breathing pattern in small babies is rather irregular, with small tidal volumes, and includes sporadic body movements. In this preclinical study the breathing pattern during CMV was quite regular and no significant motion artifacts were encountered. We have validated that the system response is not affected by the breathing frequency in vitro (Fig. 5 in the supplementary material). The feasibility of the system in newborn infants ventilated with HFOV, where the signal amplitude is very small, has been tested [9]. The effects of irregular spontaneous breathing and motion artifact should be tested in a clinical study.

Detection of asymmetric ventilation will be limited in adults with a stiff chest. The study highlights that significant information is available from monitoring a compliant chest's wall dynamics. Under relaxed conditions the chest wall compliance is larger than lung compliance in neonates and infants [28, 29].

Conclusions

Continuous monitoring of the symmetry and dynamics of the local chest wall displacement (TDi) by miniature body-surface sensors has the potential to provide early detection of complications during mechanical ventilation. The decrease in TDi is proportional to the severity of the decrease in ventilation during PIP reductions and PTX. Uneven ventilation due to one-lung intubation and PTX can be detected when the chest is flexible. The TDi provided early detection of PTX significantly (almost 1 h) before SpO₂ dropped. The potential clinical utility in pediatric patients receiving respiratory support, in the presence of spontaneous breathing and body motions, should be explored in a clinical study.

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