Frequency dependence of elastance and resistance in ventilated children with and without the chest opened

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ABSTRACT: Measurements of respiratory mechanics in mechanically-ventilated children are potentially useful for understanding the pathogenesis and progression of diseases resulting in respiratory failure. Measurement techniques that can be simply and noninvasively employed model the respiratory system as a single compartment.

The frequency dependence of elastance, both of the total respiratory system and of the lungs, was investigated in eight children (aged 2-56 months) undergoing open-heart surgery. The children were studied whilst anaesthetized, paralysed and mechanically-ventilated. Dynamic elastance (Ers) and resistance (Rrs) of the respiratory system and of the lung were calculated using a multilinear regression technique, with the chest wall intact, prior to the commencement of surgery, and with the chest wall opened via a mid-line sternotomy. Measurements were repeated after brief (60 s) changes in ventilation frequency.

The total respiratory system and the lungs demonstrated frequency-dependent behaviour, with elastance increasing and resistance decreasing with frequency. The pattern of the frequency-dependent behaviour was essentially the same, whether the chest wall was intact or opened, suggesting that the chest wall was not solely responsible for this behaviour in these children.

These data are consistent with a linear viscoelastic model containing a Kelvin body. When using measurements of respiratory mechanics to follow the progress of respiratory disease in mechanically-ventilated children, this frequency-dependent behaviour must be taken into account.

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With the increasing complexity of paediatric intensive care, objective measurements of respiratory mechanics during mechanical ventilation are desirable [1]. Study of the mechanical properties of the respiratory system during mechanical ventilation should provide a better understanding of the pathogenesis and progression of diseases causing respiratory failure, as well as providing objective evidence of the benefits of therapeutic interventions [1]. Techniques for measuring respiratory mechanics in use in paediatric intensive care units are usually based on fitting the equation of motion of a linear single-compartment to recordings of pressure, flow and volume change, measured at the airway opening, using a multilinear regression analysis [2,3]. This analysis yields values of dynamic elastance (Ers) and resistance (Rrs) for the respiratory system. The necessary equipment is commercially available (e.g. SensorMedics Corp., Yorba Linda, Ca, USA). These techniques assume that the respiratory system can be modelled as a single compartment during mechanical ventilation. The healthy adult respiratory system approximates a single compartment at frequencies above 2 Hz [4]. However, this is unlikely to be the case at normal ventilation frequencies, particularly in children [5].

Despite the above theoretical limitation to the usefulness of the multilinear regression analysis, published data show that this technique results in the model fitting the recorded signals well, with coefficients of determination (r²) usually exceeding 0.95 in ventilated children [2,3,6]. Thus, when the nonlinear respiratory system is excited at a single frequency, its behaviour can generally be described by a single-compartment linear model.

Improvement in a lung disease requiring mechanical ventilation is usually accompanied by a reduction in the amount of respiratory support required, including reductions in ventilation frequency and peak pressure required to deliver a given tidal volume. Similarly, some therapeutic interventions, such as extracorporeal membrane oxygenation [7], are usually accompanied by alterations in the ventilation pattern employed. Data published from both animal and adult human investigations have demonstrated a frequency-dependence of Ers and Rrs during sinusoidal forcing [8,9]. If the same frequency dependence of elastance and resistance is present in children,
changes in Ers and Rrs measured during the course of an illness requiring mechanical ventilation could be due to changes in ventilation frequency, rather than to any change in the mechanical properties of the respiratory system.

Data from animal experiments suggest that much of the frequency-dependent behaviour of the intact respiratory system can be explained by the chest wall, both during relaxed expiration [10], and flow interruption [11]. The adult human chest wall also exhibits frequency-dependent behaviour [12, 13]. We wanted to investigate the frequency-dependence of elastance and resistance of the respiratory system and the chest wall and, therefore, studied children undergoing open-heart surgery under anaesthetic, before and after the chest wall was opened by mid-line sternotomy.

Methods

Subjects

Eight children, aged 2–56 months, were studied during open-heart surgery. Anaesthesia was induced with thiopentone and maintained with intravenous infusions of morphine and fentanyl. The children were intubated, paralysed with atracurium, and mechanically-ventilated with 30–40% O₂ in air. Initial ventilation parameters were set by the anaesthetist, according to routine clinical criteria. Anthropometric data are shown in Table 1.

Data Collection

Following induction of anaesthesia and connection of cardiovascular monitoring equipment, but prior to commencement of surgery, an oesophageal balloon was passed into the mid to lower oesophagus in order to measure oesophageal pressure (Poës). Because occlusion tests were not possible in the paralysed subjects, the balloon was positioned to give the maximum positive deflection during positive pressure ventilation, with the smallest possible cardiac artifact. Flow (V) and pressure at the airway opening (Pao) were measured during mechanical ventilation, by inserting a pneumotachograph (Fleisch No. 0 or No. 1) and lateral pressure port between the endotracheal tube and ventilator connector. Pao and Poës were measured using piezoresistive pressure transducers (Applied Measurements, Melbourne, Australia). All signals were passed through low-pass filters (Frequency Devices 902LPF, 8-pole bessel filters) with the corner frequency set at 10 Hz, digitized at 250 Hz using a 12-bit A-D converter (Data Translation DT2801-A), and stored on computer for later analysis (Labdat & Anadat, RHT-Infodat, Montreal, Canada). Flow at the airway opening was numerically integrated to give a volume (V) signal. Any leak around the endotracheal tube was sealed by manually-applied pressure to the cricoid region. The study was approved by the local Ethics Committee, and informed parental consent was obtained.

Data Analysis

The behaviour of the respiratory system was modelled as a linear, one compartment model, described by the relationship:

\[
p(t)=ExV(t)+RxV(t)+K
\]

where \(p(t)\) is the applied pressure at time \(t\), \(V(t)\) is the volume at time \(t\), \(E\) is the dynamic elastance, \(R\) is the resistance and \(K\) is a constant term. \(E\), \(R\) and \(K\) were determined by multilinear regression.

If \(Pao\) is the applied pressure, Equation (1) describes the respiratory system in the closed-chest situation as follows:

\[
Pao(t)=ErsxV(t)+RrsxV(t)+EEP
\]

where \(EEP\) is the alveolar pressure (PA) at end-expiration [3], and can be used to measure intrinsic positive end-expiratory pressure (PEEP) [14]. If transpulmonary pressure (Pt\(p\)), calculated by subtracting Poës from \(Pao\), is used as the applied pressure, the equation of motion of the lung can be written as:

\[
Pt\(p\)(t)=ELxV(t)+RLxV(t)+K
\]

where \(EL\) is the dynamic resistance of the lungs, \(RL\) is the pulmonary resistance, and \(K\) is a constant represent-

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Age months</th>
<th>Weight kg</th>
<th>VT ml·kg⁻¹</th>
<th>Diagnosis</th>
<th>El, cmH₂O·ml⁻¹</th>
<th>RL, cmH₂O·s·ml⁻¹</th>
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</thead>
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<tr>
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VSD: ventricular septal defect; TF: tetralogy of fallot; ASD: atrial septal defect; TGA: transposition of the great arteries; VT: tidal volume at the lowest frequency; EL: pulmonary elastance; RL: pulmonary resistance.
ing the difference between $P_a$ and the elastic recoil of the lung at end-expiration, to the extent that there is complete equilibration of pressures within the bronchial tree at end-expiration. In the open-chested situation, Equation (2), with $P_a(t)$ as the applied pressure, gives estimates of pulmonary mechanics (i.e. $E_l$ and $R_l$), and $K$ is the end-expiratory $P_a$.

The presence of an endotracheal tube resistance ($R_{ett}$) adds a flow-dependent resistance to $R_{rs}$ and $R_l$ [15], that can be described by the so-called Rohrer equation.

$$R_{ett}=K_1+K_2 \times \bar{V}$$

(4)

To determine the flow-independent resistance of the respiratory system (or lungs), Equation (1) can be expanded to allow for a flow dependent resistance as follows:

$$p(t)=E \times \bar{V}(t)+R_1 \times \bar{V}(t)+R_2 \times \bar{V}(t)+R_3 \times \bar{V}(t) x \bar{V}(t)+K$$

(5)

where $R_1$ is the flow-independent, and $R_2$ is the flow-dependent, component of the resistance and $\bar{V}(t)$ is the absolute value of the flow at time $t$.

By measuring $K_1$ and $K_2$ in vivo, and using $P_a$ as the applied pressure to calculate respiratory system mechanics, and $P_{up}$ as the applied pressure to calculate lung mechanics; $R_{rs}$ corrected for $R_{ett}$, is therefore:

$$R_{rs}=(R_{rs1}-K_1)+(R_{rs2}-K_2) \times \bar{V}$$

(6)

where $\bar{V}$ is the mean absolute flow, and $R_l$, corrected for $R_{ett}$, is:

$$R_{l}=(R_{l1}-K_1)+(R_{l2}-K_2) \times \bar{V}$$

(7)

Measurements of mechanical ventilation consisted of several entire breaths (the number depended on the ventilation frequency). The estimates of $E$ and $R$ calculated by multilinear regression represent weighted-average values over the tidal volume range [2, 16]. Measurements were considered technically satisfactory if $R_1$ and $R_2$ could be determined with standard deviations of $<$10% of the mean, and if the coefficient of determination ($R^2$) for Equation (5) was $>0.95$. Estimates of $R_{rs}$ and $R_l$ were corrected for $R_{ett}$ using Equations (6) and (7), respectively.

**Study protocol**

Once the subject was stable under anaesthesia, with all cardiovascular monitoring equipment connected, but prior to commencement of surgery, three 25 s data epochs were recorded, with the ventilation parameters set by the anaesthetist. The ventilation frequency was then altered briefly (for 60 s), within clinically acceptable limits, and a further 25 s data epoch recorded. Ventilation frequency was increased or decreased in random order. The number of measurements possible in each child depended on the clinical condition of the child and the time restraints imposed by the surgical schedule.

The chest wall was then opened for cardiac surgery, using a mid-line sternotomy, and the split ends of the sternum widely retracted. The right pleural membranes were opened to provide surgical access, but those on the left were not routinely opened. The measurements of respiratory mechanics were repeated, in a manner identical to the baseline measurements.

**Statistical analysis**

To allow for the effects of different ventilation frequency ranges for the younger and older children, all variables (elastance, resistance and frequency) were expressed as a percentage of the value obtained at the lowest frequency used in each individual patient. Data were then analysed using the analysis of variance (ANOVA) and a covariance analysis on the Statistical Package for the Social Sciences, SPSS. To control for the potential influence on resistance of the change in mean flow that is likely to occur with a change in frequency, resistances were calculated for fixed flows of 60, 100 and 150 ml s$^{-1}$. Dependent variables were $E_{rs}$, $R_{rs}$, $E_l$ and $R_l$. The subject number was first entered into the analysis, the ventilation frequency was then entered as the covariate. Statistical significance was accepted at $p<0.05$.

**Results**

**Chest Wall Intact**

Technically satisfactory measurements could be obtained in five of the eight subjects (Nos. 1–3, 5 and 8).

Frequency-dependent behaviour was seen in both respiratory system and pulmonary mechanics. $E_{rs}$ increased with increasing frequency (fig 1a); the group mean value (so) at the highest frequency being 161±93% of that at the lowest frequency ($p<0.02$). $R_{rs}$ changed significantly with frequency ($p<0.001$), decreasing with increasing frequency (fig 1b); the group mean value at the highest value being 67±22% of that at the lowest frequency. Similar changes were seen in pulmonary mechanics with frequency (fig 2); $E_l$ increased to 173±113% ($p<0.01$) and $R_l$ decreased to 68±26% ($p<0.001$). The increases in elastance and the decreases in resistance were statistically significant in individual patients.

The elastance of the chest wall also increased with frequency, with the value at the highest frequency being 172±73% of that at the lowest frequency. The chest wall contributed 19±6% to total respiratory system elastance, and this contribution did not change with frequency. $PEEP_i$, derived from Equation (2), increased with increasing frequency from 3.5±1.65 to 7.0±3.47 cmH$_2$O, but tidal volume ($V_t$) did not change significantly.

**Chest opened**

Technically satisfactory measurements were obtained in six of the eight subjects (Nos. 1–5 and 7). During changes in ventilation frequency, $V_t$ was unchanged but
FREQUENCY DEPENDENCE OF ELASTANCE AND RESISTANCE

Fig. 1. - $E_r$ (a) and $R_r$ (b), with the chest closed, plotted as a function of ventilation frequency. Individual data are shown from five subjects with the chest closed. Patients: $\Delta$: No. 1; $\ast$: No. 2; $\times$: No. 3; $\circ$: No. 3; $\square$: No. 8. $E_r$: elastance of the respiratory system; $R_r$: resistance of the respiratory system.

Fig. 2. - $E_l$ (a) and $R_l$ (b), calculated from transpulmonary pressure with the chest closed, plotted as a function of ventilation frequency. Individual data are shown from 5 subjects. Patients: $\Delta$: No. 1; $\ast$: No. 2; $\times$: No. 3; $\circ$: No. 5; $\square$: No. 8. $E_l$: pulmonary elastance; $R_l$: pulmonary resistance.

Fig. 3. - $E_l$ (a) $R_l$ (b), calculated from $Pao$ with the chest wall opened by mid-line sternotomy, plotted as a function of ventilation frequency. Individual data are shown from six subjects. Patients: $\Delta$: No. 1; $\ast$: No. 3; $\times$: No. 4; $\circ$: No. 5; $\square$: No. 6; $\times$: No. 7. $Pao$: pressure at airway opening. For further abbreviations see legend to figure 2.
PEEPi increased from 2.4±1.1 cmH₂O at the lowest frequency to 5.5±2.6 cmH₂O at the highest frequency. Frequency-dependent behaviour of E₁ (increasing to 140±10%, p<0.001) and R₁ (decreasing to 54±20%, p<0.001) was seen, with the pattern of change being similar to those seen with the chest closed (fig. 3).

Discussion

The results of the present study demonstrate that mechanically-ventilated children exhibit frequency-dependent behaviour of both elastance and resistance. This is true for both the total respiratory system and for the lungs. Similar patterns were seen, whether using an oesophageal balloon to partition mechanics with the chest wall intact, or using Pao as the applied pressure in open-chested children. These results confirm the frequency-dependence of mechanics reported from animal studies and from adult humans.

The similarity in the patterns seen with the chest wall intact and with the chest opened via a mid-line sternotomy suggests that the pattern of the frequency-dependent behaviour is contributed to by both the lungs and chest wall. It is likely that the chest-wall was still contributing somewhat to the mechanical behaviour of the respiratory system with the sternum opened in the present study, as the pleural membranes usually remained intact on the left during measurements. However, if the chest wall was solely responsible for the frequency-dependent behaviour that we found, one would have expected more of a difference in frequency-dependency when the sternum was opened.

The infant chest wall is more compliant than that of the adult [18], and may contribute less to the overall behaviour of the respiratory system. We found that, on average, the chest wall contributed only 19% of the total elastance of the respiratory system, although these data must be interpreted with caution. The age range of children studied here was too small to examine the effects of age on this relationship.

There are several possible explanations for the frequency-dependent behaviour reported here. Elastance was observed to increase with frequency (fig. 1a). The lung volume was likely to have increased with frequency, i.e. end-expiratory Pao increased from 3.5±1.65 to 7.0±3.47 cmH₂O in closed-chested subjects, and from 2.4±1.1 cmH₂O at the lowest frequency to 5.5±2.6 cmH₂O at the highest frequency with the chest opened. While this increase in Pao is small, it is likely to represent an increase in end-expiratory lung volume. If the children were being ventilated on the linear portion of their pressure-volume curve, this would not result in a change in elastance. Functional residual capacity is known to fall on induction of anaesthesia [19], and is likely to be even lower in the open-chested situation. This could result in airway closure at low lung volume, with the children being ventilated on a “steep” portion of their pressure-volume volume curve, below the normal end-expiratory volume. If this were the case in the children reported here, one may expect the elastance to decrease with frequency, as the lung volume is increased to a more normal end-expiratory volume. Thus, the probable change in lung volume seen with increasing frequency is unlikely to explain the increase in elastance reported here.

A more likely explanation for the increase in elastance with increasing frequency is the viscoelastic behaviour of the pulmonary parenchyma. A model that has been found to describe the behaviour of the respiratory system under a variety of conditions is the so-called Kelvin body model [20] (fig. 4). This model consists of a dash-pot (R₁), representing the airway resistance, and a Kelvin body, i.e. a spring (E₁) in parallel with a spring (E₂) and dash-pot (R₂) in series. E₁ represents the elasticity of the lungs and E₂ and R₂ represent the viscoelasticity of the pulmonary parenchyma. Changes in lung volume are represented by changes in the distance between the bars at each end of the model. With changes in lung volume, energy is dissipated across R₁ and movement occurs in the spring E₁. At low frequencies, energy dissipation also occurs across R₂, but little movement occurs in spring E₂ and elastance approximates E₁. As ventilation frequency increases, the spring E₂ begins to move, resulting in an increase in dynamic elastance (i.e. Edyn approaches E₂=E₁+R₂). The model predictions match the data from the present study, i.e. an increase in elastance with frequency. Previous studies in animals have extended this model to include an additional resistance (dash-pot) and Kelvin body to represent the chest wall [20]. We chose not to do this, as the data were well described by the more simple model.

The data reported in the present study are also consistent with ventilation inhomogeneity in a lung with pathways of differing time-constants. As ventilation frequency increased, less time would be allowed for ventilation to occur in the lung units with longer time-constants. This would result in a fall in resistance and an increase in elastance measured at the airway opening. These two
possibilities can not be separated from measurements of pressure and flow made at the airway opening. While none of the subjects had overt lung disease, we could not claim that they were likely to have entirely normal lungs. The cardiac abnormalities necessitating surgery were associated with abnormalities of pulmonary blood flow. However, whilst we cannot be certain about the mechanism producing the frequency-dependent behaviour, it clearly exists and must be taken into account in measurements of respiratory mechanics in ventilated children.

The fall in resistance with frequency reported here is also consistent with previous reports in animals [21], and adult humans [22]. This behaviour is also predicted by the Kelvin body model. At low frequencies, energy is dissipated across both dash-pots, R1 and R2 (Rdyn(at zero frequency)=R1+R2). As frequency increases and the spring E2 begins to move, less energy is dissipated across R2, resulting in a fall in total resistance (Rdyn approaches R=R1). The falls in resistance with frequency in the present study are relatively small. Suki et al. [22] reported that the major falls in resistance in adult humans occurred below 0.03 Hz, with smaller falls between 0.03-0.1 Hz. The frequency range employed in the present study was 0.2-0.7 Hz. Thus, more marked frequency dependent behaviour may have been evident if we had been able to employ lower ventilation frequencies. It is possible that the fall in resistance with increasing frequency may be partly explained by an increase in end-expiratory lung volume, resulting in an increase in airway calibre. Whilst we feel that this is unlikely, this possibility cannot be excluded in the present study. In adult dogs, Rl has been shown to increase with an increase in lung volume, provided tidal volume remained the same [23]. This increase was due to an increase in tissue viscance, which more than compensated for a fall in airway resistance (Raw). Whether the same phenomenon would be seen in ventilated children is not known.

The estimates of Rrs and Rl reported here have been corrected for Retr. The small endotracheal tubes used in small children add a flow-dependent resistance to the respiratory system [1]. With changes in ventilation frequency, the mean flow will also change. Thus, Retr will produce a positive frequency-dependence of resistance that could diminish or mask the negative frequency-dependence reported here. The correction procedure, (Equations (6) and (7)), used the mean flow over the respiratory cycle. This seems to be a reasonable approach, as the multilinear regression yields estimates of elastance and resistance that are weighted by flow and volume changes over the respiratory cycle.

Previous investigators have suggested that frequency-dependence of Rrs and Rl may be masked by frequency components higher than the fundamental breathing frequency, if non-sinusoidal ventilation patterns are employed [8]. In the present study the ventilation pattern was sinusoidal, however, frequency-dependent behaviour has clearly been demonstrated. In the present study, children were studied, whereas Barnas et al. [8] studied adults. Also, although the subjects studied here did not have clinically overt lung disease, their pulmonary blood flows were unlikely to have been normal when they were studied. However, the subjects who would have been expected to have decreased pulmonary perfusion (Nos. 2, 6 and 8) did not show a different pattern of frequency-dependence when compared to the subjects likely to have increased pulmonary blood flow (Nos. 1, 3 and 7).

The results of the present study have important implications for studies employing measurements of respiratory mechanics in mechanically-ventilated subjects. To be able to detect the effects of therapeutic interventions on respiratory mechanics, it is necessary to take into account ventilation conditions. An apparent decrease in elastance could be produced by a reduction in ventilation frequency. Similarly, a decrease in resistance may be produced if ventilation frequency is increased. It is important, however, to also monitor the lung volume from which the subject is being ventilated. As measurements of absolute lung volume are rarely available in mechanically-ventilated subjects, the use of the estimated PEEL obtained from Equation (2) provides a useful indication of changes in lung volume [3].

In summary, elastance and resistance, of the total respiratory system and of the lung, demonstrate frequency-dependent behaviour in mechanically-ventilated children. This behaviour can be predicted using a linear viscoelastic model, and needs to be taken into account when using measurements of respiratory mechanics to assess therapeutic interventions or to indicate disease progression in mechanically-ventilated children.

References


