Original Article

Aging Effects on Alveolar Sacs Under Mechanical Ventilation

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Abstract

Alveolar sacs are primarily responsible for gas exchange in the human respiratory system and lose their functionality with aging. Three-dimensional (3D) models of young and old human alveolar sacs were constructed and fluid–solid interaction was employed to investigate the contribution of age-related changes to decline in alveolar sacs function under mechanical ventilation (MV). Simulation results illustrated that compliance and pressure reduced in the alveolar sacs of the elderly adults, and they have to work harder to breathe. Morphological changes were found to be mainly responsible for the decline in alveolar sacs function. Influence of individual differences on the alveolar sacs function was negligible and 95% confidence intervals for compliance and work of breathing (WOB) using measures from different individuals also support this finding. Moreover, higher mortality risk was recorded for elderly adults who undergo MV. Specifically, ventilator devices setting has been identified as a potential parameter for compromising respiratory function in the elderly adults. Volume-controlled ventilation applied less pressure, whereas, pressure-controlled ventilation resulted in higher compliance in the alveolar sacs and decreased WOB. Sensitivity of alveolar sacs to ventilator setting under the volume-controlled mode illustrated that increasing breathing frequency and decreasing the ratio of inhalation to exhalation times and TV caused an increase in alveolar sacs expansion and compliance in older patients. Results from this study can help clinicians to develop individualized and effective ventilator protocols and to improve respiratory function in the elderly adults.

Keywords: Alveolar sacs, FSI, Age-related changes, MV setting, Mode of MV

Human lungs mature around age 20–25 years and will start to lose functionality after approximately 35 years (1). Aging causes changes in the human body, which leads to lung function decline (2). The diaphragm is the main muscle involved in breathing and moves air in and out of the human lung. This muscle becomes weaker and its ability to inhale oxygen and exhale carbon dioxide decreases with age (3). Lung tissues, which keep airways open, also lose their elasticity with age and may cause collapse in airways (4–6). Alveoli, small sacs where gas exchange happens, can lose their shape and become baggy (6). Consequently, breathing generally becomes more difficult over time.

Generally, aging induces morphological and tissue property changes in human alveolar sacs. These changes influence alveolar

sacs mechanics and gas exchange (1,7–10). Quirk et al. (6) used MRI with hyperpolarized ³He and detected age-dependent morphological changes in the acinar region. They monitored decline in alveolar depth, alveolar density, surface area, and surface to volume ratio and increases in lumen radius, volume, mean chord length, and acinar airway radius. Moreover, an increase in alveolar wall thickness has been observed in older subjects in previous experimental studies (5,6,11,12). In addition to the structural changes, aging imposes material properties changes on alveolar sacs (4–6) and this leads to an increase in tissue bulk and shear modulus (4,5,9).

In the case of lung failure, patients often need mechanical ventilation (MV) devices to assist them in inhaling oxygen to the respiratory system. Age-related changes pose a higher risk for mortality

under MV and many important decisions have to be made once it is determined that a patient needs MV, including MV mode and parameter settings. Classically, MV modes are divided into pressure and volume-controlled modes. Volume-controlled mode has been recently identified as the preferred ventilatory mode (13). Breathing frequency, tidal volume (TV), and inhalation/exhalation (I/E) ratio are the main parameters set for the volume-controlled mode. Ventilator settings do impact respiratory system function and it is therefore important that the settings for MV devices minimize lung injury.

Many studies have focused on age-related changes and their influences on respiratory system mechanics. It has been shown that while lung static compliance increases with aging, chest wall compliance decreases due to stiffening and there is an increased outward recoil of the thoracic cage (7,14–17). In addition to compliance, work of breathing (WOB) has been identified as a major parameter that would be affected by age-related changes. Although it is anticipated that an older person sustains ventilation by smaller applied forces on the thoracic cage accompanied with a corresponding reduction in the elastic WOB, an increase in the rigidity of chest wall offsets this advantage (1,18,19). It has also been determined that airspace enlargement leads to a decrease in recoil pressure in older alveolar sacs (16,20,21). Age-related changes have been accepted as main factors that lead to a decline in lung function, but it is unclear if these changes are due to structural changes or tissue property changes in alveolar sacs. Alveolar mechanics have been investigated under normal conditions while their functionality under MV conditions has only recently been studied. It is important that age-related changes in alveolar sacs mechanics under MV be investigated as there is a possibility that the MV device settings would also affect alveolar sacs mechanics.

In this study, the contributions of morphological and tissue property changes as well as differences in ventilator device settings were investigated to assess their impact on decline in alveolar sacs function. This paper is organized into four sections. In the first section, the impact of age-related morphological and tissue property changes on alveolar sacs function is investigated, and the results are discussed. In the second section, influence of individual difference on alveolar sacs function is explored and confidence intervals for measured values for different case studies at older ages are presented that reflect the applicability of results from this study to the elderly adults. In the third section, normalized results for volume-controlled and pressure-controlled MV modes are compared to investigate the effect of MV mode on alveolar sacs mechanics in the elderly adults. The fourth section is devoted to sensitivity analysis of alveolar sacs mechanics to ventilator device settings. Influence of TV, breathing frequency, and I/E ratio in volume-controlled mode on the alveolar sacs function in the elderly adults is evaluated. Efforts were made to identify the best settings for MV devices to improve breathing conditions specifically for older patients.

FSI Approach

Quirk et al. (6) performed MRI with hyperpolarized ^3He gas on 24 healthy nonsmokers ages 19–71 years. They presented a linear correlation between adults' acinar morphometric parameters and age with 95% confidence intervals (Supplementary Table 1). As discussed in their study, alveolar depth decreases and lumen diameter and mean chord length increase in older cases (4,6). Moreover, previous experimental studies presented that older alveolar sacs have thicker walls compared to younger models (5,11). To investigate changes in alveolar sacs' function with age, 3D models of 50- (young) and 80-year-old (old) human alveolar sacs were built in CAD software based on

anatomical dimensions presented for alveolar sacs in previous experimental studies (4–6,11). Additional details/regarding the constructed models for 50- and 80-year-old alveolar sacs in this study are presented in Supplementary Figure 1 and Supplementary Table 1.

Next, constructed geometries for 50- and 80-year-old alveolar sacs were imported to ANSYS transient structural and Fluent solver. Four different case studies were considered to explore the influence of morphological and tissue property changes on alveolar sacs mechanics. Case 1 included morphological and tissue properties of the 50-year-old model. Case 2 had the geometry of the 50-year-old and the tissue properties of 80-year-old alveolar sacs. Case 3 contained the structural properties of 80-year-old alveolar sacs and tissue properties of the 50-year-old alveolar sacs, while Case 4 had the morphological and tissue properties of 80-year-old alveolar sacs. Fluid–solid interaction (FSI) was employed for all case studies to investigate the interaction of alveolar sacs structure and induced air into the model (22). Based on the number of iterations required for convergence, the time step was set to 0.1 (s). All geometries were meshed using tetrahedral elements, and dynamic mesh was activated for the fluid domain. Mesh convergence was performed, and a 2 million mesh size was set for the fluid domain, and a 1.8 million mesh size was fixed for the solid domain. Supplementary Figure 2 includes a magnified FE mesh and mesh elements for the 50- and 80-year-old alveolar sacs.

Boundary conditions were set for young and elderly patients according to the MV mode. Alveoli contain some collagen and elastic fibers, which allow the alveoli to stretch as they are filled with air during inhalation. Then they spring back during exhalation to expel the carbon dioxide-rich air. Since alveolar sacs were considered separate from the whole lung in the simulations, free displacement in radial direction and fixed longitudinal and rotational displacement were established as boundary conditions for the solid domain as shown in Figures 1 and 2.

Volume-Controlled Ventilation Mode

For the volume-controlled MV mode, flowrate waveform during MV was defined as the boundary condition for the fluid domain

Figure 1. Methodology for volume-controlled analysis.

Figure 2. Methodology for pressure-controlled analysis.

in the form of constant and exponentially decreasing flowrate profiles for inhalation and exhalation and imported as UDF files. Total breathing time (t_t) for each cycle was determined from breathing frequency (t_t is equal to $60/\text{frequency}$) and the ratio of inspiratory time (t_{in}) to expiratory time (t_{ex}) was set to 1:3 (23). Flowrate is equal to the volume change per unit time and is defined according to alveolar sacs volume change from collapsed to expanded condition during inhalation $\left(\frac{\text{Volume changes}}{t_{in}} \right)$. Since the area under the flowrate wave form is equal to TV (23), TV was set to 8.3×10^{-5} mL (volume changes of 50-year-old alveolar sacs from collapsed to expanded condition). The integral of exponential exhalation flowrate waveform was set to TV (1,23,24) and exponential function was correspondingly estimated. Flowrate waveform was generated for four breathing cycles. Since the 3D geometrical model was constructed based on expanded dimensions, flowrate was assumed to be equal to zero during inhalation time in the first breathing cycle. The air filled the alveolar sacs model during the first inhalation time then the breathing followed the whole breathing flowrate waveform for the remaining breathing cycles. The generated flowrate waveform function and the four breathing cycle patterns are presented in Supplementary Table 2.

Two-way FSI was conducted for the volume-controlled mode where governing equations for fluid and solid domain were solved iteratively as shown in Figure 1. The velocity field within the alveolar region was numerically calculated by solving 3D incompressible laminar Navier-Stokes and continuity equations in a 3D mesh domain with a control volume approximation (25). The continuity equation equation (1) and the Navier-Stokes equations equation (2) were solved numerically on a moving grid using a commercial finite-volume-based program with fully implicit time marching techniques under isothermal conditions in ANSYS fluent solver (26).

$$\nabla \cdot \mathbf{u} = 0. \quad (1)$$

$$\rho_f \left(\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} \right) = -\nabla p + \mu \nabla^2 \mathbf{u} \quad (2)$$

where $\mathbf{u}$, ρ_f , p , and μ are the velocity field, air density, pressure and dynamic viscosity, respectively. Calculated pressure from the fluid domain was transferred to the solid domain, and governing equations for the solid domain were solved corresponding to the output of the fluid domain.

The time-dependent structural equations were used as governing equations for the movement of the alveolar sac solid domain during inhalation and exhalation as shown in equations (3) and (4):

$$\frac{\partial \sigma_{ij}}{\partial x_j} + F_i = \rho_s \frac{\partial^2 x_i}{\partial t^2} \quad (3)$$

$$\sigma_{ij} = E_{ijmn} \epsilon_{mn} \quad (4)$$

where σ , F , ρ_s , x , E , and ϵ are the stress in each direction, body force, density, displacement, elasticity tensor, and strain in each direction. Hyperelastic Neo-Hookean material parameters were adopted for the alveolar wall tissue materials for the FSI simulation. For Compressible Neo-Hookean material, equation 5 gives the strain energy density function:

$$W = \frac{G}{2} (\bar{I}_1 - 3) + K_m (J - 1)^2 \quad (5)$$

Where J is equal to the determinant of deformation gradient, $\bar{I}_1 = J^{-\frac{2}{3}} I_1$ is the first invariant of the isochoric part of right Cauchy-Green deformation tensor, and I_1 is the first invariant of the right Cauchy-Green deformation tensor. G and K_m are the shear and bulk modulus, respectively. Both shear and bulk modulus increased with age. An increase in elastin content with aging has been shown to lead to an increase in alveolar diameter and tissue forces (4,5). The shear and bulk modulus values considered for the 50- and 80-year-old alveolar sacs tissues are presented in Supplementary Table 1. The displacement response from the solid domain was imported to fluid domain. These iterations were continued until convergence was reached for all data transferred and field equations (27) as shown in Figure 1.

Pressure-Controlled Ventilation Mode

For the pressure-controlled mode, one-way FSI was employed as shown in Figure 2. For this case, instead of flowrate waveform for the fluid domain, pressure was applied on the solid domain, and governing equations for the solid domain were solved until the convergence criteria were reached (28). As shown in Table 1, pressure equal to 10 cmH₂O was applied to the alveolar sacs wall and inhalation to exhalation time ratio was set equal to 1:2 (23). The calculated displacements from the solid domain were then transferred to the fluid domain, and governing equations for the fluid were solved. Then, the structure displacement was calculated for the next time step. The solution is considered to be complete when the maximum number of time steps is reached. Next, the normalized results for the volume-controlled and pressure-controlled modes were compared to explore the influence of ventilatory mode change on breathing condition in older alveolar sacs.

Statistical Analysis

Alveolar sacs wall thickness, and bulk and shear modulus for 80-year-old were varied statistically to investigate influence of individual difference on alveolar sacs function. Dimensions of

Table 1. MV Mode Effects on 80-y-old Alveolar Sacs Mechanics

Waveforms		Maximum Applied Pressure (cmH ₂ O)	WOB for Normalized Pressure and Volume Values	Compliance for Normalized Pressure and Volume Values (mL/cmH ₂ O)
Volume-controlled		1.77	0.56	0.46
Pressure-controlled		10	0.51	0.98
Remarks		80% decrease in volume-controlled	10% increase in volume-controlled	52% decrease in volume-controlled

Note: MV = Mechanical ventilation.

constructed 3D models are presented in [Supplementary Table 3](#). FSI analysis was conducted for all case studies and results for alveolar sacs compliance and WOB were compared. Significance level of $p < .05$ was considered and two-tailed z test was employed to test the null hypothesis of no significant difference relevant to individual differences. In addition, percentage of change and the confidence interval, that reflects the applicability of presented results for the given samples in this study, were calculated to be able to generalize conclusions from this study to the elderly adults.

Sensitivity Analysis

The volume-controlled ventilation mode allows for an easier approach to monitoring respiratory mechanics. Therefore, the volume-controlled mode has been recently identified as the preferred ventilation mode (13). Subsequently, the sensitivity of alveolar sacs functionality to parameter settings in the volume-controlled mode (breathing frequency, TV and ratio of inhalation to exhalation time) were investigated. In general, higher breathing frequency and lower TV are recommended for older patients (24). Consistent with this practice, considered values of these parameters in this study were increased and decreased by 10%, and FSI was conducted for all case studies. The results were compared to evaluate the influence of each parameter on older alveolar sacs mechanics.

Results

Applied Pressure

Previous studies have indicated that elastic recoil pressure of the lung decreases with age. Janssens et al. (16) identified a rate of 2 cmH₂O and Niewoehner et al. (20) reported a rate of 1.2 cmH₂O per decade for 25- and 60-year-old lungs. In addition, Subramaniam et al. (9) suggested that alveoli expansion begins when pressure reaches 25 cmH₂O. They expanded the alveolar sac model by applying pressure to internal

surfaces of the alveoli isotropically. Although applied pressure on alveolar sacs' wall increases during inhalation, it will decrease during exhalation. Accordingly, applied pressure in a volume-controlled mode in this study was recorded as 10 cmH₂O for the 50-year-old and 2 cmH₂O for the 80-year-old cases during inhalation while this value was decreased while exhaling air. Subramaniam et al. (9) presented volume increase from reference volume. Results for volume changes from reference volume for the same amount of applied pressure on the alveolar sacs wall were compared with results from Subramaniam et al. study (9). Lower pressure values resulted in lower volume changes for the same amount of applied pressure on the alveolar sacs wall. The volume changed about 0.06% and 0.2% at pressure equal to 2 cmH₂O for the 50- and 80-year-old alveolar sacs models considered in this study, while Subramaniam et al reported volume changes of 3.4% and 6.8% at pressure equal to 2 cmH₂O for 20- and 60-year-old alveolar sacs (9). One reason for the discrepancy may be due to the fact that lower pressure was applied on the alveolar sacs wall in this study. In addition, larger volume changes at the same pressure values are recorded in older alveolar sacs model compared to younger alveolar sacs models ([Supplementary Figure 3](#)).

FSI was conducted for 50- and 80-year-old alveolar sacs for the volume-controlled mode and postprocessed results were compared to evaluate contribution of age-related tissue properties and morphological changes to a decline in alveolar sacs function. In general, age-related changes decreased applied pressure on the alveolar sacs (9). [Figure 3](#) illustrates the pressure distribution in four different case studies of 50 and 80-year-old alveolar sacs models. As can be seen, during inhalation at t equal to 8 (s), a high amount of pressure was applied on the duct area by inhaling air into the model. On the other hand, during exhalation at t equal to 9.2 (s), pressure was highly distributed in the sacs region and is almost equal to zero in the duct region. Also, significant pressure values were noted at the bottom of the 50-year-old alveolar sacs model during inhalation. Finally, age-related changes decreased applied pressure on older alveolar sacs.

Figure 3. Pressure distribution during inhalation ($t = 8$ s) and exhalation ($t = 9.2$ s) for Case 1 (morphological and tissue properties of the 50-year-old alveolar sacs), Case 2 (morphological of 50-year-old alveolar sacs and tissue properties of 80-year-old alveolar sacs), Case 3 (morphological of 80-year-old alveolar sacs and tissue properties of 50-year-old alveolar sacs), and Case 4 (morphological and tissue properties of 80-year-old alveolar sacs).

Alveolar Sacs Dynamic Compliance With Aging

Alveolar sacs dynamic compliance is a measure of alveolar sacs ability to stretch and is equal to the volume change per unit pressure change. The slope of pressure–volume graph for specific pressure change illustrates the dynamic compliance. Pressure–volume loops were plotted for different breathing cycles for 50- (Figure 4B) and 80-year-old alveolar sacs (Figure 4C) under MV. It was hypothesized that cyclic breathing patterns would affect the pressure–volume loop. Figure 4 illustrates that compliance decreased in each breathing cycle and hardened the alveolar sacs expansion, and as a result, more energy would be required to inhale air into the model. Required energy for breathing, which is equal to the enclosed pressure–volume loop area, increased by 40% for the 50-year-old model and 30% for the 80-year-old model.

Pressure–volume loop testing was also employed to investigate the influence of aging on compliance. It was hypothesized that aging would decrease alveolar sacs compliance which means older alveolar sacs would have less tendency to expand compared to younger sacs. Hence, different case studies were considered to investigate the contributions of tissue properties and morphological changes on compliance decline in older alveolar sacs. Morphological changes in older alveolar

Figure 4. (A) Flowrate waveforms for four breathing cycles and pressure–volume loop for different breathing cycles for (B) Model with morphological and tissue properties of the 50-year-old alveolar sacs (Case1) and (C) Model with morphological and tissue properties of the 80-year-old alveolar sacs (Case 4).

sacs emerged as the main factor for compliance decline in older sacs (Figure 5). Compliance decreased by almost 40% for the 80-year-old as compared to the 50-year-old alveolar sacs as shown in (Figure 5B).

Effects of Age-Related Changes on WOB

WOB is defined as the energy required to inhale oxygen and exhale carbon dioxide. The area enclosed by the pressure–volume loop is a measure of the WOB. The magnitude of the WOB depends on the ventilation associated with a given effort and the mechanical efficiency of the chest wall. It is expected that an older person could sustain a given ventilation by applying smaller forces to the thoracic cage, with a corresponding reduction in the elastic WOB (19). The area enclosed by pressure–volume loops for 50- and 80-year-old alveolar sacs were calculated. It was hypothesized that older alveolar sacs would have smaller WOB compared to younger models, and results confirmed that morphological changes are the main reason for the decrease in WOB magnitude (see Figure 5C).

However, increase in the rigidity of the chest wall and airway collapse both augment resistive work, so the total WOB is likely to be greater in an older person in comparison to a younger person. In order to capture the increase in WOB, applied pressure on the diaphragm has to be considered in future in the simulations.

Influence of MV Mode on Alveolar Sacs Function

MV mode influence on alveolar sacs mechanics was evaluated for the 80-year-old alveolar sacs model. According to previous studies, volume-controlled mode decreases distending pressure compared to pressure-controlled mode (13). It was therefore hypothesized that applied pressure in volume-controlled mode would be smaller compared to applied pressure in pressure-controlled mode. Furthermore, measured pressure and volume for volume-controlled and pressure-controlled mode were normalized and corresponding WOB and compliance values for volume-controlled and pressure-controlled modes were calculated and compared. As shown in Table 1, WOB increased by 10% for volume-controlled mode while volume-controlled mode decreased compliance by almost 52% compared to pressure-controlled mode.

Figure 5. (A₁–A₃) Pressure–volume plots for considered case studies (Case 1 with morphological and tissue properties of the 50-year-old alveolar sacs, Case 2 morphological of 50-year-old alveolar sacs and tissue properties of 80-year-old alveolar sacs, Case 3 with morphological of 80-year-old alveolar sacs and tissue properties of 50-year-old alveolar sacs, Case 4 with morphological and tissue properties of 80-year-old alveolar sacs) and contribution of tissue properties and morphological changes in older alveolar sacs' compliance decline (B) and WOB decrease (C). WOB = Work of breathing.

Influence of Individual Differences on Alveolar Sacs Function

A 0.05 significance level and two-tailed z test were employed in this study. Accordingly, upper and lower tail were set equal to 0.025. The z values that corresponds to upper and lower tail are -1.96 and 1.96 . Thus, the null hypothesis of no difference will be rejected if the computed z statistic falls outside the range of -1.96 to 1.96 . Computed z statistics for alveolar sacs compliance and WOB were equal to -0.95 and -1.55 , respectively. Therefore, the null hypothesis of no difference could not be rejected. Moreover, estimated range of values that include 95% of compliance and WOB values from considered case studies with morphological and tissue properties between 75- and 85-year-old alveolar sacs are presented in [Supplementary Table 4](#). It was observed that individual differences resulted in less than 10% difference for both compliance and WOB values in the elderly adults (see [Supplementary Table 4](#)). This difference is considered negligible. Therefore, results from this study are applicable and can be generalized to the elderly adults.

Sensitivity of Alveolar Sacs Function to MV Devices Setting

Since volume-controlled mode has been recently identified as the preferred mode for ventilator devices, sensitivity of alveolar sacs mechanics (WOB, strain, and compliance) to ventilator devices settings in the volume-controlled mode (TV, breathing frequency, and I/E) was measured. Changing MV parameters can improve breathing condition. For instance, previous studies have shown that the adoption of a slower expiration may reduce premature airway collapse occurrence. This will not only be helpful in its own right but will also reduce the WOB and ventilatory demand (19). Therefore, the considered values for TV, breathing frequency, and I/E in this study were

Figure 6. Sensitivity of WOB, strain and compliance to volume-controlled mode parameters (TV, breathing frequency, and I/E). I/E = Inhalation to exhalation ratio; TV = Tidal volume; WOB = Work of breathing.

increased and decreased by 10% and FSI was conducted for all case studies. Results indicated that decreasing I/E increases WOB, compliance, and strain significantly. An increase in frequency also increased WOB and strain and compliance. Increasing frequency had the most influence on strain enhancement. Decreasing TV also decreased WOB and strain but increased alveolar sacs compliance as shown in [Figure 6](#). Although, increasing frequency and decreasing I/E increases WOB, it also increases alveolar sacs and compliance. Therefore, increasing breathing frequency and decreasing I/E and TV would improve breathing conditions for older alveolar sacs under MV.

Limitations

Fixed longitudinal displacement was considered as a boundary condition for the solid domain in the FSI analysis in this study. Although elastic support could be considered in future studies, access to bronchiole tissue properties changes with age will be required. In addition, a decrease in WOB of older alveolar sacs was observed while an

increase in the rigidity of the chest wall and airway collapse resulted in greater total WOB in an older person in comparison to a younger person. Therefore, applied pressure on the diaphragm has to be considered in the simulations to capture the increase in WOB.

Conclusions

Aging is associated with morphological and tissue properties changes in alveolar sacs that would decline alveolar sacs functionality significantly. FSI was employed to study younger (50) and older (80) alveolar sacs models under MV. Older alveolar sacs had lower pressure compared to younger alveolar sacs models. Findings also indicated that morphological changes have a major impact on decline in alveolar sacs function. Alveolar sacs enlargement in older models led to a decrease in compliance of alveolar sacs and WOB. Although WOB is decreased in single alveolar sacs, an increase in the rigidity of the chest wall would neutralize this decrease in WOB. In reality, WOB would increase in older patients. Apart from morphological and tissue properties changes in alveolar sacs, ventilator device settings may also influence their functionality, specifically in older patients. MV mode was altered from volume-controlled mode to pressure-controlled mode and it was observed that applied pressure on alveolar sacs wall decreased in volume targeted mode and WOB increased in volume-controlled mode as compared to pressure-controlled mode while compliance decreased significantly in volume-controlled mode. Statistical analysis illustrated that influence of individual differences on alveolar sacs function is negligible and results are applicable to the elderly adults. The results of sensitivity of alveolar sacs under volume-controlled mode showed that their function is highly sensitive to I/E and breathing frequency. Therefore, increasing frequency and decreasing I/E would increase alveolar sacs expansion and compliance. Decreasing TV decreases WOB while increases in the other two parameters increases WOB. Consequently, increasing breathing frequency and decreasing I/E and TV would help improve breathing conditions for older patients under MV.

Supplementary Material

Supplementary data is available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

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Conflict of Interest

None reported.

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