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Research Article

Entropy Generation and Exergy Destruction During and After Weaning from Mechanical Ventilation in Patients with Respiratory Failure

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Abstract

BACKGROUND: Mechanical ventilation is a useful supportive treatment for patients with respiratory failure who are not able to maintain the level of ventilation required to maintain the oxygenation and carbon dioxide elimination. Mechanical ventilation is often life-saving, but it also has risks. Thermodynamic analyses are used to test the feasibility of processes leading to a better understanding of the system's overall performance. Energy losses (entropy) and the destruction of maximum useful work (exergy) leading to reduced respiratory work of breathing efficiency, can be calculated by thermodynamic analysis of the respiratory muscles.
OBJECTIVE: To determine the entropy generation, exergy destruction, and glucose consumption during and after weaning from mechanical ventilation in patients with respiratory failure by thermodynamic analysis.
METHODS: In this study, a human respiratory system during and after weaning from mechanical ventilation modeled thermodynamically using the first and second laws of thermodynamics. The work of breathing data adapted from the literature. Mass and energy analyzes are carried out according to the 1st law of thermodynamics, while entropy generation is calculated according to the 2nd law of thermodynamics which enables us to measure energy losses. In this thermodynamic model, the body temperature was considered at 37 °C, and the surrounding air condition was taken at 25 °C.
RESULTS: Exergy destructions during and after weaning from mechanical ventilation were calculated as $2.23\text{x}10^{-2}$ and $1.75\text{x}10^{-2}$ kJ/min, respectively. Entropy generation by the patients through the breathing cycle was $7.48\text{x}10^{-5}$ (kJ/K)/min during mechanical ventilation while $5.89\text{x}10^{-5}$ (kJ/K)/min after weaning from mechanical ventilation, respectively. The glucose consumed for work of breathing in patients during and after weaning from mechanical ventilation was calculated as 0.58-0.45 mmol/min, respectively.
CONCLUSION: After weaning from mechanical ventilation, the patients have significantly decreased entropy generation, exergy destruction, and glucose consumption, indicating to the improvements in the structure of respiratory mechanics and diaphragm perfusion. The reductions in entropy generation and exergy destruction after weaning from mechanical ventilation also indicates an increase in the mechanical efficiency of the respiratory muscles. According to the results of the energy balance analysis, the decrease in muscle energy requirement, was determined and the calculations found that the patient used 1.3 times more glucose during mechanical ventilation than after weaning from mechanical ventilation for work of breathing. In this study, the thermodynamic approach was used to determine the benefit of mechanical ventilation. More powerful work and multidisciplinary data are needed to progress reliable procedures.

Keywords: Mechanical ventilation, Entropy generation, Exergy destruction, Respiratory thermodynamics, Thermodynamic analysis

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1. Introduction

Mechanical ventilation (MV) is a useful supportive treatment for patients with respiratory failure who are not able to maintain the level of ventilation required to maintain the oxygenation and carbon dioxide elimination. Critically ill patients may require ventilator support, and they are regarded ventilator-dependent due to their insufficiency to tolerate weaning attempts. The use of MV varies significantly from short term to long term and from acute care in the hospital to extended care at home. One of the most common applications of MV is for the management of postoperative patients recovering from anesthesia and medications [1, 2].

Work of breathing (wob) is the performance necessary to respire air into the lungs (energy expenditure of respiratory muscles), which constitutes 5% of total body oxygen consumption in a normal resting state but can increase significantly during acute illness. Wob values range from 2.4 to 7.5 J/min and from 0.2 to 0.9 J/L in healthy subjects at rest [3]. Wob is measured in joules/L, joules/min, and sometimes kg/m/min and may be computed concerning the oxygen cost of breathing or the pulmonary pressure manifolded by the exchange in pulmonary volume. The measurement of the wob in respiratory physiology (work = pressure x volume) is analogous to the typical definition of work in physics (work = force x distance) [1].

Increased work of breathing and respiratory muscle weakness are considered as the main reasons for respiratory failure after thoracic surgery [2]. During critical illness, many patients become dependent on the ventilator. The measurement of the wob was found to be a useful objective variable to determine the capability for independent ventilation and an objective indicator of dependence on mechanical ventilation [4, 5].

The first law of thermodynamics claims that energy can neither be created nor destroyed, but transformed from one form to another or transported through heat, mass, and work transfer. The second law of thermodynamics describes entropy. Entropy is used to measure energy losses in a system. The randomness of a system measured by entropy. Exergy is described as the maximum useful work, in every irreversible process like breathing, entropy production leading to the destruction of the exergy. Accordingly, exergy determines the usable energy loss caused by entropy generation.

Respiration is the production of adenosine 5’-triphosphate (ATP) energy by the chemical degradation of organic nutrients in various ways which are taken from foods and found in the human body. Nutrient and oxygen are transported to our cells through the bloodstream. The nutrients carried to our cells are burned by oxygen, and thus, the energy state formed by the nutrient-oxygen combination causes respiration [6].

Respiratory muscle can be regarded as a thermodynamic machine like piston that converts chemical energy into mechanical work (wob) during each breathing cycle. The energy utilized is converted to wob by respiratory muscles during each breathing cycle. During the breathing process, heat is generated as a by-product and dissipated to the surroundings by generating entropy based on the second law of thermodynamics. The tissue randomness increases due to entropy accumulation in this periodically breathing process, which may lead to a decrease in wob efficiency over time and eventually may lead to damage in respiratory muscle.

Thermodynamic analyses are used to test the feasibility of processes leading to a better understanding of the system’s overall performance. The sources of losses due to irreversibilities in each breathing process in the system can be identified by thermodynamic analyses. Energy losses (entropy) and the destruction of maximum useful work (exergy) leading to reduced respiratory wob efficiency can be calculated by thermodynamic analysis of the respiratory muscles.

In recent years, numerous studies have been published on thermodynamic analysis of processes based on metabolism in the biological systems [7-19]. However, in the literature, there is a limited number of studies on respiratory thermodynamics [8, 10, 15,19]. It has been observed from the literature survey that no such research has been done regarding the work of breathing in mechanical ventilation evaluated by thermodynamically. Therefore, this study was carried out in order to characterize the structure of damaged respiratory mechanics by thermodynamic analysis in patients with respiratory failure and to resolve the thermodynamic changes in respiratory mechanics.

2. Material and Method

2.1. Model Description

A human respiratory system during and after weaning from MV was modeled thermodynamically using the first and second laws of thermodynamics. The data of work of breathing by the respiratory muscles of the patients during and after weaning from MV is adapted from the literature [2]. Calculations were done by applying the first and second laws of thermodynamics. Mass and energy analyzes are carried out according to the 1st law of thermodynamics by energy balance equation, while entropy generation is calculated according to the 2nd law of thermodynamics, which enables us to measure energy losses. In the blood concentration, consumed glucose alters with the second law efficiency (η_{II}) So, the energy, mass, entropy, and exergy equations are carried out around the respiratory muscles for calculating the glucose consumed, exergy destructed and entropy generated as a function of 2nd law efficiency and the 2nd law efficiency has been assumed 0.3. Experimental outcomes on the first law efficiencies which performed with animals such as mouse and frog are reported within the range 0.14 and 0.35 while the 2nd law efficiencies are given between 0.17 and 0.42 [20]. In this thermodynamic model, the body temperature was considered at 37 °C, and the surrounding air condition was taken at 25 °C. This study is limited by the consumption of glucose to produce ATP in the respiratory muscle cells.

3. Results and Discussion

3.1. Mathematical Formulation

In this thermodynamic analysis, glucose consumption, exergy destruction, and entropy production were calculated for the work of breathing of the patients by the respiratory muscles during and after weaning from MV. Wob done by the respiratory muscles by using adenosine triphosphate (ATP), which produced in the metabolic pathways. To reposition the myosin head, ATP is dissociated into adenosine diphosphate (ADP), to provide the relaxation of the actin-myosin complex following the contraction of the muscle fibres [21]. By conversion of the glucose to the metabolic end-products heat is generated, which equals nearly 2/3 of the enthalpy change and a cause of the entropy accumulation.

3.2. Energy Balance

The energy balance equation around the respiratory muscle system (Fig. 1),

$$Q - W + \sum_i (mh)_{in} - \sum_i (mh)_{out} = \Delta E = 0 \qquad (1)$$

where i=1, 2, 3, and 4 mean glucose, oxygen, carbon dioxide, and water, respectively. Under the steady-state conditions, ΔE = 0 during respiratory muscle contracting. We modified the wob data from the literature during and after weaning from mechanical ventilation (Table 1) [2].

Table 1. *Ventilatory parameters and wob during and after weaning from MV in five patients [2].*

Variable	Unit	During MV	After weaning from MV
VE	L/min	11	10.3
Wob	J/min	8.90	7.01
Wob	kJ/min	8.9×10^{-3}	7.01×10^{-3}

MV, mechanical ventilation; VE, minute ventilation; Wob, work of breathing per minute (Values are mean ± SD, paired t-test).

After substituting the enthalpy of formation (ΔE), the heat released during work of breathing from the respiratory muscle was calculated. We calculated the mass exchanges by Çatak et al. [11] which lists the thermodynamic data of each constituent (absolute entropy, chemical composition chemical exergy, enthalpy of formation, heat capacity, and mass) entering and leaving through the muscle system boundaries.

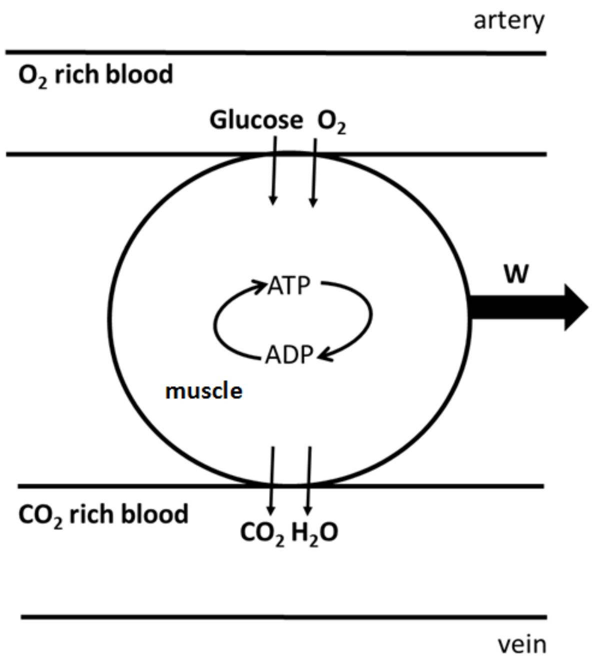

Figure 1. *The schematic definition of the process of muscle contraction, ATP generation, and work performance in the respiratory muscle.*

3.3. Exergy Destruction

Exergy destroyed in the blood is calculated from Dinçer and Çengel [7]:

$$Ex_{destroyesd} = Q\left(1 - \frac{T_0}{T}\right) - W + (mex)_{in} - (mex)_{out} \qquad (2)$$

T_0 is the reference temperature, and T is the boundary temperature of the respiratory muscle system. Based on their thermophysical state and chemical composition, the specific exergy of the species is calculated:

$$ex = ex_{ch} + h - T_0 s - \sum x_i \mu_i^0 \qquad (3)$$

where, μ_i^0 is pure species' chemical potential and $Ex_{destroyed}$ refer to the exergy loss in the bloodstream, which equals (entropy accumulation in the bloodstream) x (the body temperature). $T_0 = T_{out}$ is the reference temperature, and $T = T_{in}$ is the boundary temperature of the respiratory muscle system. In this analysis, it has been assumed that the respiratory system keeps on the fixed temperature at 37 °C. Exergy of formation is given in Çatak et al. [11] for each chemical when $T_0 = T_{out}$ = 298 K. Also, $T=T_{in}$= 310 K. Firstly, the amount of heat released from the respiratory muscle during the work of breathing process and transferred by the blood is calculated. Then the exergy loss in the blood is calculated (Fig. 1).

3.4. Entropy Generation

Assuming that heat transfer occurs at 37 ºC (310 K) from blood to the respiratory muscle and from respiratory muscle to the air at 25 ºC (298 K), substituting the exergy destroyed and the respiratory muscle cell temperature we calculated the s_{gen} (J/K) as:

$$s_{gen} = \frac{Ex_{destroyed}}{T_0} \qquad (4)$$

The respiratory muscle produces the wob by the consumption of the internal energy of the nutrients. The number of produced ATP moles relies on the kind of the nutrient and metabolic pathway employed as a result of catabolism. Such as, 30 to 38 moles of ATP are produced in the course of the oxidation of glucose. The complex energy metabolism can be simplified as one chemical reaction namely glycolysis, assuming that only glucose is catabolized and 30 moles of ATP is formed by the muscle cells:

$$C_6H_{12}O_6 \xrightarrow{30ADP+30P \rightarrow 30ATP} 6CO_2 + 6H_2O \qquad (5)$$

Accordingly, the production of wob can be described as:

$$ATP \xrightarrow{musclecontaction} ADP + P_i \qquad (6)$$

Pioneering study regarding muscle work was done by Hill [22], who proved that both force and the heat released in the course of the contraction of a muscle could be scripted as a function of the contraction velocity by experimentation.

3.5. Efficiency

External work acquired from the input chemical energy is measured by the efficiency of muscle contraction [23]. A muscle contracts and shortens against a load, and then it acts work with the use of metabolic energy. The measure of the thermodynamic efficiency is obtained by comparing the cross-bridge work component of the remainder to the Gibbs free energy of hydrolysis of ATP [20]. The 1st law efficiency also denoted the thermodynamic efficiency or mechanical efficiency, is described as:

$$\eta_I = \frac{W}{\Delta H_{glycolysis}} \qquad (7)$$

The 1st law is pertinent even in an irreversible process, and energy is still conserved in this process. However, the 2nd law of thermodynamics says that something is lost and irrecoverable. The 2nd law efficiency is known as the ratio of the actually produced work done to the maximum available work:

$$\eta_{II} = \frac{W}{W_{max}} = \frac{W}{\Delta G_{glycolysis}} \qquad (8)$$

Numerical values of the entropy generation, exergy destruction, and glucose consumption in the respiratory system with the given second law efficiency of η_{II}=0.3 are listed in Table 2.

As a result of the thermodynamic analysis of the work of breathing performed by the patients, the values of the exergy destruction during and after weaning from MV were calculated as 2.23×10^{-2} kJ/min and 1.75×10^{-2} kJ/min, respectively.

Entropy generation by the patients through the breathing cycle was 7.48×10^{-5} (kJ/K)/min during MV while 5.89×10^{-5} (kJ/K)/min after weaning from MV, respectively.

According to the first law of thermodynamics, the glucose used by the respiratory muscle, which absorbed from the blood flow was calculated by energy balance analysis. The glucose consumed for wob of patients during and after weaning from MV was calculated as 0.58-0.45 mmol/min, respectively.

Table 2. *Variation of the glucose consumption, exergy destruction, and the entropy generation rate in patients during and after weaning from MV with the second law efficiency.*

η_{II} (0.3)	$m_{glucose}$ (mol/min)	$m_{glucose}$ (mmol/min)	Glucose concentration in blood (mmol/L)	$Ex_{destroyed,muscle}$ (kJ/min)	$S_{gen,muscle}$ (kJ/K)/min
During MV	7.67×10^{-6}	0.58	0.12	2.23×10^{-2}	7.48×10^{-5}
After weaning MV	6.04×10^{-6}	0.45	0.09	1.75×10^{-2}	5.89×10^{-5}

MV, mechanical ventilation; η_{II}, second law efficiency; $m_{glucose}$, mass of glucose; $Ex_{destroyed,muscle}$, exergy destruction in respiratory muscle; $S_{gen,muscle}$, entropy generation in respiratory muscle.

With this thermodynamic analysis, it was determined that exergy destruction and entropy generation decreased after weaning from MV with lowering the wob of the respiratory muscles of the patients. Decreases in entropy production and also exergy destruction after weaning from MV indicate that an increase in the mechanical efficiency of the respiratory muscles. There is a definite and expected association between entropy generation as well as exergy destruction and the mechanical ventilation process.

According to the results of the energy balance analyzes, a decrease in respiratory muscle energy requirement was found, and the calculations determined that the patients used 1.3 times more glucose during MV than after weaning from MV for work of breathing in respiration.

The energy balance calculated mass of consumed glucose in the respiratory muscle. Depending on the reduced work of breathing after weaning from MV, a reduction of 23% was also determined in the amount of consumed glucose which used for the work of breathing.

MV can be lifesaving, but it also has risks and may be harmful to the lungs as well. The health professionals always try to help a patient leave the ventilator as early as possible. Weaning mentions, the process of moving the patient from the ventilator. Some patients may remain in the ventilator for only a few hours or days, while others may need the ventilator for a long time depending on many factors namely, overall strength affected other organs like kidney, brain, and heart. Some patients do not improve enough to be weaning from the MV entirely or at all.

Wob is the amount of effort used to expand the lungs; therefore, it is the total consumption of energy required to achieve the act of breathing. In predicting the potential for weaning and extubation, the standard evaluation criteria may not be accurate at all times. In accordance with our study, in the literature there are clinical studies on the importance of wob in mechanical ventilation.

Henning et al. [4] reported the routine measurement of the wob is a potentially useful quantification of ventilator status and dependence on mechanical ventilation. In their study, they had measured the wob in 10 healthy subjects and 28 critically ill patients with obstructive airway disease treated with assisted ventilation.

Shikora et al. [5] investigated the wob whether the wob was a more trustworthy predictor of ventilator dependence. In their study, 20 consecutive ventilator-dependent patients had prospectively studied. Using a metabolic gas monitor, oxygen consumption (VO_2) and resting energy expenditure had measured. By the change in VO_2 between spontaneous and mechanical ventilation, the wob had determined and represented as a percentage of VO_2 during MV. They had two groups applying a reference value for the work of breathing of 15% and statistically significant differences in the wob between two groups. This study supported the use of wob determinations in the assessment of extubation potential and had verified to be of higher predictive value than conventional criteria.

The pressure of putting air into the lungs and the use of very high levels of oxygen in MV can damage the lungs. This damage can be explained by thermodynamically. In the breathing process, the randomness of the tissue increases due to entropy accumulation that may cause a decrease in wob efficiency over time and eventually may cause damage in respiratory muscle [24]. Health care professionals try to maintain this risk at a minimum level by the management of pressure and, oxygen getting enough to provide vital organs. In some cases, it is challenging to decrease this risk when the lungs are damaged. Nevertheless, this damage may heal if a patient can recover from critical illness.

Previous studies revealed that thermodynamic analysis of associated respiratory problems is beneficial to understand the behavior of the system [15, 19]. The study of Çatak [15] stated that respiratory problems are related to entropy accumulation in the body. The respiratory muscle cell of the patient with respiratory failure becomes different than a healthy individual's cell. Metabolic heat generation may be considered among the primary sources of these structural alterations. Recently, the studies have reported that the released metabolic heat during ATP hydrolysis and glycolysis may change depending on metabolic conditions like Ca^{2+} concentration. The measured heat release ranges from 879 to 4017 kJ per mole of glucose consumption [12].

A reduction in mitochondrial function can affect the cellular energy production, that may limit the ATP dependent processes in the cell. The ability to maintain a given level of work of breathing depends on the balance between the energy needs of the breathing activity and the metabolic capacity of the respiratory muscle to provide energy. The level of work of breathing cannot be sustained if the energetic needs of the respiration surpass the capacity to supply energy. The maximum capacity of the body to accomplish wob may also be decreased in a patient. MV can be useful to sustain the life. Therefore, there may be an association between the positive effects of mechanical ventilation and changes in ATP supply-to-demand mechanisms in a patient.

In this study, respiratory muscles were evaluated thermodynamically with the limited data provided from the literature. Data of critically ill patients are studied to simulate the respiratory failure process during and after weaning from MV in terms of the work of breathing. The ability of respiratory muscles to use glucose seems to be the most critical factor determining their work of breathing performance within limits of the data analyzed here.

The assessment of living organisms by thermodynamic analysis offers vast opportunities for the determination of diseases, treatments, and control of the system. Entropy generation regarding the second law is associated with the different losses of a system that block the thermodynamic performance of a system.

4. Conclusions

In this study, the importance of wob for potential clinical applications is explained numerically, and a thermodynamic approach is used to determine the benefit of MV. After weaning from MV, the patients have significantly decreased glucose consumption, exergy destruction, and entropy generation. In conclusion, it is thought that MV can lead to improvements in the structure of respiratory mechanics and diaphragm perfusion by increasing the work of breathing efficiency in respiration.

This study shows that thermodynamic analyzes may make a significant contribution when studied with clinical practices to the improvement of measures for the prevention of respiratory failure. More powerful work and multidisciplinary data are needed to progress reliable procedures for the prevention of respiratory failure.

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Conflicts of interest

There are no conflicts of interest.

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