Proceedings on Automation in Medical Engineering
Proc AUTOMED, Vol 2, No 1 (2023): Article Ref 733
www.journals.infinite-science.de/automed/article/view/733

A lung model considering age, sex and height: an *in-silico* study – gas exchange

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Abstract: In this article, we present an in-silico study of simulating the respiratory system of a healthy cohort depending on age, sex and height by focusing on the individual gas exchange. The virtual cohort simulation, consisting of the lung mechanics and the gas exchange, can be used to test automated functions in highly automated ventilators. To achieve this, a gas exchange model is adapted with the goal to represent the changes in gas exchange by the influence of age, sex and height. For evaluating the individual gas exchange, the arterial partial pressures of oxygen and carbon dioxide are of particular interest. First cohort simulations show a decreasing arterial partial pressure of oxygen with increasing age, while the arterial partial pressure of carbon dioxide increases slightly. Those simulation results are in good agreement with the literature data.

I. Introduction

To improve patient safety during mechanical ventilation, highly automated functions may be beneficial, as they can react independently to the patient's behaviour [1]. Thus, these functions could generally allow a greater focus on individual therapy. It is essential to test the functions by examining them for a variety of combined physiological parameters to ensure the safety of medical devices. In terms of testing these functions, we propose a first approach of simulating the gas exchange of a healthy virtual cohort of various subjects, considering the effects of age, sex and height. Based on an existing gas exchange model, model parameters have been adapted to the different physiological properties using literature references. The resulting cohort simulations can be used to test the automated functions in highly mechanical ventilators.

For the modelling of an individual gas exchange, the lung mechanics model, which is further discussed in [2], is extended by the gas exchange, resulting in a gas exchange model introduced in [3]. The model structure with the relevant input model parameters is shown in *Fig.1*.

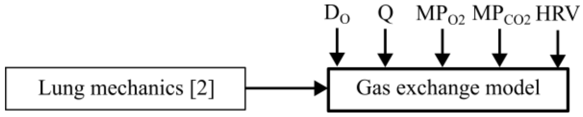

Figure 1: Model structure of respiration with input parameters: oxygen diffusion capacity D_O, cardiac output Q, metabolic rate of oxygen MP_{O2} and carbon dioxide MP_{CO2} and heart rate HRV.

II. Material and methods

In order to simulate the gas exchange of a cohort of various subjects, the breath- and heartbeat-resolved gas exchange model of Hennigs et al. [3] is used.

Regarding the evaluation of the individual gas exchange of a simulated cohort, the determined arterial partial pressures of oxygen $P_{a_{O2}}$ and carbon dioxide $P_{a_{CO2}}$ are of particular interest. They provide information about the efficiency of the respiratory gas diffusion and thus are verified of physiological correctness by comparison with literature [4].

A cohort simulation of the gas exchange of healthy, resting, recumbent subjects considering age, sex and height is achieved by adjusting the following model parameters. The diffusion of oxygen is of particular interest, represented by the oxygen diffusion capacity D_O. To determine D_O, the age-, sex- and height-depending results of a widely used method of measuring the carbon monoxide diffusion capacity D_{CO} are used [5]. Due to the fixed diffusion ratio of oxygen and carbon monoxide, the sex-specific equations of D_{CO} are multiplied by the transfer factor TLCO of 1.2 to obtain the D_O with the standard deviation (*Table 1, l.1*) [6].

Luisada et al. [7] established age- and sex-related changes of the cardiac output Q based on an impedance cardiographic study. A linear approximation of the measurements results in sex- and age-specific equations with their corresponding standard deviation (*Table 1, l.2*).

Since the person's metabolism is affected by factors such as age, sex and height, the metabolic rate for oxygen MP_{O2} and carbon dioxide MP_{CO2} should be adjusted to the individual. The MP_{O2} is closely related to the age-, sex- and height-depending resting energy expenditure REE and can therefore be determined based on the latter [8]. Using the caloric equivalent, a connection between the energy consumption and the MP_{O2} is made by assuming that the simulated subjects eat mixed European diet, so that 20.2 kJ of energy can be extracted from 1 L oxygen [9]. Next, based on the connection of kilojoule and kilocalorie the MP_{O2} can be determined (*Table 1, l.3*) [9]. The PAL-factor considers the individual activity level and is set according to a subject under resting conditions [10]. To determine the MP_{CO2}, the

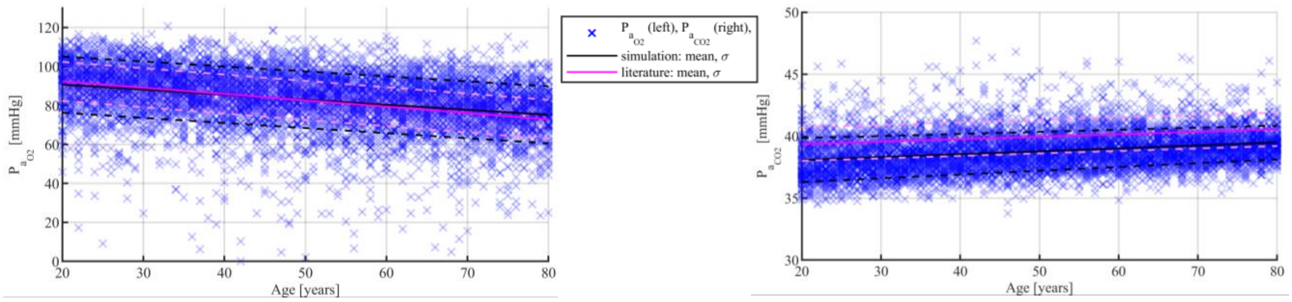

Figure 2: Age-related changes of the arterial partial pressures $P_{a_{O_2}}$ (left) and $P_{a_{CO_2}}$ (right) of a male cohort with an average height of 1.78 m. The cohort is simulated with 6000 males, consisting of 100 different people of each age in the range of 20 to 80 years. The person's variability is achieved by a Gaussian distributed selection of D_O, Q, C_L, C_{CW} and HRV. The solid black line represents the determined mean of the simulation results, with the standard deviation illustrated by the dashed black lines. For comparison, the pink lines show the mean and standard deviation of the literature with the same visualisation [4].

respiratory coefficient RQ is chosen to be 0.84, corresponding to a subject at rest (*Table 1, l.4*) [6].

Based on literature we assumed an age-independent Gaussian distributed average HRV of sleeping subjects of 65 bpm with the standard deviation, as seen in *Table 1, l.5* [11]. All other parameters of the gas exchange model correspond to the choice presented in [3].

The sex-specific cohort simulations regarding the gas exchange were performed by the Gaussian distributed D_O, Q and HRV and their respective standard deviation, as well as the Gaussian distributed C_L and C_{CW}, representing the lung mechanics (cf. [2]). All cohorts consisted of 6000 subjects, evenly distributed between 20 to 80 years of age.

*Table 1: Literature-based model functions and the standard derivation σ of the gas exchange parameters for males (m) and females (f) with A = age [y] and * = based on.*

Parameter		Function	
D_O [L/(s · mmHg)]		$\left(D_{CO,i} \cdot \left((10^{-3} \cdot 22.4)/(60 \cdot 7.5)\right)\right) \cdot \mathrm{TLCO}$ for i = m, f; σ: $(5\%\ \mathrm{Percentile} - D_{CO,i})/1.96$	[5,6]*
Q [L/min]	m	$7.2638 - 0.0265 \cdot A$; σ: $1.8723 + 0.0111 \cdot A$	[7]*
	f	$5.6974 - 0.0190 \cdot A$; σ: $1.8150 - 0.0140 \cdot A$	[7]*
MP_{O2} [L/min]		$\left((REE_i/4.83)/(24 \cdot 60)\right) \cdot PAL$ for i = m, f; $PAL = 0.95$	[8,9, 10]*
MP_{CO2} [L/min]		$MP_{O2} \cdot RQ$ for $RQ = 0.84$	[6]
HRV [bpm]		65; σ: 8.6	[11]

III. Results and discussion

For illustrational purposes, the simulation results shown in *Fig.2* refer to an exemplarily selected simulation of a male cohort with a fixed average height of 1.78 m. As depicted in *Fig.2*, on average the $P_{a_{O2}}$ decreases with increasing age. The different $P_{a_{O2}}$ of the simulated virtual cohort are predominantly located at the expected literature data [4], as the slope of their calculated mean deviates only slightly from the literature mean. The $P_{a_{CO2}}$ in turn increases slightly with rising age and is on average about 1.5 mmHg below the literature mean [4]. The deviation might be due to the choice of MP_{CO2} and RQ. Both the simulation results of $P_{a_{O2}}$ and $P_{a_{CO2}}$ are in good agreement with the literature, as the calculated mean values lie within the physiological range of the standard deviation throughout the aging process [4]. Nonetheless, the cohort simulation computed a few outliers that deviate from reality. This is probably due to a non-physiological composition of the individually selected model parameters and will be addressed in a subsequent work.

IV. Conclusions

An approach of simulating the gas exchange of a cohort with respect to age, sex and height as a second part of an in-silico study is proposed. First simulations show that the model may generally represent the essential changes of the gas exchange in a cohort simulation taking the anthropometric data into account. This work could thus be a first step for the testing of highly automated functions in ventilators. Our future work will focus on expanding the in-silico study by adjusting it to pathological lung diseases such as the acute respiratory distress syndrome (ARDS) and the occurring changes.

AUTHOR'S STATEMENT

This work was partially supported by the German Federal Ministry for Economic Affairs and Climate Action (BMWK) through the KI-SIGS - Project (FKZ: 01MK20012B). A. Oltmann was supported by the European Union – European Regional Development Fund (ERDF), the Federal Government and Land Schleswig Holstein, Project No. 12420002.

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