Mini-Symposium (MS) Proposal for IEEE EMBC20 Montreal

MS Title: Heart–Lungs–Kidneys
Theme 5: Cardiovascular and Respiratory Systems Engineering

Proposer: Nicolas W. Chbat, PhD
The heart, lungs, and kidneys are core organs to sustain life. In the Intensive Care Unit (ICU) predicting, even detecting, the health of one or more of these organs could determine life or death. Understanding their physiology and articulating it mathematically is a way to better understand the function and dysfunction of these core organs, their interactions, and effects on the health of the patient.
This session gathers clinical experts, R&D engineers, and doctoral students to share their experience into the understanding of the function and dysfunction of these organs, in the hope to shed light on the corresponding normo- and patho-physiology, and eventual appropriate therapy.
The authors develop mathematical models to understand underlying physiological mechanisms and validate their models on animals and humans to prove clinical hypotheses. The session comprises five talks each addressing the organs or their interactions in the following order: Heart, Lungs, Kidneys, Heart-Kidneys, Heart-Lungs. I expect to have sequels to such a session in future EMB conferences as well since the topic is fertile. Here is a synopsis of the five talks: Dr. Cristhian Potes, R&D Engineer at Edward Life Sciences, will start the session and explains left ventricular failure and a hypothesis validated on animals. Mr. Jiayao Yuan, a doctoral student of biomedical engineering at Columbia University, then explains how alveolar surfactants affect lung mechanics. Dr. Alan Weinstein of Weill Cornell Medical Center, then introduces us to the clinical renal world by talking about Modeling Kidney Function. Mr. Ben Czerwin, a mechanical engineering doctoral student at Columbia University, then applies a developed a kidney model to relate cardiovascular blood pressure effect on kidney function. Finally, Dr. Nikos Karamolegkos of Philips Research, closes the session by talking to us about cardiovascular and pulmonary interactions under ventilatory support.
The hope of this session is to present work that enables better understanding of the engineering workings of these three organs through the eyes of physiology.

Here are brief synopses of the proposed presentations:

Talk #1: A Porcine Model of Acute Right Ventricular Dysfunction
Presenter: Cristhian Potes, PhD, Research & Development Engineer, Edwards Lifesciences
Contributors: Kevin Moses, Cristhian Potes: Edwards Lifesciences; Etienne Couture, Andre Denault: Montreal Heart Institute, Univeriste de Montreal; Ignacio Monge: Hospital del SAS – Jerez de le Frontera

The talk will shed light on cardiovascular physiology, with spotlight on left ventricular function and failure. An animal study was done to validate results. He will present the set of results from the animal tests that furthers the understanding on this important and common type of heart failure.

Talk #2: Alveolar Tissue Fiber and Surfactant Effects on Lung Mechanics – Validation on ARDS Patients
Presenter: Jiayao Yuan, Doctoral Candidate in Biomedical Engineering, Columbia University
Contributors: Caitlyn Chiofolo, Nicolas Chbat, Quadrus Medical Technologies

The talk will shed light on the effect that the material property and geometry of the alveoli have on lung compliance. In turn, the compliance of the alveoli depends on tissue elasticity and surface tension, which directly affect lung mechanics and hence respiration. In early stage Acute Respiratory Distress Syndrome (ARDS), lung edema collapses the alveoli due to an increase in surface tension. In late stage ARDS, lung fibrosis develops resulting from an increase in collagen fibers volume. To better understand the normo- and patho-physiology of the lungs, we have developed a physiology-based lung model that describes the effect of the lung edema on the amount of air in the alveolar space. The model will be validated on ARDS patient data.

Talk #3: Modeling Kidney Function: Transforming Classical Physiology Into Systems Biology
Presenter: Alan M. Weinstein, MD, Professor of Medicine, Nephrology, Weill Cornell Medical Center

The talk will inaugurate the modeling of the kidneys as a part of the Cardiovascular and Pulmonary Systems Engineering theme, effectively expanding the core organs that define the theme focus from Heart & Lungs only to also include Kidneys. The spotlight will be on the importance that mathematical modeling has on the understanding of the function and dysfunction of the kidneys. Examples will highlight his work, notably how Potassium acts to enhance renal Sodium excretion to effectively reduce blood pressure.

Talk #4: Renal Control Mechanism Effective Threshold for Hypotension in Humans
Presenter: Benjamin Czerwin, Doctoral Candidate in Mechanical Engineering, Columbia University
Contributor: Nicolas Chbat, Quadrus Medical Technologies

The talk will highlight how renal diseases have detrimental effect on the body. While there are several causes of kidney disease, one major risk factor is heart disease because the heart supplies blood to the kidneys. This coupling between the heart and kidneys can lead to hypotension (decreased blood pressure due to heart disease) affecting kidney

function. This prompts the question: at what stage of hypotension does the myogenic response and the tubuloglomerular feedback mechanism become infeasible for controlling the proximal tubule? By including these two feedback mechanisms into a lumped human kidney model, we can study the effects of hypotension on glomerular filtration rate (GFR). We will observe what blood pressure inputs cause the GFR to become unstable. This study is important for the classification of the effect that hypotension has on kidneys and determining at what point can hypotension no longer be controlled by the kidneys.

Talk #5: Right Ventricular Failure in ARDS: Are Heart-Lung Interactions to Blame?
Presenter: Nikolaos Karamolegkos, PhD, Research & Development Engineer, Philips Research
Contributor: Nicolas Chbat, Quadrus Medical Technologies

The talk will highlight heart-lung interaction mechanisms, since they are generally not well understood, especially during mechanical ventilation (MV). They arise due to the location of the heart inside the thoracic cavity. General clinical protocols suggest institution of positive end-expiratory pressure (PEEP) to patients with acute respiratory distress syndrome (ARDS). PEEP induces changes in systemic venous and pulmonary system impedance. Consequently, PEEP affects RV preload and afterload. We can relate such changes in RV function to the partitioning of the respiratory system elastance (E_{rs}) into lung and chest wall components (E_L and E_{cw}).

Short Biographies

Speaker 1 short bio: Cristhian is Distinguished Engineer and Senior Manager of the Applied Machine Learning Group at Edwards Lifesciences. He has obtained his PhD from the University of Texas at El Paso in Electrical and Computer Engineering in 2013. He has a wide experience spanning: 4 years at the Air Force Research Lab (Human Muscle Fatigue) while a doctoral student, 2 years at the Wadsworth Center (ECG), and 2 years at Philips Research North America (Clinical Decision Support).

Speaker 2 short bio: Jiayao plans to graduate in 2021 under the supervision of Dr. Chbat. His expertise is in Respiratory System Modeling and System Identification. His first publication is on micro-vessel exchange system, which is the transport of fluid and protein from blood capillaries to the alveolar space. He was granted the top 10 Award for his work at EMBC19.

Speaker 3 short bio: Alan graduated from Harvard Medical School in 1975. He has numerous journal publications and is renowned as a world expert in renal modeling. He is a Nephrologist at the New York Presbyterian Hospital, and Professor of Medicine as well as of Physiology and Biophysics at the Weill Cornell Medical College, Cornell University.

Speaker 4 short bio: Benjamin plans to graduate in 2020 under the supervision of Dr. Chbat. His expertise is in Renal System Modeling, as well as numerical solutions to Differential-Algebraic Equations. He has developed a modular mathematical model of the dynamics of solute and fluid transports in the kidneys. He recently submitted this work for journal publication.

Speaker 5 short bio: Nikoloas obtained his PhD in Biomedical Engineering in 2017 from Columbia University. In 2018 he has joined Philips Research North America. His expertise is in first-principle modeling of dynamic systems and System Identification. He has several publications and patents.

Organizer short bio: Nicolas is the CEO of Quadrus Medical Technologies, and Adjunct Professor at Columbia University. He is also the Chairman of the Technical Committee of Theme 5, Cardiovascular and Respiratory Systems Engineering, at IEEE EMBS.

Speaker 1: Cristhian Potes, PhD, Edwards Lifesciences

Title of Talk: A Porcine Model of Acute Right Ventricular Dysfunction

***Abstract*— Right ventricular dysfunction (RVD) is associated with a decrease in contractility and/or an increase in afterload. RVD has been associated with increased mortality in the ICU and cardiac surgical patients. Therefore, early identification of this condition at less severe stages will allow for earlier intervention and potentially better patient outcomes. Unfortunately, early recognition of RVD using standard hemodynamic and ultrasound parameters is non-specific and clinically challenging. In this study, we developed a swine model to create ischemic myocardial dysfunction/failure of the right ventricle. In line with previous human observational studies, our animal results confirmed that changes in the morphology of the right ventricular pressure waveform are significantly correlated with echocardiography measurements and could be used to continuously monitor right ventricular function.**

I. INTRODUCTION

Acute right ventricular dysfunction (RVD) remains an important complication in patients undergoing cardiac surgery and has been associated with increased major organ dysfunction and mortality [1]. There is strong evidence from human studies that specific hemodynamic features derived from the morphology of the right ventricular pressure waveform are highly correlated with hepatic venous congestion and other clinical variables associated with RVD [1]. We developed a swine model of RVD to evaluate changes in the right ventricular pressure waveform associated to ischemic myocardial dysfunction.

I. METHODS

Right ventricular dysfunction/failure was induced by injecting microspheres in the right coronary artery. Biventricular pressure-volume (PV) loops and echocardiography measurements (tricuspid annular plane systolic excursion – TAPSE, peak strain, and fractional area change - FAC) were taken during baseline and after every microsphere injection with the ventilator off. PV loops were recorded during inferior vena cava (IVC) occlusions (every third injection) to assess the myocardial contractility of both ventricles by using the slope of the end-systolic pressure volume relationship (ESPVR). During the entire protocol hemodynamic parameters such as pulmonary artery pressure, central venous pressure, femoral artery pressure and mixed venous oxygen saturation (SvO2) were continuously recorded.

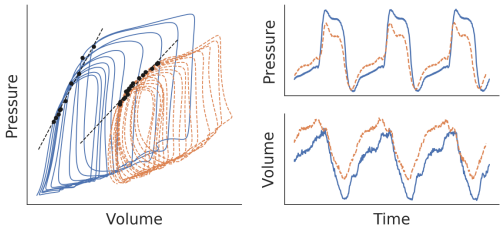

Figure 1. Pressure-volume loops of the right ventricle during baseline (in blue and continuous line) and end of protocol (in orange and dashed line). Black dots correspond to the end-systolic pressures and volumes (ESPVR) obtained during IVC occlussions. The slope of ESPVR represents the end-systolic elastance, which provides an index of myocardial contractility

II. RESULTS

Acute RVD was successfully induced in 10 pigs. Contractility of the right ventricle decreased by an average of 48.5% from baseline to the end of the protocol. Compared to baseline, TAPSE decreased from 17 mm to 7 mm, peak strain went from -28% to -14% and FAC decreased from 39% to 19.5%. Increases in both end-diastolic pressure (EDP) and pressure gradient (EDP minus proto-diastolic) were negatively correlated with contractility of the right ventricle. Increases in the pressure gradient greater than 4 mmHg have been significantly associated with venous congestion caused by RVD [2]. The average global impact of the dysfunction was reducing right ventricle stroke volume from 84.5 ml to 70 ml, SvO2 from 68.3% to 44%, and femoral artery pressure from 72.88 mmHg to 55.7 mmHg. These hemodynamic changes were below normal clinical thresholds late in the protocol.

III. DISCUSSION & CONCLUSION

Ischemic myocardial dysfunction of the right ventricle was induced by injecting microspheres in the right coronary artery. A significant decreased in contractility of the right ventricle was significantly correlated with TAPSE, peak strain, RVFAC, and RV waveform parameters. Changes in the RV pressure waveform could be used for early detection of RVD and continuous monitoring of RV function.

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Speaker 2: Jiayao Yuan, Columbia University

Title of Talk: Alveolar Tissue Fiber and Surfactant Effects on Lung Mechanics – Simulation of ARDS

Abstract— **The air flow goes in and out of the lungs is closely related to the compliance of the alveoli (gas exchange units). The compliance of the alveoli is determined by alveolar tissue fiber (elastin and collagen) elastic properties, tissue fiber volume and surface tension effect. The alveolar compliance varies within every breath due to the nonlinear fiber elastic property and surface tension effect. To better understand the normo- and patho-physiology of the lungs, we developed a physiology-based lung model that describes the effect of a time-varying alveolar compliance on the lung mechanics. To prove the feasibility of this model, Acute Respiratory Distress Syndrome (ARDS) was simulated.**

IV. INTRODUCTION

The lung parenchyma, comprising a large number of thin-walled alveoli, has a complex internal structure with maximized inner surface area to support gas exchange. The alveoli are held open under the balance of three pressures: 1) the transmural pressure, which is the difference between pleural cavity pressure and the alveolar pressure, 2) tissue fiber stress, and 3) the alveolar surface tension, decided by the concentration of surfactant lining inside the alveoli surface. Surfactant plays a critical role in reducing the surface tension in alveoli. Patients who have acute lung injury (ALI), or ARDS, have severely reduced gas exchange due to alveoli collapsing and fluid occlusion of the small pulmonary airways. It is important to recruit the collapsed alveoli, because hypoxemia can cause tissue and hence organ failure. The tissue elasticity of late stage ARDS patients would further change due to the development of fibrosis.

As shown in Figure 1, we defined a lung mechanics module to compute air flow goes into the lungs during breathing, and an alveolus elasticity module to quantify the effect of tissue fiber elasticity and surfactant concertation on the time-varying alveolar compliance.

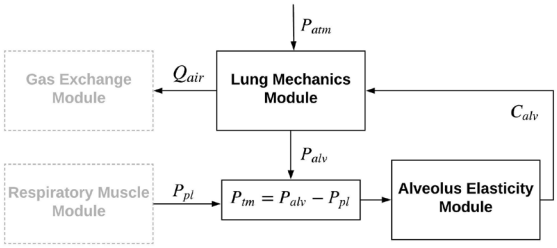

Figure 1. Linkage of Lung Mechanics and Alveolus Elasticity Module

V. METHODS

In the lung mechanics module, we combined air tubes that are in parallel and showing similar geometric and functional properties into one single compartment. Following Rideout's work [4], we defined four series segments to present the lung structure: larynx, trachea, bronchi and alveoli. Rideout used a constant alveolar compliance, while we computed a time-varying alveoli compliance as a function of tissue fiber elasticity and surfactant concentration from alveolus elasticity module.

In the alveolus elasticity module, we adopted the shape of alveolus to be truncated octahedron, as Fung found that the most common shapes of alveoli were hexagons and rectangles [2]. The mechanical properties of an alveoli tissue are mainly determined by elastin, collagen and surface tension [3]. We leveraged Fujioka's model [1] to solve for the volume of one single alveolus, given pleural cavity pressure. The change of the alveoli volume is computed by multiplying the alveolus volume by the number of alveoli in the lungs [5].

VI. RESULTS

Preliminary result of air flow in early and late stage of ARDS with different severity levels was shown in Figure 2. In an early stage of ARDS, alveoli collapse due to an increase of surface tension. To show early stage of ARDS, 20% and 40% surfactant reduction were simulated. In a late stage of ARDS, the lung fibrosis develops, stiffening the lungs resulting from an increasing volume of collagen fibers. Four and eight times increasing of collagen volume were simulated. Figure 2 shows reducing air flow goes into the lungs as the lungs get stiffer.

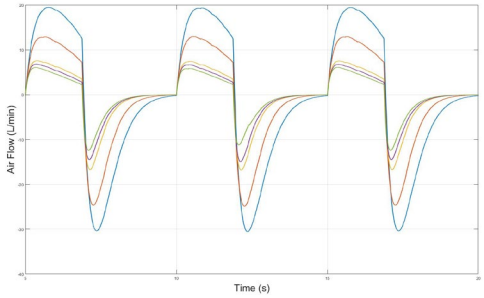

Figure 2. Air flow in healthy (blue), 20% (red) and 40% (yellow) surfactant reduction, 4 (purple) and 8 times (green) increasing of collagen volume (with 40% surfactant reduction)

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Speaker 3: Alan Weinstein, MD, Weill Cornell Medical Center

Title of Talk: Modeling Kidney Function: Transforming Classical Physiology Into Systems Biology

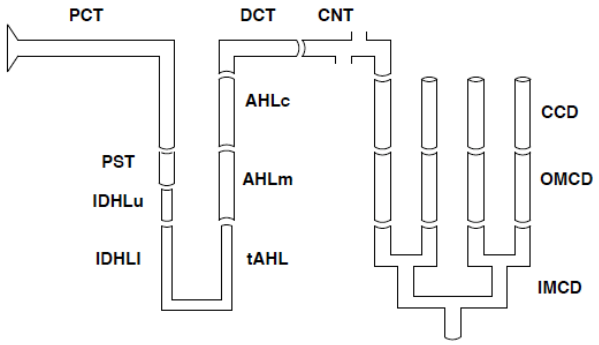
Abstract— **The spotlight will be on the importance that mathematical modeling has on the understanding of the function and dysfunction of the kidneys. Examples will highlight his work, notably how potassium acts to enhance renal sodium excretion to reduce blood pressure, and connections of microvascular function and tubular metabolism to renal water conservation.**

I. Background

The ability of the kidney to conserve water and excrete concentrated urine (antidiuresis) has been the focus of chemical engineers and renal physiologists for over a half century. In order to decipher the underlying physiology, workers have developed mathematical models of the kidney that focus on this aspect of its function. All have been dedicated to understanding renal water conservation, specifically maximizing urine osmolality in the antidiuretic state. With rare exception, these models have been stripped down to two solutes, neutral NaCl and urea. What these models provided was insight into the role of the tapering multinephron and multivessel configuration, and of segmental permeability differences, in protecting deep interstitial solute gradients within the kidney medulla. Absent from these models was the impact of electrolyte metabolism on kidney function. There have been no model predictions of the medullary acid-base milieu.

II. Methods

The mathematical difficulty of a kidney model derives from the fact that within the renal medulla, both proximal and distal nephron segments contribute to the interstitial composition, so that late events impact early events along the tubule (figure). This kidney model is comprised of an ensemble of superficial and juxtamedullary nephrons, medullary vasculature, and an axial interstitial compartment, whose local composition is determined by conservation equations which balance nephron and vascular fluxes (Weinstein, 2017). The model solutes for tubules and interstitium include Na^+, K^+, Cl^-, HCO_3^-, H_2CO_3, CO_2, HPO_4^{2-}, $H_2PO_4^-$, urea, NH_3, NH_4^+, H^+, and glucose, so that their concentrations, along with hydrostatic pressure constitute the variables to be determined at interstitial grid points. Their conservation equations are complicated by titration of buffers (including vascular hemoglobin species), and by CO_2 generation, which derives from metabolically driven solute transport.



III. Results

The first application of this kidney model focused on the salutary effect of dietary K^+ to reduce blood pressure by promoting Na^+ excretion. There is ample evidence that the natriuresis is due to a direct impact of elevated blood K^+ concentration to depress renal Na^+ reabsorption, and there are several plausible segmental loci for this effect. What this model predicts is that the extra Na^+ that appears in the final urine derives from the effect of K^+ on proximal convoluted tubule. Attention was next turned to determinants of water conservation, and in comparison to its predecessors, this model did not do well. A key difference here is insistence on realistic vascular reflection coefficients (near zero), which has worsened the ability to concentrate the urine, by providing substantial convective solute uptake from the medullary interstitium. An unanticipated finding from these calculations was the prediction that a consequence of water conservation would be high medullary pCO_2. Layton and collaborators had already noted that the antidiuretic kidney was functioning with low medullary blood flow, but which was sufficient to provide that all active transport could be aerobic. What this model adds to the discussion is that those metabolic estimates must produce high medullary pCO_2, which becomes unrealistically high as countercurrent exchange becomes more efficient.

IV. Conclusion

Simulation of kidney function at the cellular level highlights aspects of electrolyte transport, microvascular function, and renal oxygen metabolism, which have important translational impact, but which require considerably more experimental definition.

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Speaker 4: Benjamin Czerwin, Columbia University

Title of Talk: Renal Control Mechanism Effective Threshold for Hypotension in Humans

Abstract— **While there are several causes of kidney disease, one major risk factor is heart disease because the heart supplies blood to the kidneys. This coupling between the heart and kidneys can lead to hypotension (decreased blood pressure due to heart disease) affecting kidney function. This prompts the question: at what stage of hypotension does the myogenic response and the tubuloglomerular feedback mechanism become infeasible for controlling glomerular filtration rate (GFR)? By including these two feedback mechanisms into a lumped human kidney model, we can study the effects of hypotension on glomerular filtration rate (GFR). We observe what blood pressure inputs cause the GFR to become unstable. This study is important for the classification of the effect that hypotension has on kidneys and determining at what point can hypotension no longer be controlled by the kidneys.**

I. INTRODUCTION

All organs in the body function in a highly coupled system where inputs and outputs of certain organs affect others. One such important coupling is the heart and kidneys. A major risk factor for kidney disease is heart disease whereby blood flow into the kidneys is altered in such a way that the kidneys are no longer able to function. We look to investigate the thresholds where intrinsic control mechanisms within the nephron are no longer able to compensate for altered blood flow from hypotensive heart disease.

II. METHODS

A lumped full kidney human model has been developed capable of simulating several scenarios. This model was developed using linear graphs [1] – lineal, graphical representations of the biology – and subsequent continuity and compatibility equations. The model contains nodes (compartments) with fluid pressure and salt concentration values throughout the kidney (represented by a single, lumped nephron). The model consists of hydraulic flow of fluid, advective flow of solutes, and reabsorption (proportional to node inflow) flow for both. Resistance and reabsorption percentage parameters (largely unknown for humans) were determined via optimization using feasible human nephron lengths, pressures, and salt concentrations.

The afferent arteriole diameter is the actuator for both the myogenic and tubuloglomerular feedback mechanisms. This diameter is a direct factor for the fluid resistance parameter given by $R = 8L\mu/\pi r^4$ where L is the arteriole length, μ the viscosity, and r the radius. This resistance determines the rate at which fluid moves through the afferent arteriole, given by Hagen-Poiseuille flow, as the $Q = \Delta P/R$, where ΔP is the difference in pressure between two nodes.

III. RESULTS

For a healthy case, sodium, and chloride concentrations can be seen in Table 1 along with comparisons against Layton and Layton's model [2]. It can be seen that the concentrations are in good standing with those expected. Fluid flows were compared with Uttamsingh *et al.* [3] and were within 7%.

[mM]	Current Model		Layton and Layton [2]	
	Na	**Cl**	**Na**	**Cl**
B	137	110	140	110
P	137	120	140	120
N	210	185	215	200
K	98	92	100	100
D	29	28	30	30

Table 1. Sodium, and chloride concentrations in millimolar under healthy conditions in Bowman's space (B), proximal tubule (P), descending loop of Henle (N), ascending loop of Henle (K), and distal tubule (D).

Congestive heart failure can often lead to hypotension and decreased cardiac output. In this case, we simulated several cardiac output values over a wide range and observed glomerular filtration rate (GFR) to see when it fell below the healthy limit of 90 mL/min. This plot can be seen in Fig. 1 without the presence of intrinsic controllers to dampen the changes in cardiac output.

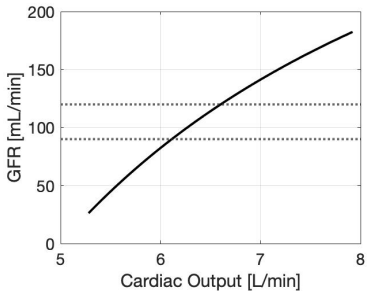

Figure 1. Glomerular filtration rate (GFR) as a function of cardiac output. Healthy GFR range between dotted lines. Open loop simulation.

IV. DISCUSSION & CONCLUSION

It is apparent from Fig. 1 that control mechanisms are imperative for kidney function as a healthy cardiac output of 6.1 L/min would otherwise threaten kidney health. We will present our investigation into the system's response and GFR values with the myogenic and tubuloglomerular feedback mechanisms under hypotensive scenarios. This will allow us to determine the degree of hypotension where the kidneys will be seriously affected.

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Speaker 5: Nikolaos Karamolegkos, PhD, Philips Research North America

Title of Talk: RV Failure in ARDS: Are Heart-Lung Interactions to Blame?

***Abstract*— Heart-lung interaction mechanisms are generally not well understood. Mechanical ventilation (MV) accentuates such interactions and could compromise cardiac activity. MV with positive end-expiratory pressure (PEEP) is used for patients with acute respiratory distress syndrome. However, PEEP can affect right ventricular function, potentially causing right ventricular (RV) failure. In this paper, we use a cardiopulmonary model to provide physiological hypothesis to the underlying mechanisms causing RV failure.**

***Clinical Relevance*—Assessment of ventilation-induced changes in cardiac function is considered an unmet clinical need.**

V. INTRODUCTION

Heart-lung interaction mechanisms are generally not well understood and often dismissed during mechanical ventilation (MV). They arise due to the location of the heart inside the thoracic cavity (Figure 1). Ventilation-induced lung volume and pleural pressure changes are transmitted to any structure within the thorax. MV accentuates heart-lung interactions and could compromise cardiac activity. General clinical protocols [1] suggest institution of positive end-expiratory pressure (PEEP) to patients with acute respiratory distress syndrome (ARDS). ARDS is a common inflammatory condition that causes increased permeability of the pulmonary vascular wall [2]. PEEP application has become the recommended method to treat such patients by expanding the fluid-filled alveoli and reducing the edema. However, PEEP induces changes in systemic venous return and pulmonary system impedance. Consequently, PEEP affects right ventricular (RV) preload and afterload, which can lead to adverse effects on cardiac activity.

VI. RESULTS

We can relate PEEP-induced changes in RV function to the partitioning of the respiratory system elastance (E_{rs}) into lung and chest wall components (E_L and E_{cw}, respectively) [3]. In other words, for a given value of E_{rs}, the same change in PEEP would result in different changes in RV function depending on the ratio between E_L and E_{cw}. For instance, two different groups of ARDS patients (pulmonary ARDS, $ARDS_p$ and extra-pulmonary ARDS, $ARDS_{exp}$) may have the same value of E_{rs} but different partitioning to E_L and E_{cw} [3]. Such a difference alters the effect of PEEP on the loading status of the right ventricle (right-hand side plots in Figure 2). Observations, like those from Figure 2 from a cardiopulmonary model, then suggest that institution of PEEP on a patient with $ARDS_p$ may lead to right ventricular overloading, potentially causing right ventricular failure [4], despite the overall decrease in systemic venous return and cardiac output.

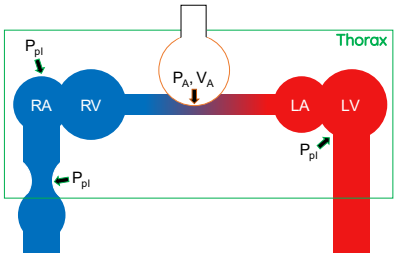

Figure 1. Graphic illustration of heart-lung interaction mechanisms. RA, right atrium; RV, right ventricle; LA, left atrium; LV, left ventricle, P_A, alveolar pressure; V_A, alveolar (lung) volume; P_{pl}, pleural pressure.

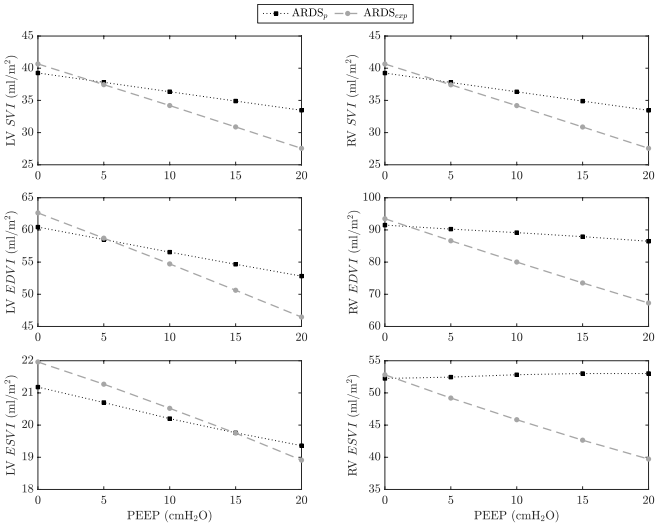

Figure 2. Cardiovascular response to step changes in the level of positive end-expiratory pressure (PEEP) for pulmonary ARDS ($ARDS_p$, black squares) and extra-pulmonary ARDS ($ARDS_{exp}$, gray circles). LV, left ventricular; RV, right ventricular; SVI, stroke volume index; EDVI, end-diastolic volume index (indicator of preload); ESVI, end-systolic volume index (indicator of afterload).

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