Patient-specific computational models of acute pulmonary embolism: relating regional occlusion to clinical symptoms

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Abstract— The pulmonary circulation is a unique low resistance system that carries almost the entire cardiac output. Full or partial occlusion of pulmonary arteries by thromboemboli can result in acute elevation of right ventricular pressure, and/or hypoxaemia, but the relationship between clinical symptoms and the size or distribution of embolus is poorly described. Here we review the development and application of multi-scale, anatomically based models of the pulmonary circulation that have been used to provide new insight into structure-function mechanisms in acute pulmonary embolism.

I. BACKGROUND

Thromboembolic occlusion of pulmonary arteries in acute pulmonary embolism (APE) leads to a redistribution of blood flow and pressures, which can elevate pulmonary arterial pressure (PAP) sufficient to cause right ventricular (RV) dysfunction or failure. Obstruction of large pulmonary arteries could theoretically increase the pulmonary vascular resistance (PVR) sufficiently to elevate PAP, however, because patients can present with the same apparent obstruction load yet have markedly different RV response, this has been discounted as important. Thrombus-mediated vasoconstriction has been proposed as a potential alternative mechanism. The unresolved question as to what is responsible for variable patient response hinders the stratification of patients into high risk or low risk groups, and hence the appropriate treatment strategy. The development of anatomically based computational models of the pulmonary circulation has enabled model-based investigation of heterogeneous clot distribution and comparison of individuals with the same clot load, but different distributions of clot, to provide a rational basis for patient stratification.

II. MODELING PRE- AND POST-EMBOLIC OCCLUSION

We have established computational methods that model the geometry and perfusion of the pulmonary circulation over multiple spatial scales of interest [1]. The geometric models include definition of the geometry of arteries and veins resolvable on computed tomography pulmonary angiograms (CTPAs) for an individual, supplementation of these vessels with a 1D branching tree to the level of the gas exchange tissue that fills the five lobes, and a model for each pulmonary acinus as a ‘ladder-like’ structure with recruitable and distensible capillary sheets [2]. The model is embedded within a deformable parenchymal tissue, so it responds to changes in lung inflation and orientation (with gravity), and it is accompanied by an airway tree for simulation of ventilation distribution. Pulmonary emboli are identified using a semi-automated method [3], and their full or partial obstruction is imposed on the vascular model. We consider only the steady-state distribution of perfusion, to enable prediction of main pulmonary artery pressure and gas exchange. Blood is modeled as a Newtonian fluid in the arteries, using Poiseuille resistance, and a sheet-flow model is adopted in the capillaries.

III. STRUCTURE-FUNCTION OUTCOMES

We have used estimates of metabolic rate at rest, fidgeting, and walking to estimate the level of activity required to induce hypertension in nine subject-specific models representing patients clinically presenting with APE [4]. Hypertension can be predicted in patients whose cardiac output was consistent with upright fidgeting in the absence of any active response to embolization. We have since supplemented this with further subjects. Of the patients included in the study, those with model-predicted global hypoxia (P_{O2} < 80 mmHg) all had RV dysfunction in the clinical setting, whereas none of the patients without predicted global hypoxia had RV dysfunction. Outcome was dependent on the spatial location of the emboli and their size, hence explaining different outcomes in individuals with the same obstruction load but different patterns of occlusion.

REFERENCES


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