Pulmonary Arterial Wave Intensity Analysis in Health and Disease.

By

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Abstract

Wave intensity analysis (WIA) is a time-domain technique utilising high fidelity pressure and velocity measurements to determine the intensity, direction, type and timing of waves that may simultaneously exist. Travelling wavefronts represent elemental units of energy transmitted within and between the heart and blood vessels. Thus, WIA allows us to study ventricular-arterial interactions providing information on ventricular performance and the state of the circulation. In the pulmonary circulation WIA allows the study of upstream and downstream events that influence net pulmonary arterial blood flow.

WIA was performed in the pulmonary arteries of anaesthetised open-chest sheep, determining a normal mean wave speed of 2.1 ms$^{-1}$. Whilst wave reflection was minimal in healthy resting pulmonary arteries, two minor but clearly discernible backward travelling waves were identified that serve as important physiological markers. The first was an early systolic backward expansion wave representing open-end reflection from a site approximately 3 cm downstream, most likely from the main pulmonary bifurcation, and would serve to augment flow out of the right ventricle. The second was a late systolic backward compression wave representing closed-end reflection from a site approximately 20 cm downstream, most likely from the pulmonary microcirculation, and would serve to oppose flow out of the right ventricle. The open-end reflection was enhanced by increased pulmonary blood flow or circulating blood volume. With pulmonary vasoconstriction or obstruction, WIA was able to accurately determine the distance to the newly developed closed-end reflection site from which a backward compression arrives in mid-systole and opposes flow out of the right ventricle.

In human volunteers with normal or diseased pulmonary vasculature, wave speed was shown to increase linearly with pulmonary vascular resistance. The difficulties in reproducing instantaneous pulmonary blood velocity accurately in-vivo limited assessment of reflected waves.
Foreword

The current definition of pulmonary vascular disease in terms of the presence or absence of pulmonary hypertension, that is a mean pulmonary artery pressure $\geq 25$ mmHg (Badesch et al., 2009), is inadequate. As the pulmonary circulation is highly compliant with a substantial ability to recruit blood vessels, 50-60% of the pulmonary microcirculation is diseased before a pressure rise is manifest (Dalen et al., 1967). Thus, pulmonary hypertension is a late manifestation of pulmonary vascular disease and therefore new techniques are required to define the condition at its earliest and perhaps more treatable stages.

The trend to explore genetic and subcellular processes means that important haemodynamic principles such as ventricular-vascular interactions have been neglected, particularly in the pulmonary vascular bed. A relatively new method called wave intensity analysis (WIA), relying on the simultaneous acquisition of blood velocity and pressure, has the potential to provide exciting insights into right ventricular-pulmonary arterial interactions. The basis of this approach is that a cardiac cycle is associated with the propagation of infinitesimal wavefronts defined by changes in pressure and velocity. WIA allows the identification of forward-travelling waves that arise from the heart and backward-travelling waves that are reflected from the distal vasculature, as well as the calculation of the instantaneous energy carried by these waves. These waves are further defined as compression waves that increase pressure or expansion waves that decrease pressure. With calculation of the wave speed, the wave intensity can be separated into the four potential wave types that may simultaneously exist; forward compression waves that increase pressure and velocity, forward expansion waves that decrease pressure and velocity, backward compression waves that increase pressure but decrease velocity, and backward expansion waves that decrease pressure but increase velocity. As WIA remains in the time domain, it has advantages over the prevailing frequency domain approach to wave reflection.

By potentially identifying reflected waves from the pulmonary vasculature WIA may have a role in the early detection and diagnosis of pulmonary vascular
disease, allowing targeted therapy before right ventricular dysfunction becomes irreversible.

This thesis is divided into 10 chapters and may be thought of as a collection of experiments and observations that may be used as a foundation to extend our understanding of wave travel and reflection in the pulmonary circulation of sheep and humans using WIA. Chapter 1 is introductory in nature, describing the historical evolution of cardiopulmonary knowledge, outlining our current understanding of pulmonary circulatory physiology, and critically explores the literature related to investigation of wave reflection. Chapter 2 reports the methodology, experimental protocol and data analysis techniques in both the sheep and human studies. Chapter 3 qualitatively and quantitatively investigates wave intensity in the resting healthy pulmonary artery of sheep. Chapter 4 reports on the marked influences that pressure-velocity signal delays or wave speed calculation errors may have on wave intensity parameters. Chapter 5 explores the effects of high pulmonary blood flow on wave intensity parameters in sheep. Chapter 6 reports on the influence of reversible and irreversible acute changes in right ventricular afterload on wave intensity parameters in sheep. Chapter 7 explores whether progressive microsphere obliteration of the sheep’s pulmonary microcirculation would lead to detectable changes in the wave speed or wave intensity parameters before a significant rise in mean pulmonary artery pressure manifests. Chapter 8 investigates the possible changes on wave intensity parameters after accounting for the pulmonary Windkessel (reservoir) pressure. Chapter 9 reports on the first study in humans to investigate pulmonary arterial wave intensity in healthy and diseased volunteers. Chapter 10 summarises the thesis, draws conclusions and plans new directions for pulmonary arterial WIA. A list of references is documented after Chapter 10.
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Intensity may have to be modified because of disease severity, symptom limitation and co-morbidities. (21). 3.1.2.2 Strength and endurance training of upper and lower limbs Muscle atrophy is common in chronic respiratory disease. A reduction in peripheral muscle mass compared to normal subjects has been demonstrated. (22) Low intensity peripheral muscle training has been found to improve muscle bulk and strength. (22) Management of Chronic Obstructive Pulmonary Disease in Adults in Primary and Secondary Care. Roche, N. (2009). Activity limitation: a major consequence of dyspnoea in COPD. (22) National Institute for Health and Clinical Excellence. Mean pulmonary arterial pressure and pulmonary vascular resistance (PVR) remain the most common haemodynamic measures to evaluate the severity and prognosis of pulmonary hypertension. However, PVR only captures the non-oscillatory component of the right ventricular hydraulic load and neglects the dynamic compliance of the pulmonary arteries and the contribution of wave transmission. Wave intensity analysis offers an alternative way to assess the pulmonary vasculature in health and disease. Wave speed is a measure of arterial stiffness, and the magnitude and timing of wave reflection provide in Clinical usefulness of wave intensity analysis. Abstract. Introduction. Abstract Wave intensity (WI) is a hemodynamic index, which can evaluate the working condition of the heart interacting with the arterial system. It can be dened at any site in the circulatory system and provides a great deal of information. In the coronary artery disease group, the magnitude of the rst peak of carotid arterial WI (W1) increased with LV max. dP/dt (r = 0.74, P \ 0.001), and the amplitude of the second peak (W2) decreased with an increase in the time constant of LV pressure decay (r = -0.77, P \ 0.001). In the dilated car-diomyopathy group, the values of W1 were much lower than those in the normal group (P \ 0.0001).