

EDITORIAL

Clinical significance of pulmonary arterial input impedance

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Pulmonary arterial input impedance excites the attention of few clinicians, but there are compelling reasons why they should be more interested in this subject. Physicians are well-versed in the intricacies of pulmonary vascular resistance, which is a measure of the opposition to the mean components of flow. Impedance is a measure of the opposition to the pulsatile components of flow. Right ventricular afterload is usually considered in terms of pulmonary vascular resistance. Yet, between one third and one half of the hydraulic power in the main pulmonary artery is contained in the pulsatile components of flow [1]. Therefore, measurement of arterial input impedance is needed to obtain a complete description of ventricular afterload [2]. The primary cause of cor pulmonale is an increase in the right ventricular afterload [3]. Therefore, impedance is likely to make a substantial contribution to this perennial problem.

Most pulmonary vascular research has focused on the small pulmonary arteries, which appear to be the main site of resistance. Impedance is dependent on the mechanical properties and the geometry of the proximal pulmonary arteries. The pulmonary arterial input impedance spectrum is dependent primarily on the first five orders from the main pulmonary artery in decreasing levels of importance [4]. The proximal pulmonary arteries are the first line of opposition to right ventricular output and have a dominant effect on the input impedance. The fact that the mean and the pulsatile components of flow are dependent on different portions of the pulmonary circulation suggests that they could be controlled separately, without much overlap. It seems likely that this may be an unexplored avenue that may open the possibility of developing new therapeutic interventions.

Although the factors that affect pulmonary vascular resistance are many, resistance, unlike impedance, can be expressed as a single number. Impedance is a function of frequency and requires a graphical display of the spectrum to show its magnitude and the phase relation between pressure and flow over a range of frequencies that are contained in the measured pressure and flow waveforms. The magnitude of impedance varies with frequency because of wave reflection [5]. The pulmonary circulation is pulsatile with multiple

bifurcations; wave reflection is an inevitable consequence. When the forward pressure wave from the heart collides with the backward pressure wave that was reflected from the bifurcations, pressure increases. In contrast, when the forward flow wave from the heart meets the backward flow wave that was reflected from the bifurcations, flow decreases. As a result of wave reflections, the pressure and flow waves are not in phase with each other. Although not easily appreciated clinically, except perhaps in severe pulmonary hypertension, wave reflection occurs even under physiological conditions. Pressure lags flow at normal cardiac frequency in normal subjects.

Because resistance is the opposition to mean flow, it is represented by only one frequency, zero, and there is no phase relation to consider because it is zero, the mean pressure and mean flow change simultaneously under steady-state conditions. To circumvent the need for a display of the entire impedance spectrum and the associated complexity that occurs with a statistical evaluation, there have been several approaches to representing the essential features of the spectrum as one or two numbers.

Some investigators have used lumped parameter models to represent impedance [6]. These models are simple electrical circuits of resistors, capacitors and inductors. The values of these elements are altered to produce an input impedance that is similar to the input impedance of the pulmonary circulation. The value of these elements has been shown to reflect certain aspects of the haemodynamic properties of the pulmonary vasculature. Nevertheless, the lumped parameter model has several drawbacks. For example, lumped parameter models do not have any explicit representation of wave reflection, although the elements responsible for its occurrence are represented. Wave reflection does not occur in the electrical circuit because current is transmitted instantaneously.

To circumvent this limitation, others have used transmission line theory of fluid dynamics. Transmission line theory emphasizes the importance of characteristic impedance [7]. Characteristic impedance is the input impedance in the absence of wave reflection. Although wave reflection cannot be eliminated from the pulmonary circulation under normal circumstances, wave reflection is minimal at high frequencies. The viscoelastic properties of the vessel wall dampen wave propagation at these frequencies. As a result, the pressure and flow are in phase, so that the phase shift is close to zero and characteristic impedance can be represented by a single number. Theory indicates that it is dependent on the calibre and compliant properties of the main pulmonary artery.

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Importance of input impedance on right ventricular performance

The need to consider the elastic properties of the pulmonary circulation and impedance rather than the pure resistive properties on right ventricular performance is abundantly apparent at the limit. The heart could not function if it were not for the elastic properties of pulmonary vasculature. During systole, the pulmonary valve is open but the mitral valve is shut. Therefore, the heart could not pump if it were not for the elastic properties of the pulmonary vasculature. Hence, the importance of the ventricular-vascular interaction is easy to demonstrate at this extreme; the more pertinent question is whether or not it is important under circumstances that arise in pathophysiology.

The relationship between input impedance and ventricular performance has been well established, largely with *in vitro* preparations for the left ventricle [8]. There is also some evidence from *in vivo* experimentation. MORITA *et al.* [9] demonstrated that the compliance of the aorta is inversely related to characteristic impedance and to pulse pressure. Similarly, we have shown that stiffening of the main pulmonary artery by placement of a cuffed electromagnetic flow probe around the vessel results in an immediate 25% increase in pulmonary arterial pulse pressure [10].

MORITA *et al.* [11] have also shown in a preliminary study that increased characteristic impedance causes left ventricular hypertrophy in dogs. In fact, their study was stimulated by reports of left ventricular hypertrophy occurring in patients after bypass between the ascending aorta and the abdominal aorta for thoracoabdominal aortic aneurysm [12]. They reasoned that the abnormal proximal arteries imposed an increased opposition to pulsatile flow. As a result, aortic impedance was altered without affecting resistance. This increase in impedance was sufficient to result in left ventricular hypertrophy. We have used a similar experimental approach in rats. We used monocrotaline to induce pulmonary hypertension and stiffened the main pulmonary artery with plastic tubing to increase pulse pressure. We found that the degree of right ventricular hypertrophy was dependent on the increase in pulse pressure rather than the increased mean pulmonary arterial pressure [13].

Wave reflection and impedance

Wave reflection is, in part, responsible for the increased burden on the heart under pathological conditions. The increased pressure in pulmonary hypertension may be accentuated by wave reflection. By knowing the characteristic impedance, the measured pressure and flow waves can be resolved into the two components: a forward wave and a reflected wave [5]. The effect of wave reflection on hydraulic power can be assessed by calculating the energy transmission ratio. The energy transmission ratio is the ratio of hydraulic power in the measured pressure and flow waves to the hydraulic power in the forward pressure and flow waves. Previously, we have shown that acute elevation of cardiac output increases the energy transmission ratio [4]. Therefore, the pulmonary circulation becomes more efficient with

this physiological disturbance. The energy transmission ratio decreases markedly after acute pulmonary thromboembolism [13]. Therefore, the pulmonary circulation becomes inefficient after this pathological haemodynamic disturbance.

In the pulmonary circulation, several investigators [14–17] have shown that the precise form of pulmonary vascular obstruction has differing effects on input impedance and resistance depending on the site of obstruction. All forms of obstruction caused increased input resistance. Positive end-expiratory pressure compresses the pulmonary microcirculation. It increases resistance, but has little effect on input impedance and wave reflection. Obstruction of a large pulmonary artery by ensnarement of the left pulmonary artery increases pulse pressure and characteristic impedance, but has little effect on wave reflection. The increased characteristic impedance appeared to prevent an increase in wave reflection and was mediated, at least in part, by serotonin. In contrast, acute thromboembolism with obstruction of medium-sized pulmonary arteries decreases characteristic impedance and pulse pressure. As a result, it has a detrimental effect on wave reflection and systemic hypotension [13]. It appears that the passive decrease in characteristic impedance due to distension of the pulmonary trunk, rather than the active increase in characteristic impedance that occurs with ensnarement of the left main pulmonary artery, results in greater wave reflection. Perhaps the severe haemodynamic disturbance that can occur with pulmonary embolism compared with the milder changes that occur with unilateral pulmonary arterial occlusion is due to the differing effects that these forms of obstruction have on wave reflection.

Is impedance affected by breathing?

The article by CASTIGLIONI *et al.* [18], in this issue of the Journal, raises an old question that is important to engineers and clinicians. Engineers are interested because it strikes at the haemodynamic basis for the measurement of input impedance. The concept of impedance assumes that the system is passive and time invariant. Passivity means that the only energy supplied actively to the system occurs at the input, the rest of the system is passive. For the pulmonary circulation, it would require that the right ventricle is the sole energy source and that cardiac motion has no effect on the pulmonary circulation. Causality means that the output depends only on the input at any moment or previous moment of time. For the pulmonary circulation, it would require that any change in flow at the input of the circulation is due to an alteration in the measured pressure at the input.

Although these requirements seem reasonable approximations for the left ventricle and systemic circulation, it may not necessarily be the case in the pulmonary circulation. More recently, we have shown that the geometry of the main pulmonary artery does not change in a manner predicted by haemodynamic theory and may be due to direct ventricular-vascular interaction [19]. Pulmonary flow may be affected not only by the heart, but also by movement of the lungs. Over 50 yrs ago, MACKLIN [20] pointed out that the pulmonary vasculature could act as a pump. There is a contrasting effect

of lung volume on the extra-alveolar and the alveolar vessels. An increase in lung volume tends to increase the volume of the extra-alveolar vessels and decrease the volume of the alveolar vessels [21]. As a result, blood can be pumped through the lungs by a milking action due to the cyclical changes of lung volume. Backflow is prevented by the pulmonary and mitral valves. If the system is not passive, then it could be anticipated that impedance would not be time invariant but would alter during the respiratory cycle.

Experiments in our laboratory have indicated that there are, indeed, changes in pulmonary arterial input impedance during the respiratory cycle [22–24]. Although this open-chest preparation is quite different from spontaneous breathing (the respiratory cycle can be controlled accurately) it is easier to ascertain the pressures imposed on the lung and the pulmonary vasculature and allows the use of accurate probes to measure flow instantaneously. In contrast, CASTIGLIONI *et al.* [18] found no significant changes of impedance during the respiratory cycle. They used velocity tipped catheters in the closed-chest animal as a surrogate for flow, and assumed that the velocity profile across the main pulmonary artery is uniform or that the catheter remains in the same site within the velocity profile throughout the respiratory cycle. In light of the negative result, it would seem that this issue is not a major concern. Current technology permits the possibility of evaluating the velocity profile across the entire vessel [25]. Of greater importance is the relatively poor signal-to-noise ratio of the velocity probe, which may have resulted in a type 2 error (no statistical difference when one actually exists). Another possibility of a type 2 error is that impedance was measured only at three specific points in the respiratory cycle. Ideally, a measure of impedance throughout the respiratory cycle is needed to ensure that differences are not being missed because the sampling intervals are suboptimal. Calculation of impedance throughout the respiratory cycle by the classic Fourier analysis is not possible because of limitations inherent in that approach.

Calculation of impedance

As with any physiological measurement, impedance has a number of caveats that require attention to obtain accurate measurements. Firstly, pressure and flow need to be measured at the same site. If this ideal is not possible, the sites of measurement need to be very close to each other and appropriate corrections applied. Secondly, corrections need to be made for the frequency response of the equipment used to measure and record pressure and flow. Thirdly, attention needs to be given to period of data collection, sampling frequency and analysis. Detailed accounts of these problems are readily available [7], but the analytical methods used have tended to lag behind more recent advances in this area which have used, primarily, Fourier analysis.

Fourier analysis was developed after the Napoleonic wars (1822). The bicycle was invented during this period by Kirkpatrick Macmillan in 1839. Like the bicycle, Fourier analysis has its place because it is easy to use and its limitations are well-known. A major limitation

is that it assumes that the data have no beginning or end. If the data are collected over a long period of many cardiac cycles with respiration suspended, this requirement might be satisfied. The fact that single cardiac samples are needed gives rise to difficulties because the beginning and end of each cycle may differ. Fourier analysis causes the appearance of high frequency waves to simulate this abrupt change. As a result, systematic errors can occur, particularly in the measurement of characteristic impedance.

To circumvent the limitations of Fourier analysis, three approaches can be made: either avoid the frequency domain and remain in the time domain, use more modern methods of frequency analysis that either avoid Fourier analysis or work around its deficiencies. To avoid the frequency domain, we used a lumped parameter model with time varying parameter values in the time domain. Parameter values were altered iteratively to match the flow predicted from the model when the actual pressure wave was used as the input to the actual flow waves. A drawback to this approach is that impedance is not measured directly and the parameter values of the elements of the model are not independent of each other. The other approach is to use methods of frequency analysis that do not have the same limitations as Fourier analysis. For example, the maximum entropy method based on autoregression does not require long data records and has been used for earthquake analysis [26]. It assumes only that the system is causal: that the output of the system is dependent on present and past values at the input. We elected to use another approach to this problem that still uses Fourier analysis but decomposes each cardiac cycle into a series of transient wavelets [24]. The development of the new methods remove some of the difficulties that arise with classic Fourier analysis, and are likely to be used increasingly as investigators become more familiar with their application.

Summary

With the widespread availability of computers and software, the mathematical and logistical difficulties that prevented their application in the past are being removed and will enhance investigation in this field. The data available indicate that there is a strong likelihood that impedance properties of the pulmonary circulation play an important role in pathophysiology. This conclusion is based, to a large extent, on haemodynamic theory and *in vitro* experimental data. Nevertheless, there are some *in vivo* experiments and clinical observations which support the hypothesis that the mechanical properties of the proximal arteries are important for right ventricular performance.

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