A step towards clinically applicable non-invasive coronary wave intensity analysis

Joseph J. Smolich, Jonathan P. Mynard

Heart Research, Clinical Sciences, Murdoch Childrens Research Institute and Department of Paediatrics, University of Melbourne

The mechanisms underlying a striking diastolic predominance of left ventricular coronary arterial blood flow have been the subject of intensive investigation for many years, starting with the first reliable measurements of phasic coronary arterial flow by Gregg and Green in 1940 (9). Subsequent detailed and elegant experimental studies (3, 20, 23-25) have shown that an increased coronary perfusion pressure during systole is counteracted by a rise in intramyocardial pressure which not only throttles, but actively pumps, blood out of the coronary microcirculation. With ventricular relaxation, perfusion pressure decreases but the accompanying lower extravascular compression results in a prominent diastolic surge of coronary flow.

Until the relatively recent introduction of wave intensity analysis (18, 19), however, there was no straightforward method for quantifying the specific upstream and downstream forces contributing to the complex morphology of coronary arterial flow waveforms. Performed in the time-domain, this analysis quantifies pressure-velocity waves that give rise to instantaneous changes in local flow and pressure (17). Wave intensity is calculated as the product of blood pressure and velocity time-derivatives (i.e. dP/dt × dU/dt) and can distinguish between waves propagating in a forward (positive intensity, by convention) or backward direction (negative intensity), waves that have pressure-increasing or pressure-decreasing effects (compression and decompression waves respectively), and waves that accelerate or decelerate flow. Four possible wave types exist: 1) forward-running compression waves that increase pressure and velocity, 2) forward-running decompression waves that decrease pressure and velocity, 3) backward-running compression waves that increase pressure but decrease velocity, and 4) backward-running decompression waves that decrease...
pressure but increase velocity. Identifying such waves and studying their sequence and magnitude throughout the cardiac cycle can provide a wealth of information regarding physiological mechanisms underlying measured pressure and flow/velocity signals (1, 17, 21, 22).

Characterization of coronary arterial flow patterns using wave intensity analysis was first performed in anesthetized dogs by Sun et al (27), via passage into the circumflex artery of a thin micromanometer-tipped catheter to measure high-fidelity pressure and a guidewire with a Doppler sensor mounted on its tip to obtain velocity. An important finding arising from initial studies was that backward-running compression waves, generated within the myocardium during the isovolumic contraction and early ejection periods, were key actuators of systolic flow impediment, as they countered the forward flow-promoting effects of an aortic forward-running compression wave generated in the early phase of ventricular ejection (26, 27).

Coronary wave intensity analysis was subsequently extended to the clinical sphere by Davies et al (6), using Doppler and high-fidelity pressure sensors mounted singly or in combination on guidewires that were inserted into a coronary artery during cardiac catheterization. This and subsequent studies suggested that a backward decompression wave, which was a manifestation of distal suction generated by ventricular relaxation and untwisting, was the dominant wave responsible for the surge in blood flow that occurred while blood pressure was falling in early diastole (6, 10). Moreover, this wave appeared to have considerable clinical significance, as its magnitude was reduced in hypertension-related left ventricular hypertrophy in proportion to the degree of hypertrophy (6), and increased with elevations in coronary flow that occurred with rises in heart rate during exercise (13) or after cardiac resynchronization therapy in patients with heart failure (11). Furthermore, the amplitude of this wave was not only reduced in proportion to the extent of myocardial infarction in acute coronary syndromes, but was also predictive of myocardial recovery in the territory of the infarct-related artery (8).

A major factor limiting wider clinical use of coronary wave intensity analysis to date, however, has been the need to acquire blood pressure and velocity measurements invasively
during cardiac catheterization. In this issue of the *American Journal of Physiology Heart and Circulatory Physiology*, Broyd et al (2) describe a novel technique for obtaining coronary wave intensity non-invasively in humans, with blood velocity measured in the left anterior descending coronary artery via pulsed wave Doppler using a clinical echocardiography machine, and central aortic blood pressure derived with a Pulsecor cuff-based brachial blood pressure device. Two types of validation were performed. The first was a comparison with coronary wave intensity profiles generated from high-fidelity coronary arterial pressure and velocity waveforms obtained invasively during cardiac catheterization. This indicated that the magnitudes of non-invasive and invasive backward decompression waves were similar and exhibited significant concordance, while other waves were substantially smaller non-invasively than invasively, with no significant concordance. The second validation was to demonstrate that the non-invasive approach was able to detect expected rises in the magnitude of the backward decompression wave during semi-recumbent exercise on an ergometer bike.

This study represents a significant step towards a more readily accessible clinical means of evaluating mechanisms underlying impaired or disturbed myocardial perfusion, and post-therapeutic changes in this perfusion. However, the proposed method for non-invasive coronary wave intensity relies on a number of assumptions. For example, use of central aortic blood pressure as a surrogate of coronary arterial blood pressure in the calculation of wave intensity is generally a reasonable assumption, as pressure in normal epicardial coronary arteries closely resembles that of the proximal aorta (7, 27). However, because substantial pressure loss may occur along the course of these arteries in the presence of diffuse atherosclerosis (7), the resultant aorto-coronary pressure difference may introduce error into the estimate of dP/dt, and thus calculation of coronary wave intensity. The clinical settings where it is appropriate (or more importantly, inappropriate) to use central aortic blood pressure as a surrogate for coronary arterial blood pressure therefore need to be clearly defined.

The assumption that the backward decompression wave (the sole wave showing agreement between invasive and non-invasive approaches) is the most clinically important
wave for myocardial perfusion holds true in many settings (4, 6, 8, 11, 13). However, recent evidence points to substantial increases in not only the backward decompression wave, but also the early-systolic forward compression wave, during improved coronary perfusion occurring with endocardial pacing in cardiac resynchronization therapy (4) or after stenting of a coronary artery stenosis (15). Thus, the approach of (2) may not provide a complete picture of coronary wave dynamics if multiple wave mechanisms contribute to enhanced coronary flow after therapeutic interventions.

Finally, while a clear advantage of the Pulsecor device is that central aortic pressure can be obtained non-invasively at the same time as coronary Doppler velocity profiles are being acquired, prior studies have shown that this device does not provide a high-fidelity representation of the invasively-measured blood pressure waveform, as peak systolic pressure is lower and diastolic pressure higher (5, 12, 14, 16), while waveform features are smoothed (12, 16). The Pulsecor device thus yields an attenuated $dP/dt$ waveform, consistent with the finding that the intensity of coronary forward compression and decompression waves was smaller non-invasively than invasively. However, that the backward decompression wave was of similar magnitude non-invasively and invasively (2) suggests that an attenuated Pulsecor-derived $dP/dt$ was offset by a near-equal amplification of $dU/dt$ calculated from Doppler during the period of the backward decompression wave. Why such a fortuitous ‘aligning of the stars’ occurred for the backward decompression wave (but not the forward decompression wave occurring in the same time window) is unclear and needs to be clarified.

The clinical value and utility of non-invasive coronary wave intensity will be greatest if the method used to derive it is accurate (i.e. qualitatively and quantitatively reproduces wave intensity waveforms obtained invasively), robust (i.e. validly applicable in a wide range of clinical settings) and demonstrates good reproducibility between different investigators and centers. Optimizing methodological aspects of non-invasive coronary wave intensity analysis is thus an important and essential goal, as an accurate and robust technique would be an invaluable asset in numerous clinical settings, many of which have been identified in (2). These include 1) study of patients with cardiac disease in whom cardiac catheterization is not
required or cannot be justified, 2) detailed assessment of coronary blood flow effects of cardiovascular therapies in population studies, 3) follow-up of patients who have undergone an interventional cardiology procedure, 4) monitoring the progression of cardiac disease to optimize the timing of an interventional procedure, and 5) incorporation of the technique into screening programs for identifying patients at heightened risk of future cardiovascular events.

Broyd et al (2) are to be complimented for paving the way towards practical and clinically applicable non-invasive coronary wave intensity analysis. The numerous potential benefits of this analysis for clinical practice and research will undoubtedly provide considerable impetus for further studies directed towards optimizing the methodology of the technique.

**Source of funding**

This work was supported by the Victorian Government’s Operational Infrastructure Support Program. JPM was supported by a CJ Martin Early Career Research Fellowship from the National Health and Medical Research Council of Australia.

**References**


25. **Spaan JA, Breuls NP, and Laird JD.** Forward coronary flow normally seen in systole is the result of both forward and concealed back flow. *Basic Res Cardiol* 76: 582-586, 1981.
