Chapter 2.2

Non-invasive assessment of arterial pressure, cardiac stroke volume and central blood volume

For a better understanding of the cardiovascular dynamics during orthostatic stress in humans a continuous recording of blood pressure, cardiac stroke volume (SV) and changes in central blood volume (CBV) is required because events proceed rapidly. Non-invasive recordings are preferable since the invasive recording procedures itself may promote neurally mediated syncope. In this chapter we describe how blood pressure can be measured non-invasively by a continuous recording of finger blood pressure. The principle of and relation to intra-arterial pressure is described. Application of pulse wave analysis to the arterial finger pressure offers a non-invasive and continuous recording of stroke volume. The Modelflow method computes a flow wave from the arterial pressure wave that is integrated to obtain the SV of the heart. We describe in this chapter the theoretical and physiological background of the Modelflow method and how thoracic impedance can be used as a non-invasive index of changes in CBV.

Non-invasive finger blood pressure

Finapres principle

For a continuous measure of blood pressure, cannulation of an artery was necessary until the early 1980s when two devices, the “Finapres” and “Portapres” were developed by Wesseling et al. (1995) based on the volume-clamp method introduced by the Czech physiologist Peñáz (1973). By doing so, continuous non-invasive measurement of arterial pressure was introduced both for research purposes and clinical medicine (23, 105). Finger blood pressure is measured non-invasively using the Finapres (FINger Arterial PRESsure) principle (105). From the finger pressure waveform, heart beats are detected and systolic, diastolic and mean pressure and pulse rate are output in a beat-to-beat mode. Blood pressure measurement devices based on the Finapres principle use an inflatable finger cuff which comprises an infrared plethysmograph and a small box attached to the wrist enclosing a fast servo-controlled pressurising system for the continuous adjustment of cuff pressure according to changes in the plethysmographic output (Figure 1). The cuff and wrist-box are connected to a main unit which holds the air pump, electronics and a computer.
Arterial pressure in the finger is measured making use of the volume-clamp method (203). The method is based on the development of the dynamic (pulsatile) unloading of the finger arterial walls using an inflatable finger cuff with a built-in photo-electric plethysmograph (105, 301). In this method the diameter of an artery under a cuff wrapped around the finger is kept constant (clamped) at a certain diameter, the “set-point”, in spite of the changes in arterial pressure during each heart beat. Changes in diameter are detected by means of an infrared photo-plethysmograph built into a finger cuff. If during systole an increase is detected in arterial diameter the finger cuff pressure is immediately increased by a rapid servo-controller system to prevent the diameter change. A fast pneumatic servo system and a dynamic servo setpoint adjuster assure arterial unloading at zero transmural pressure and consequent full transmission of arterial pressure to cuff air pressure (105, 203, 300). To fully collapse the finger artery requires a cuff pressure larger than the finger intra-arterial pressure. At zero transmural pressure the artery is not collapsed (unstressed arteries still have \( \approx \frac{1}{3} \) or \( \frac{1}{2} \) their original cross-sectional area and volume) but “unloaded”, that is, the arterial walls are held at zero transmural pressure which corresponds with their unstressed diameter (105, 301). As a result, finger cuff pressure equals intra-arterial pressure when the volume-clamp method is active at the proper unloaded diameter of the finger artery. Defining the correct unloaded diameter of a finger artery is not straightforward. The unloaded diameter is close to the average diameter at a pressure where the amplitude of the pulsations in the plethysmogram is largest. Changes in stress and tone of smooth muscle in the arterial wall and in hematocrit affect the unloaded diameter. Therefore, the unloaded diameter is usually not constant during a measurement and has to be verified at intervals.
An important feature is an expert system (Physiocal®) consisting of a dynamic servo setpoint adjuster, it defines and maintains the diameter at which the finger artery is clamped (301). The Physiocal algorithm includes the search procedure and criterion for the automated determination and periodic adjustment of the arterial unloaded volume. It explores part of the pressure-diameter relation by analysing the plethysmogram at a number of steady pressure levels, and is able to track the unloaded diameter of a finger artery even if smooth muscle tone changes. To adjust the correct unloaded diameter of the finger artery based on the signal from the finger cuff plethysmograph, cuff pressure is kept constant at regular intervals (23). A consequence is that the measurement of blood pressure is temporarily interrupted. Activation of the Physiocal procedure is considered mandatory to maintain accuracy during measurements (304).

**Finger arterial pressure vs intra-arterial pressure**
In a review of 43 studies comprising a total of 1031 subjects the accuracy of finger pressure vs. intra-arterial pressure was studied (105). The weighted accuracy for systolic pressure was \(-0.8 \pm 11.7\) mmHg (range \(-48\) to 30 mmHg) for mean pressure \(-1.6 \pm 8.5\) mmHg (\(-20\) to 19 mmHg) and for diastolic pressure \(-1.6 \pm 7.7\) mmHg (\(-13\) to 25 mmHg). This, precision is too low for systolic and mean pressures and does not meet the acceptable limit of the 8 mmHg SD of the American Association for the Advancement of Medical Instrumentation (AAMI) recommendations. Although for diastolic pressure the accuracy and precision values are within the limits the overall performance does not permit finger arterial pressure measurements for assessment of absolute blood pressure levels in individual patients (105). Continuous finger arterial pressure reliably follows intra-arterial pressure under a variety of circumstances (Figure 2) (103, 104, 199).

Reconstruction of brachial arterial pressure from finger arterial pressure, as implemented in the Finometer, reduces the pressure differences and thereby meets the AAMI criteria (24, 27, 82, 243). In conclusion finger arterial pressure is in general a reliable alternative for intra-arterial measurements method for the assessment of beat-to-beat changes in arterial pressure (105). Especially in clinical practice for the assessment of blood pressure regulation by autonomic function testing, orthostatic hypotension and syncope it has established its place, where application of intravascular instrumentation may affect these responses.
Figure 2.
Original intra-arterial (IAP) and non-invasive finger arterial pressure (FINAP) registration during active standing in 23-year old male subject. Open bar indicates period of light-headedness, sweating and “not feeling well”. Arrow indicate lying down. IAP is tracked by FINAP for all levels of arterial pressure including impending vasovagal syncope. Note physiocals in FINAP registration (small arrows).
Non-invasive cardiac stroke volume

The Modelflow method

The Modelflow method computes an aortic flow waveform from a peripheral arterial pressure signal. It uses a non-linear three-element model of the aortic input impedance. The hemodynamic behaviour of the aorta in opposing ejection of blood from the left ventricle has been described by a three-element model of the arterial input impedance (34, 39, 278). The three elements correspond to the characteristic impedance of the aorta (the opposition to the pulsatile flow from the left ventricle), the total arterial compliance (opposition to an increase in aortic blood volume), and a peripheral vascular resistance.

The first element in the model is the aortic characteristic impedance ($Z_0$); it describes the relation between pulsatile flow and pressure at the entrance of the aorta. The rise in pressure will depend on the instantaneous flow, on the cross-sectional area of the aorta and on the aortic compliance. Hence, $Z_0$ represents the aortic opposition to pulsatile inflow from the contracting left ventricle. $Z_0$ has the dimension of pressure divided by flow. The second model element is the arterial compliance ($C_w$); it describes how much the aortic pressure rises for a given volume of blood and represents the aortic opposition to an increase in blood volume. Compliance is defined as a change in volume ($dV$) divided by a change in pressure ($dP$). The third element in the model is peripheral vascular resistance ($R_p$). $R_p$ is a measure for the ease of constant blood drainage from the Windkessel into the peripheral vascular beds. $R_p$ is defined as the ratio of mean pressure to mean flow, and is not a major determinant of systolic inflow (303).

The first two elements of the model, $Z_0$ and $C_w$, are thus dependent on the elastic properties of the aorta. In earlier models of the arterial system, changes in aortic volume were assumed to be linearly related to the aortic pressure (34, 39, 278). From Langewouters’ studies on the elastic properties of human thoracic and abdominal aortas it was found that the aortic properties vary in a non-linear manner with distending pressure. The change in thoracic aortic cross-sectional areas was described as an arctangent function of transmural pressure (138).

The model uses this property and is non-linear thus mimicking the hemodynamic behaviour of the aorta in detail (Figure 3). It computes two of the model parameters, $Z_0$ and $C_w$, making use of a built-in database of arctangent area-pressure relationships given subject gender and age as input (138). Instantaneous values of $C_w$ and $Z_0$ are used in the model simulation resulting in the computation of an aortic flow waveform. $R_p$ as the third element is calculated each beat by the model simulation and updated.
Thus the Modelflow method computes SV from the arterial pressure wave with continuous non-linear corrections for variations in aortic diameter, compliance and impedance during the arterial pulsation (303). Integrating the aortic flow waveform per beat provides left ventricular SV. Cardiac output (CO) is computed by multiplying SV and heart rate. Only if absolute values for SV are requested, Modelflow SV needs calibration against a "golden" standard, e.g. thermodilution or inert gas rebreathing. Otherwise, SV can be expressed as changes from control with the same precision in SV tracking.

Aortic pressure, theoretically preferred as model input, is not routinely available in clinical practice, and therefore a peripheral arterial pressure is used. Peripherally measured arterial pressure is, however, distorted in comparison with aortic pressure. Although the calculated flow waveform is therefore distorted also, the area under the flow wave which equals the SV, was shown to be affected only minimally by such distortion (303). The effect is that peripheral arterial pressures, including non-invasive finger arterial pressure, appear sufficiently close to aortic pressure to be applied in the model and still compute SV reliably (119, 303). Correct tracking of intra-arterial pressure by non-invasive finger arterial pressure is a prerequisite for such a proper computation of model simulated SV as demonstrated in healthy subjects (60, 118, 209) and in patients with coexisting hypertension and vascular disease (26).

The cross-sectional area of the aorta is increased in arteriosclerotic aortas with an increased stiffness. The net effect of both increments is that they compensate for each in their effects on compliance, such that the compliant behaviour of an arteriosclerotic is almost identical with that of a non-sclerotic aorta over the physiological pressure range (139). Studies in patients
with cardiovascular disease demonstrated that Modelflow accurately track changes in CO in both direction and degree when compared with thermodilution-based estimates (119, 240, 303).

**Thoracic impedance as a non-invasive index of the central blood volume**

As most methods for measuring CBV require extensive apparatus, it is useful to apply Ohm’s law to the body and evaluate volume directly (186). Such assessment of the volume of the body, and more specifically of the volume contained within the central vessels and the heart, is readily available with the use of either band or ECG electrodes. Given a constant field, the current depends on the resistance it is exposed to (246). For assessment of CBV, the thoracic region is of interest. Transthoracic electrical impedance, or its reciprocal value admittance, correlates to changes in central blood volume (41, 54, 167, 207, 211, 246). Electrical impedance is based on the principal that conductivity is a basic property of biological tissue. Accordingly, alterations of thoracic fluid volume must be followed by alterations in impedance (186, 242). Therefore a decrease in CBV results in a reduction in conductance and an increase in impedance. To evaluate the volume within the thoracic region, including the central vessels and the heart two electrodes are placed on the sternocleidomastoid muscle and two electrodes on the lower contralateral ribs in the midaxillary line (206, 246, 253). The outer two electrodes serve as current electrodes with a frequency of 100 kHz and are spaced 5 cm from the inner electrodes. The latter monitor changes in voltage (Figure 4).

![Figure 4](image-url)

*Figure 4.* Thoracic impedance as a non-invasive index of changes in central blood volume. Two electrodes are placed on the sternocleidomastoid muscle and two electrodes on the lower contralateral ribs in the midaxillary line. The outer two electrodes serve as current electrodes with a frequency of 100 kHz and are spaced 5 cm from the inner electrodes. The latter monitor changes in voltage.
Impedance differs considerably between subjects (242, 246). Therefore comparison of sequential measurements is feasible only in one and the same subject. This difference is probably due to the fact that basic electrical impedance depends on the electrical conductivity of the thorax which in turn is determined by its anatomical structure. The result is that individual differences in the architecture and dimensions of the chest affect impedance (140, 242, 246). Impedance measurements may be influenced by electrode position and replacement, tissue movement between the recording electrodes and body position (125, 167, 211, 242). In severe respiratory failure there is no change in electrical impedance due to fixation of fluid within the lung (242). Emphysema results in higher electrical impedance due to the large amount of air in the chest which is a poor conductor (125). A direct evaluation of the electrical properties of the thorax is made during thoracocentesis where the change in fluid volume is known. The correlation coefficient between changes in thoracic impedance and the amount of fluid withdrawn is satisfactory ($r=0.97$) (208). Measurement of central blood volume by thoracic impedance show high correlations, for instance with the volume deficit during haemorrhage and following reperfusion in the pig (130), and allows for the prediction of hypotension when the central blood volume is reduced, for instance during head-up tilt (167, 206), lower body negative pressure (41), syncope (189) and hemodialysis (42).