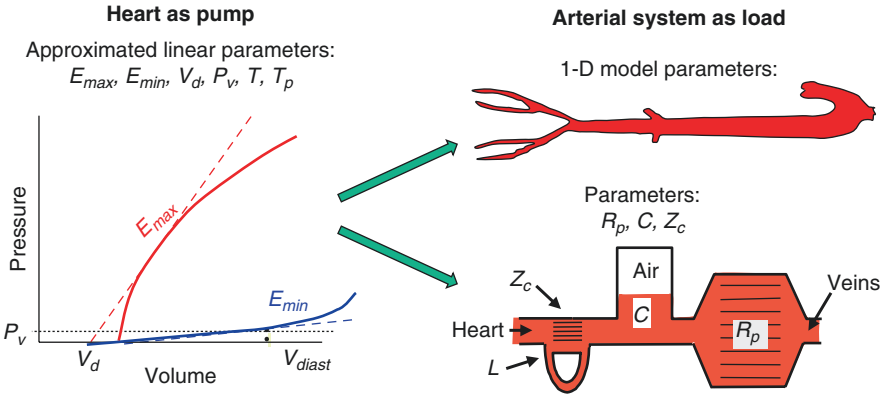
Chapter 31
Determinants of Pressure and Flow



Pressure and flow result from the interaction of the heart, the pump, and the arterial system, the load. Understanding the quantitative contribution of the heart and the arterial system to pressure and flow is important in the study of hypertension, cardiac failure and other cardiovascular diseases. The heart can be described on the basis of the pressure-volume relation, left, or from muscle properties. The arterial load, can be described by a Windkessel or 1-D model, right. A simple approach is to use the pressure-volume relation for the heart and the three-element Windkessel for the load. When we linearize the pressure volume relations the total number of parameters to describe cardiac pump function is 6, and for the Windkessel it is 3. Using this limited number of parameters, their quantitative contribution to systolic and diastolic pressure and Stroke Volume can be worked out. Dimensional analysis shows that $R_p \cdot C/T$ and $C \cdot E_{max}$ are parameters that couple the heart and load, and they play an important role in pressure and Stroke Volume. The normalized $E_N(t_N)$ curve describing, the heart and the normalized input impedance, describing the arterial system, are similar in different mammals, explaining the similarities of pressure and flow wave shapes in mammals

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31.1 Description

Blood pressure and Cardiac Output result from the interaction of the heart and arterial load. It is also known that changes in cardiac and arterial properties are related as has been shown in aging [1]. However, quantitative information about the contribution of heart and arterial load to pressure and flow under different physiological conditions and during various diseased states is limited. To quantitatively analyze the cardiac and arterial contributions to systolic and diastolic pressure and Stroke Volume models have been developed describing the cardiac pump and the arterial load. Cardiac models are mostly based on the time-varying elastance concept (Chap. 14), and the requires only a limited number of parameters, the diastolic and systolic pressure volume relations, E_{max}, E_{min}, (model terms for linearized E_{es} and E_{ed}, Chap. 14), and the time varying function $E(t)$, which, when normalized in magnitude and timing of the peak, T_p, can be written as $E_N(t_N)$ [2]. This general approach is used by several authors, with differences in the details [3–6]. Other heart models, based on strain modeling, have been used as well [7, 8].

The arterial system can be described by the three-element Windkessel model (Chap. 25) [3] or by 1-D arterial models [4–6]. Below we discuss a model based on the time-varying elastance concept and the three-element Windkessel, where the number of parameters is limited.

31.1.1 Dimensional Analysis

Dimensional analysis, or the concept of similitude, is a powerful method to systematically derive relations of a system and offers two major advantages [9]. First, it reduces the number of variables, and second, it groups the cardiac and arterial parameters in dimensionless terms, which are automatically scaled to Heart Rate and body size. This will be a particularly important issue when we discuss comparative physiology (Chap. 32). The parameters that describe the heart as a pump, including venous filling pressure are E_{max}, E_{min}, V_d, T_p, and venous filling pressure, P_v, and heart period (1/Heart Rate), T. The arterial load is mimicked by the three-element Windkessel, with parameters Z_c, R_p and C (Chap. 25). The total number of parameters is 9, namely 6 for the heart and 3 for the arterial system. Figure in the Box and Fig. 31.1.

The dependent variables systolic and diastolic pressure (P_s and P_d) and Stroke Volume, SV, can be written as a function of these nine cardiac and arterial parameters. Dimensional analysis implies that when the variables and the parameters are non-dimensionalized, the number of non-dimensional parameters can be reduced by three. Three is the number of reference dimensions (time, force and length) describing the variables [9]. Thus six non-dimensional parameters remain. An intelligent choice is the following [3]:

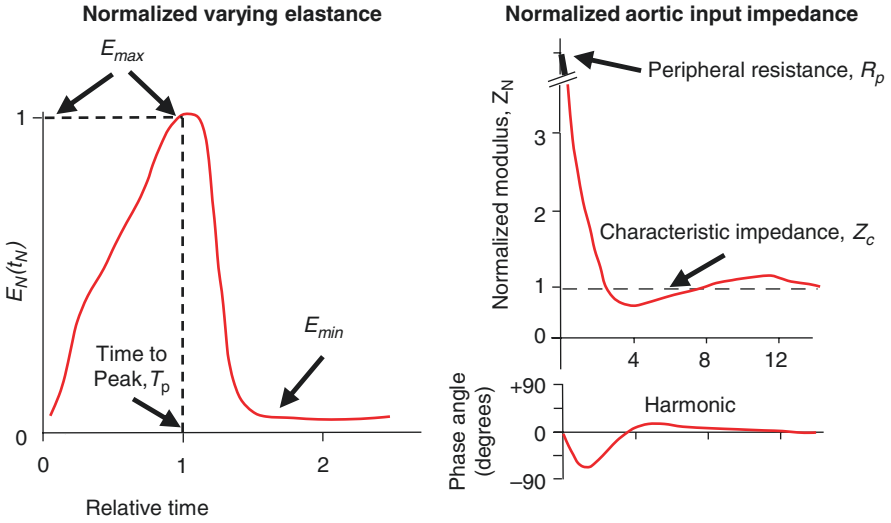

Fig. 31.1 The normalized elastance curve, $E_N(t_N)$, and the normalized input impedance, Z_{in}/Z_c, are independent of animal size, resulting in similar wave shapes of aortic pressure and flow in mammals, and with pressures even having the same in magnitude

$$P_s / P_v = \Phi_1\left(Z_c / R_p, R_pC / T, CE_{\min}, E_{\max} / E_{\min}, E_{\min}V_d / P_v, T_p / T\right)$$

$$P_d / P_v = \Phi_2\left(Z_c / R_p, R_pC / T, CE_{\min}, E_{\max} / E_{\min}, E_{\min}V_d / P_v, T_p / T\right)$$

$$SV \cdot E_{\min} / P_v = \Phi_3\left(Z_c / R_p, R_pC / T, CE_{\min}, E_{\max} / E_{\min}, E_{\min}V_d / P_v, T_p / T\right)$$

The next step is to find the dependence of the non-dimensional variables on the non-dimensional parameters. The normalized $E_N(t_N)$ (Fig. 31.1) is fixed [2], and the contribution of T_p/T to P_s/P_v, P_d/P_v, and $SV{\cdot}E_{min}/P_v$ is small and can be neglected. It turns out experimentally that the parameter $E_{min}{\cdot}V_d/P_v$ does not contribute to P_s/P_v and P_d/P_v; that Z_c/R_p does not determine P_d/P_v and SV/V_d; while E_{max}/E_{min} does not determine $SV{\cdot}E_{min}/P_v$. The contribution of Z_c/R_p to P_s/P_v turns out to be small and is neglected as well [3]. The relations then can be simplified to:

$$P_s / P_v \approx \Phi_1\left(R_pC / T, CE_{\min}, E_{\max} / E_{\min}\right)$$

$$P_d / P_v \approx \Phi_2\left(R_pC / T, CE_{\min}, E_{\max} / E_{\min}\right)$$

$$SV \cdot E_{\min} / P_v \approx \Phi_3\left(R_pC / T, CE_{\min}, E_{\min} \cdot V_d / P_v\right)$$

In all non-dimensional variables we see that the parameters R_pC/T, (arterial time constant and heart period) and $C{\cdot}E_{min}$ (arterial compliance i.e. 1/arterial stiffness and

ventricular diastolic elastance) appear. We call them ventriculo-arterial coupling parameters. This emphasizes the fact that the interaction of pump and load determines pressure and flow.

The Frank-Starling mechanism also emerges from the above equations. Leaving all parameters the same, the pressures are simply proportional to venous pressure, P_v. Stroke Volume is also related to filling pressure, but in a more complex way. In reality the diastolic Pressure-Volume relation is not straight and therefore the effect of filling is in reality more complex than shown here.

The pressures also depend on E_{max}/E_{min} a measure of contractility of the heart. The Stroke Volume is also described by the rather complex term $E_{min} \cdot V_d / P_v$, which is related to diastolic ventricular filling and can be written as $V_d/(V_{diast} - V_d)$, with V_{diast} end-diastolic ventricular volume.

On the basis of the results obtained with the dimensional analysis we can perform a sensitivity analysis of pressure and Stroke Volume to individual parameters. The results are given in the Table 31.1.

We note that the normalized parameters R_pC/T, CE_{min}, E_{max}/E_{min} do not depend on body size, (Chap. 32) so that for similar venous pressures, aortic systolic and diastolic pressures will be similar in all mammals. Stroke Volume does depend on body size.

The wave shapes of pressure and flow result from the shape of the $E(t)$-curve describing the pump and the input impedance describing the arterial load, Z_{in}. When both are normalized, $E_N(t_N)$ and $Z_{in,N}$ [10] they are independent of body size, explaining why aortic pressure and flow have similar shapes in mammals (Chap. 32).

31.2 Physiological and Clinical Relevance

The analysis shows in quantitative terms the contribution of cardiac and arterial parameters to blood pressure and Stroke Volume. It may be seen from Table 31.1 that resistance has a much stronger effect on systolic blood pressure than compliance has. However, changes in compliance are often considerably larger than resistance changes. For instance, between the ages of 20 and 80 years PWV may increase a

Table 31.1 Quantitative contribution of heart and arterial system to pressure and Stroke Volume

Parameter	$P_{systole}$	$P_{diastole}$	SV
Z_c	+9	0	0
R_p	+41	+90	−28
C	−10	+22	+5
T	−50	−90	+28
E_{max}	+40	+32	+33
E_{min}	−100	−100	−100
P_v	+100	+100	+100

Percent changes in systolic, diastolic pressure and Stroke Volume, resulting from a 100% increase in a single cardiac or arterial parameter. The minus sign indicates a decrease with an increase in a parameter. Thus, a 20% change in heart period (T) results in a – (20/100)·50 = −10% change in systolic pressure and a −18% change in diastolic pressure

factor 2 (Fig. 21.5) implying a compliance decrease by a factor of 3–4, while the resistance increase is about 15%. Thus the decrease in compliance predicts an increase systolic blood pressure by 15%, while the age related resistance increase predicts a systolic pressure increase of slightly over 4%. This prediction is assuming no role of changes in cardiac properties (see below).

On the basis of the dimensionless parameters shown above it may be suggested that E_{max}/E_{min} is a better measure of contractility than E_{max} alone, because this ratio is size independent, while the E_{max} is depending on the ventricular volume.

The theoretical results can be compared with biological data. Experimental data [11] obtained from the isolated heart loaded with a Windkessel model indeed show that compliance changes alone have a small effect on systolic blood pressure and a larger effect on diastolic blood pressure (Chap. 25). When compliance is decreased *in vivo* (Chap. 11) other parameters also change and systolic pressure increases and diastolic pressure decreases [12]. The main difference between the *ex vivo* and *in vivo* results is the adaptation of the heart during the decrease in compliance. The *ex vivo* heart, was unchanged in terms of filling and contractility (Chap. 25), while *in vivo* the heart does adapt and Cardiac Output diminishes less than in the *ex vivo* situation (see Fig. 11.7, Chap. 11). Thus, the changed cardiac function *in vivo* has an effect on blood pressure.

31.2.1 Contribution of Arterial System and Heart in Systolic Hypertension

The contributions of both heart and arterial system to the increase in aortic pressure with age is shown in Fig. 31.2 [13]. In the literature it is well established that hypertension results in ventricular hypertrophy and therefore a higher E_{max} [1]. However, it is often not realized that cardiac hypertrophy causes changes in the properties of the cardiac pump such as increased wall thickness (i.e. increased E_{min} and E_{max}) and that these changes may, in turn, contribute to a further increase in blood pressure. Using the models, as given in the Box, the contributions of the heart and arterial system to systolic aortic pressure in four groups of hypertensive patients were calculated and the results are shown in Fig. 31.3 [14]. It may be seen that in concentric remodeling the increase in systolic blood pressure is mainly the result of the altered arterial system, while in eccentric hypertrophy the contribution to the increased systolic pressure is mainly the result of changed cardiac properties. This example therefore shows that both heart and arterial system need to be considered in hypertension research.

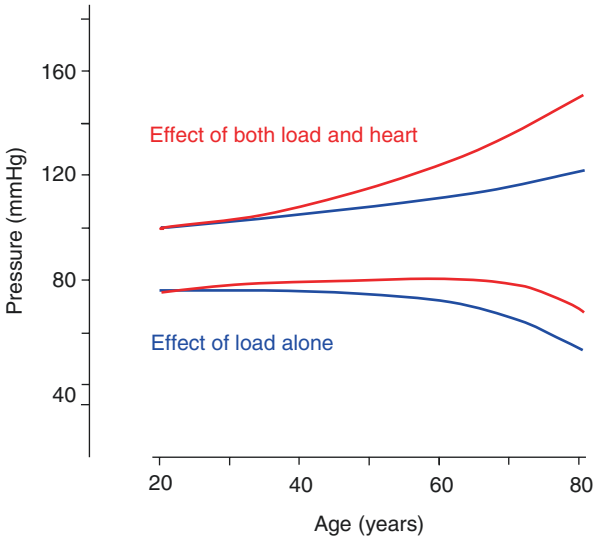

Fig. 31.2 The effect of aging on systolic and diastolic aortic pressure, resulting from arterial changes alone (blue) and from both arterial and cardiac changes (red). (Adapted from Ref. [13], used by permission)

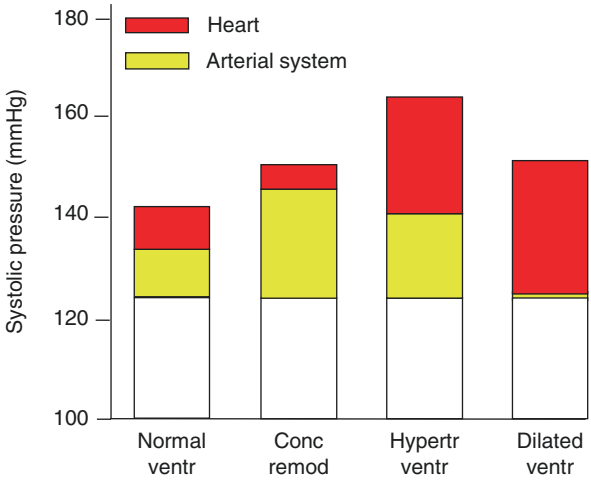

Fig. 31.3 Cardiac and arterial contributions to systolic pressure increase in four groups of hypertensive patients. Several stages in cardiac changes are depicted, (1) Normal ventricle; (2) Concentric remodeling; (3) Hypertrophied left ventricle; and (4) Dilated left ventricle. The white bars give the systolic pressure of the normal cardiovascular system. In concentric remodeling most of the systolic pressure increase results from the change in the arterial system (yellow) while the cardiac change has a small effect (red). When the ventricle is dilated in hypertension most of the pressure increase is caused by the heart. (Adapted from Ref. [14], by permission)

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