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Arterial Reservoir-Excess Pressure and Ventricular Work (Supplementary Material)

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1 The arterial network

We assume that the arterial network is made up of N vessels with a single inlet from the ventricle, denoted as 0, and K terminal vessels through which blood is conducted from the arterial system into the microcirculation (see Figure 1). Note that the network is not necessarily a simple bifurcating tree, but can contain loops. Also note that nonuniform vessels can be divided into segments that are effectively uniform, making the analysis applicable to realistic arterial networks.

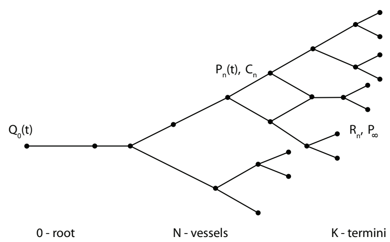

Fig. 1 Sketch of the arterial network. The network consists of N vessels, each of which has an average instantaneous pressure $P_n(t)$ and constant compliance C_n. The root of the network, denoted as 0, is connected to the ventricle which generates a volume flow rate $Q_0(t)$. There are K terminal vessels connected to the local microcirculation. The flow out of the terminal vessels is assumed to be resistive with resistance R_n and back pressure P_∞.

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2 Estimating the reservoir pressure

The lack of a general analytical solution for the reservoir pressure $\bar{P}$ defined by Eq. (7) is unfortunate. The existence of a unique solution is adequate for the calculus of variations analysis of the excess work, but there are many applications where a solution would be useful. We note, however, that a general solution of Eq. (7) would depend upon the compliances of all of the vessels $C_n,\ n \in N$ and the resistances of all of the terminal vessels $R_n,\ n \in K$; information that is clinically unavailable. It is, therefore, necessary to find a way of estimating $\bar{P}$ if the reservoir-excess pressure hypothesis is to be useful clinically.

To do this, we observe that the time that it takes for a wave to propagate through the arterial system is generally much less than the cardiac period T. For example, measurements in the human aorta show that the time it takes the initial compression wave to traverse the length of the aorta is $\sim 50\ ms$ whereas $T \sim 1\ s$. If τ_n is small compared to T we can use Taylor's theorem to expand $\bar{P}_n(t)$,

$$\bar{P}_n(t) \equiv \bar{P}(t-\tau_n) = \bar{P}(t) - \tau_n \frac{d\bar{P}(t)}{dt} + \mathcal{O}(\tau_n^2).$$

Substituting into equation (4), we obtain the linear ODE

$$\sum_{n\in N} C_n \Big(\frac{d\bar{P}(t)}{dt} - \tau_n \frac{d^2\bar{P}(t)}{dt^2} + \mathcal{O}(\tau_n^2) \Big) + \sum_{n\in K} \frac{\bar{P}(t) - P_\infty - \tau_n \frac{d\bar{P}(t)}{dt} + \mathcal{O}(\tau_n^2)}{R_n} = Q_0(t),$$

which, neglecting terms of $\mathcal{O}(\tau_n^1)$, reduces to the ODE

$$C\frac{d\bar{P}(t)}{dt} + \frac{\bar{P}(t) - P_\infty}{R} = Q_0(t),$$

where we have used the previously defined C and R for the net compliance and resistance of the arterial system. This is the classical Windkessel equation (2).

We see, therefore, that the solution to the Windkessel equation provides a first estimate to the reservoir pressure. This argument has been developed into an algorithm that can be used to estimate the reservoir pressure from a measured pressure waveform [1]. This algorithm has been used to calculate the reservoir pressures in Fig. 2.

Briefly, the algorithm is based on three assumptions: 1) that the reservoir pressure can be represented by an exponential fall-off during diastole, 2) the flow at the aortic root is proportional to the excess pressure there and 3) the arteries are well-matched for forward waves so that the excess pressure at the aortic root propagates without significant change to the more distal arteries. The first assumption follows from the solution of the global conservation equation during diastole when $Q_0 = 0$ and can be seen from the figure to be a good one in most cases, although more complex pressure waveforms are seen during

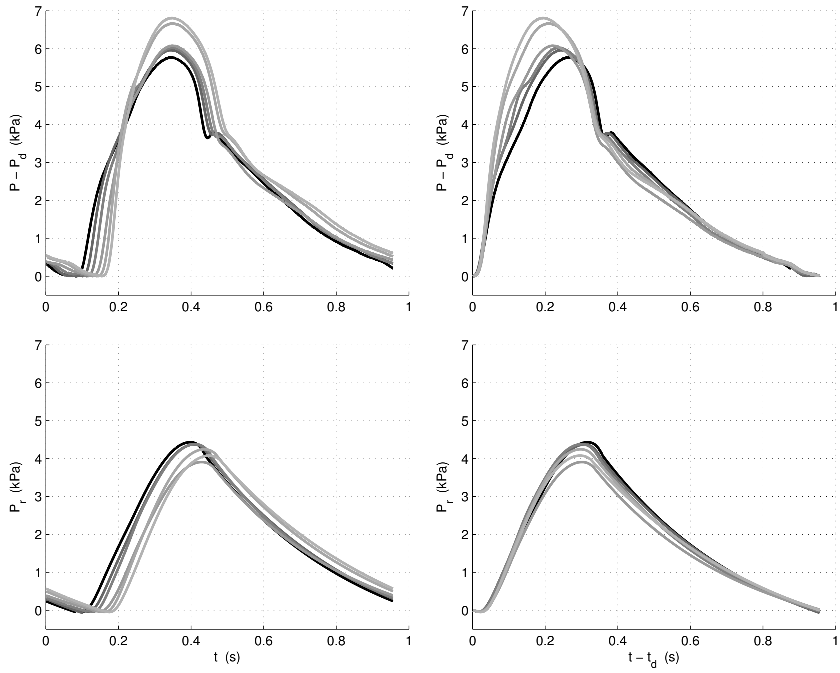

Fig. 2 Pressure measurements from 6 locations starting approximately 5 cm from the aortic valve (black curve) at intervals of 10 cm along the length of a normal human aorta (successively lighter gray curves). Upper left: the data plotted as a function of time relative to the peak of the R-wave of the simultaneously measured ECG. Lower left: The reservoir pressure calculated from each of the measured pressure waveforms plotted on the same time axis [1]. Upper right: the data shifted so that the end diastolic point (the time of minimum pressure, t_d) corresponds to $P = 0$ and $t = 0$. Lower right: the reservoir pressure plotted on the same axes. For ease of comparison, all pressures are shown relative to the diastolic pressure, P_d. Although the waveforms measured at the different sites are very different from each other, the reservoir pressure plotted relative to the foot of the measured pressure waveform is very similar.

diastole in some cases. The other assumptions are based on experimental observations reported in [1] and [2]. These assumptions require further testing, but the algorithm has proven to be robust and has given reasonable results when applied to clinically measured pressure waveforms.

3 Minimum excess work when $S \ll 1$

The nondimensional equation for the minimum excess work, Eq. (19), can be written in asymptotic form when $S = T_s/RC \ll 1$. For small times, the exponential terms can be expanded using $e^{\pm t} = 1 \pm t + \mathcal{O}(t^2)$. Thus, the indefinite integral in the first term can be written

$$\int_0^t \dot{v}(\gamma)e^{-\gamma}d\gamma = \int_0^t \dot{v}(\gamma)d\gamma - \int_0^t \gamma\dot{v}(\gamma)d\gamma + \dots = v(t) - \Big(tv(t) - \int_0^t v(\gamma)d\gamma\Big) + \dots$$

where the last equation follows from integration by parts and ... refers to terms of $\mathcal{O}(t^2)$. Using this, the first term on the rhs of Eq. (19) can be written

$$\int_0^S \dot{v}(t)e^t \int_0^t \dot{v}(\gamma)e^{-\gamma}d\gamma dt = \int_0^S \dot{v}(t)\big(1+t+\dots\big)\Big(v(t) - tv(t) + \int_0^t v(\gamma)d\gamma + \dots\Big)$$

$$= \int_0^S v(t)\dot{v}(t)dt + \int_0^S \dot{v}(t)\int_0^t v(\gamma)d\gamma dt + \dots = \tfrac{1}{2}\big(v(S)\big)^2 + v(S)\int_0^S v(\gamma)d\gamma - \int_0^S v^2(t)dt$$

$$= \tfrac{1}{2} + S\big(\langle v\rangle - \langle v^2\rangle\big) + \dots$$

where we have used integration by parts and $v(S) = 1$, which follows from the use of the stroke volume in the nondimensionalisation, and define the average over the time of systole $\langle\cdot\rangle = \frac{1}{S}\int_0^S \cdot \, dt$. The various factors in the second term on the rhs of Eq. (19) can similarly be written

$$\frac{e^{\kappa S}}{e^{\kappa S}-1} = \frac{1}{1-(1-\kappa S + \frac{1}{2}(\kappa S)^2 + \dots)} = \frac{1}{S}\left(\frac{1}{\kappa} + \frac{S}{2} + \dots\right)$$

$$\int_0^S \dot{v}(t)e^{-t}dt = \int_0^S \dot{v}(t)(1-t+\dots)dt = 1 - S\big(1-\langle v\rangle\big) + \dots$$

$$\int_0^S \dot{v}(t)e^t dt - 1 = \int_0^S \dot{v}(t)(1+t+\tfrac{1}{2}t^2+\dots)dt - 1 = S\Big(\big(1-\langle v\rangle\big) + S\big(\tfrac{1}{2}-m\big) + \dots\Big)$$

The term $m = \frac{\langle tv\rangle}{S}$ is the first moment of the ejected volume over the time of systole. Combining these results and neglecting terms of $\mathcal{O}(S^2)$, we have

$$\dot{w} = \frac{1}{2} + S\big(\langle v\rangle - \langle v^2\rangle\big) - \frac{1}{S}\left(\frac{1}{\kappa} + \frac{S}{2}\right)\Big(1 - S\big(1-\langle v\rangle\big)\Big)S\Big(\big(1-\langle v\rangle\big) + S\big(\frac{1}{2}-m\big)\Big) + \dots$$

$$= \left(\frac{1}{2} - \frac{1}{\kappa} + \frac{\langle v\rangle}{\kappa}\right) + S\left(-\frac{1}{2}\Big(1-\frac{1}{\kappa}\Big) + \Big(\frac{3}{2} - \frac{2}{\kappa}\Big)\langle v\rangle - \langle v^2\rangle + \frac{\langle v\rangle^2}{\kappa} + \frac{m}{\kappa}\right) + \dots$$

4 Minimum excess work when S is $\mathcal{O}(1)$

When S is not small, it is possible to solve Eq. (19) for a number of idealised volume flow rate functions $Q(t)$ to find the conditions for which $\hat{w} > 0$. Similarly, for any given $q(t)$ it is possible to determine if the excess work is positive by solving the equation, numerically if necessary. We have obtained general results for three idealised cases; constant flow, half-sinusoidal flow and a general triangular flow during systole. The nondimensional minimum excess work is given by Eq. (19)

$$\hat{w} = \int_0^S q(t)e^t \int_0^t q(\gamma)e^{-\gamma}d\gamma\, dt - \frac{e^{\kappa S}}{e^{\kappa S}-1}\int_0^S q(\gamma)e^{-\gamma}d\gamma\left(\int_0^S q(\sigma)e^{\sigma}d\sigma - 1\right).$$

Constant flow during systole

Assume the nondimensional volume flow rate is $q(t) = 1/S$ during systole, $0 \le t \le S$, and zero during diastole $S < t \le \kappa S$. The value of the constant flow rate follows because $\int_0^{\kappa S} q(t)dt = 1$ by our choice of scalings. Using

$$\int_0^S qe^t dt = \frac{1}{S}(e^S - 1), \quad \int_0^S qe^{-t}dt = \frac{1}{S}(1-e^{-S}) \quad \text{and}$$

$$\int_0^S q(t)e^t \int_0^t q(\gamma)e^{-\gamma}d\gamma dt = \frac{1}{S^2}(e^S - 1 - S),$$

we obtain

$$\begin{aligned}\hat{w} &= \frac{e^S-1}{S^2} - \frac{1}{S} - \frac{e^{\kappa S}(1-e^{-S})}{S(e^{\kappa S}-1)}\left(\frac{e^S-1}{S} - 1\right)\\ &= \frac{1}{S}\left(\frac{e^S-1}{S} - 1\right)\left(1 - \frac{e^{(\kappa-1)S}(e^S-1)}{(e^{\kappa S}-1}\right)\right).\end{aligned}$$

Looking at the two bracketed terms, using $\frac{e^S-1}{S} \ge 1$, we see that both brackets are greater or equal to zero and so we conclude that $\hat{w} \ge 0$ for constant flow during systole.

Half-sinusoidal flow during systole

A more realistic, but still very idealistic, volume flow waveform is a half-sinusoidal flow, $q(t) = \frac{\pi}{2S}\sin\left(\frac{\pi t}{S}\right)$ during systole $0 \le t \le S$ and zero during diastole $S < t \le \kappa S$. Again, the amplitude of the sinusoidal flow arises from the condition $\int_0^{\kappa S} q(t)dt = 1$ imposed by our choice of scalings. We can write the excess work

$$\hat{w} = I_3 - \frac{e^{\kappa S}I_2(I_1-1)}{e^{\kappa S}-1}$$

where

$$I_1 = \int_0^S q(t)e^t dt = \frac{\pi^2(e^S+1)}{2(S^2+\pi^2)},$$

$$I_2 = \int_0^S q(t)e^{-t}dt = \frac{\pi^2(e^S+1)}{2e^S(S^2+\pi^2)},$$

$$I_3 = \int_0^S q(t)e^{-t}\int_0^t q(\gamma)e^{\gamma}d\gamma dt = \frac{\pi^2}{8S} - \frac{\pi^4(1-e^{-S})}{2S^2(S^2+4\pi^2)}.$$

Again we see that $\hat{w} > 0$ for any half-sinusoidal ventricular flow rate.

Triangular flow during systole

Measured volume flow rates from the ventricle are generally skewed during systole. We explore the effect of skew by assuming that the flow is triangular with the peak velocity occurring at $t = U$, where $0 \leq U \leq S$ and $q(0) = 0$ and $q(S) = 0$. That is, when $U = 0$ the flow accelerates immediately to its maximum value at the start of systole and decreases linearly to zero. When $U = S$ the flow increases linearly throughout systole, reaching its peak at the end of systole when it decreases immediately to zero. Other values of U correspond to different degrees of skew. Because $\int_0^{\kappa S} q(t)dt = 1$, it is easy to show that the peak volume flow rate $q(U) = \frac{2}{S}$, so that the volume flow rate can be written

$$q(t) = \begin{cases} \frac{2t}{SU} & 0 \leq t \leq U \\ \frac{2(S-t)}{S(S-U)} & U \leq t \leq S \end{cases} \tag{1}$$

The analytical solution is plotted in Fig. 3 for the three cases, $U = 0$, $U = \frac{1}{2}S$ and $U = S$. For the triangular flow profile, we see that $\hat{w}$ can be negative when the peak flow rate occurs late in systole. For these cases, we can no longer conclude that the reservoir pressure waveform results in the minimum ventricular work. We note, however, that peak ventricular flow rate generally occurs early in systole and so our general conclusion stands.

General flow waveforms

It is difficult to find analytical solutions for $\hat{w}$ for more general ventricular flow rate waveforms, which frequently involve backward flow at the end of systole. It is therefore impossible to state general conditions for which $\hat{w} > 0$. However, given any flow waveform $Q_0(t)$, the positivity of $\hat{w}$ can always be checked numerically using Eq. (19).

References

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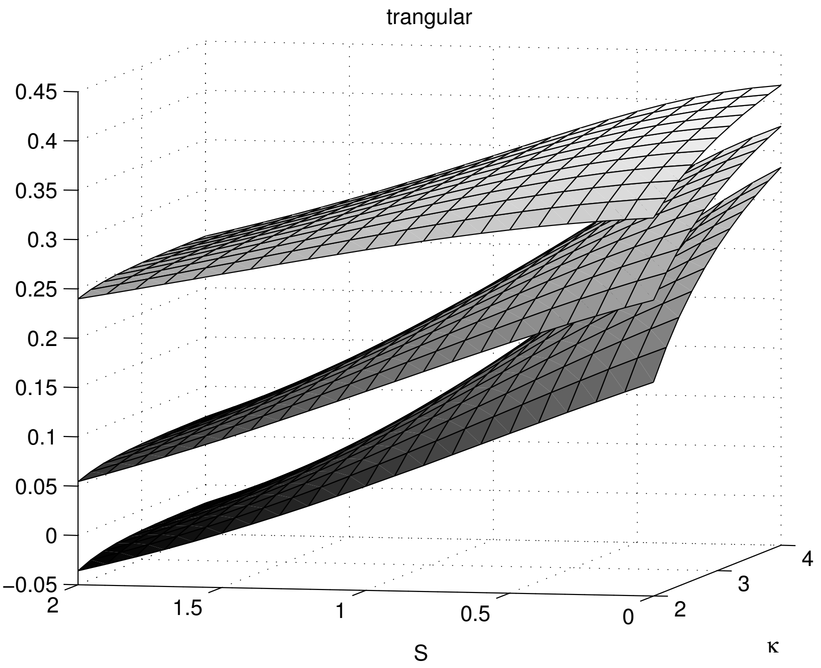

Fig. 3 Nondimensional minimum excess work, $\hat{w}$, for triangular input flow waveforms as a function of the nondimensional time of systole $S = T_s/RC$ and the cardiac period expressed in terms of the time of systole $\kappa = T/T_s$. Three cases are shown. The top values are for a left-triangular waveform where the peak flow rate occurs at the start of systole and falls linearly to the end of systole, the bottom values are for a right-triangular waveform where the flow rate increases linearly throughout systole reaching its peak at the end of systole, and the middle values are for a symmetrical triangular waveform where the peak flow rate is reached at mid-systole. Note that $\hat{w}$ becomes negative for the right-triangular waveform when S is greater than about 1.5 and is positive for all other cases. This condition is physiologically unrealistic since it means that the time of systole is longer than the time constant of the pressure fall-off during diastole which means that the diastolic pressure would be very low. However, it does indicate that $\hat{w}$ can be negative under some conditions of ventricular flow rate and arterial properties.