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Letter to Editor

Modeling predicts a connection between sinus vortex effects and aortic compliance

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ABSTRACT

We submit this letter in order to clarify some methodological issues and concerns raised by Spronck et al. (2015) related to our mathematical modeling of aortic valve dynamics during systole Aboelkassem et al. (2015). It is important to note at the outset that these clarifications do not impact the simulation output or conclusions we originally reported in that paper. However, Spronck et al. have led us to recognize some unfortunate omissions and minor typographical errors in the methods portion of our report that, once corrected, will allow others to more easily reproduce and understand our results.

1. Variable systemic vascular resistance using pulsed wave velocity

Pulse wave velocity (V_p) is directly related to the mechanical properties of the vascular walls and is widely used to determine wall distensibility (Mcdonald, 1998; Milnor, 1989; Lehmann et al., 1996; Westerhof et al., 2010). In Eqs. (7)–(13) of our report (Aboelkassem et al., 2015), the pulse wave and momentum equations were used to derive a constitutive relationship between the systemic vascular resistance R_{sc}, area A_{sa}, and capacitance C_{sa}, i.e., $R_{sc}=R_{sc}$ (A_{sa}, C_{sa}). Our analysis assumed R_{sc}, A_{sa}, and C_{sa} to be time-dependent to account for possible distensibility D during the cardiac cycle.

Spronck et al. (2015) correctly noted some unfortunate inconsistencies in our derivation of an expression for R_{sc} as a function of V_p. We inadvertently used the symbol V_p when we had actually intended to refer to the flow velocity, V_F, in Eqs. (7)–(10) (Aboelkassem et al.). Furthermore, we omitted some details in the derivation that made it difficult to follow the development of the final governing equation relating R_{sc} to V_p (Eq. (13) in Aboelkassem et al.). We present here an alternate derivation that we feel is a simpler method for obtaining the final equation for R_{sc}. In this derivation, there is no need to assume $\partial R_{sc}/\partial A_{sc}=0$ or involve this derivative term in any way. In Point 2 below, we will also show an alternative approach to reach the same R_{sc} expression using a derivative approach to both flow resistance and pulsed (water-hammer) equations.

Consider the laminar blood flow V_F through the proximal aorta to the systemic veins. The pressure drop can be given using Poiseuille formula

$$\Delta P = P_{sc} - P_{sv} = R_{sc}Q_{sc} = R_{sc}A_{sc}V_F \tag{1}$$

Next, we make the assumptions that the pressure wave pulsatility along the proximal aorta does not completely decay, that there is no reflection, and that the venous pressures are invariant and negligible. Accordingly, the "water-hammer" equation (Allieve, 1909; Khir et al., 2001; Wang and Parker, 2004) can be used to relate changes in pressure and flow velocity along the forward (+) characteristic line:

$$\Delta P \cong \rho V_p V_F \tag{2}$$

From Eqs. (1) and (2), an expression for the systemic vascular resistance R_{sc} can be found as a function of the pulse wave velocity V_p:

$$R_{sc} = \frac{\rho}{A_{sc}} V_p \tag{3}$$

Recall the relationship between pulse wave velocity V_p and wall distensibility D by Bramwell and Hill (1922), $V_p = +\sqrt{1/(\rho D)} = \sqrt{A_{sc}/(\rho C_{sc})}$, where $D=(1/A_{sc})\partial A_{sc}/\partial p_{sc}$ and $C_{sc}=\partial A_{sc}/\partial p_{sc}$. If this expression for V_p is substituted back into Eq. (3) while assuming that the lumped area $A_{sa}=A_{sc}$ and that the compliance of capillary walls are similar to that of the very end of the proximal aorta, the systemic vascular resistance can be given as

$$R_{sc} = \sqrt{\rho/(A_{sa}C_{sa})} \tag{4}$$

Alternatively, one can define the pulse wave velocity in terms of inertance L using the Langewouters model (Langewouters et al., 1984), $V_p=\sqrt{1/(LC_{sc})}$, where $L=\rho/A_{sc}$ and substitute this back into Eq. (3) to obtain similar expression for R_{sc}. While the earlier mistakes and omissions are regrettable, it should be noted that they did not affect the final expression in Eq. (13) in the original report, and hence our previously presented results remain unchanged.

2. Variable systemic resistance during a cardiac cycle

Spronck et al. (2015) also raise concerns about our formulation of a variable systemic vascular resistance (VSVR). We believe that the confusion arises from thinking of resistance as only arising from fluid shear. However, this combined resistance term accounts not only for the vascular flow resistance but also considers the contribution

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induced by wall distensibility and blood inertia. Our derived expression for VSVR can be shown to be analogous to the expression given by Eqs. (1) and (5) in the papers by Wesseling et al. (1993) and Langewouters et al. (1984), respectively. Hence, unlike a simple Poiseuille-type resistance that represents the ratio of average pressure drop to average flow, VSVR accounts for the effects of wall distention and inertia, not unlike the afterload provided by a four-element Windkessel model (Stergiopulos et al., 1999).

In Figure 2d of our paper (Aboelkassem et al., 2015), we showed the VSVR distribution over a cardiac cycle. This distribution is governed by a set of coupled non-linear equations (5, 14, and 16 therein). The variations of VSVR during the cardiac cycle can be understood from a mathematical standpoint as follows: the resistance is no longer coupled to the average pressure only but also to the gradient of the blood flow ($dQ_{sc}/dt \equiv$ acceleration/deceleration effects) and the lumped area A_{sa} as given by Eq. (5) in Aboelkassem et al. (2015). This suggests that the VSVR has to change during the cardiac cycle in order to balance the inertial effect represented by the term $\rho L_{sa}/A_{sa}$, which takes into account the blood flow acceleration during systole and deceleration during diastole from the aortic root to systemic the veins. In addition, we noted that the VSVR distribution over a cardiac cycle has a profile that looks similar to the aortic pressure profile. This similarity in shape arises from the fact that both A_{sa} and C_{sa} are strong functions of the aortic pressure.

Although VSVR as formulated fluctuates by 30 % during the cardiac cycle, the entire distribution still falls within the physiological range of healthy human vasculature, which varies between 1 and 1.5 mmHg s/ml as reported in many sources. For instance, according to Kusumoto, the value of SVR for a normal subject can range between 1170 $\pm$ 270 dyns s/cm^5), which is about 0.675–1.08 mmHg s/ml (see Table 1-1 in Kusumoto, 1999). In another source, SVR was reported between 700 and 1600 dyns s/cm^5, which is about 0.525-1.2 mmHg s/ml (see Table 30-1 in Klingensmith et al., 2008). Furthermore, Virag and Lulić (2008) used a value of $R_{sc}=1.429$ mmHg s/ml in their simulations. It should be noted that our average value of VSVR during a cardiac cycle was about $R_{sc}=1.216$ mmHg s/ml (Aboelkassem et al., 2015).

Gu et al. (2012) have shown the relationship between the systemic vascular resistance and the mean arterial pressure (MAP), which we reproduce here in Fig. 1(a). The mean VSVR and the mean pressure for both Virag and Lulić (MAP=97.3 mmHg) and Aboelkassem et al. (MAP=94.53 mmHg) are plotted on the same axes to show that these values are actually within the physiological range, assuming that MAP for healthy human hearts is in the range of 100 $\pm$ 10 mmHg (grey shaded area).

Spronck et al. (2015) also note that they were unsuccessful in repeating our calculations of VSVR, and while investigating this we became aware of the fact that some of the parameter values we reported were actually initial literature values, and not the final values we obtained after optimization. Final values for the parameters A_{max}, P_o, and P_1 (appearing in Eqs. (14) and (15)) were optimized in order to reproduce physiological pressure wave forms for both left ventricle and aorta. The initial values for these parameters were $A_{max}=1.75$ cm^2, $P_o=74$ mmHg, and $P_1=57$ mmHg. We imposed physiological systolic and diastolic pressures as well as dicrotic notch constraints during the optimization procedure. Sample results for the optimization procedure are given here in Fig. 1(b) and (c). The procedure yielded values of $A_{max}=0.505$ cm^2, $P_o=46.5$ mmHg, and $P_1=35.8$ mmHg, with the corresponding results shown in Fig. 2 in our paper (Aboelkassem et al., 2015). A quick test for this result can be done manually by using diastolic and systolic arterial pressures of 80 and 120 mmHg with the optimized parameters (above), which will render the systemic diastolic and systolic resistances to be 0.938 and 1.4548 mmHg s/ml, respectively.

Finally, there was also a question about our assumption $\partial R_{sc}/\partial A_{sc}=0$ that we used when deriving the R_{sc} expression. Although we have shown in point 1 in this letter that you can reach the same expression without neglecting this term or even having to take the derivative at all. However, herein we show some extra details on how to derive the same constitutive relationship and why we have neglected this term. If we recall again the Poiseuille law (Eq. (1)), and differentiate with respect to A_{sc},

$$\frac{\partial \Delta P}{\partial A_{sc}} = R_{sc}V_F + A_{sc}V_F\frac{\partial R_{sc}}{\partial A_{sc}} \tag{5}$$

by using the chain rule $\frac{\partial R_{sc}}{\partial A_{sc}} = \frac{\partial R_{sc}}{\partial p_{sc}}\frac{\partial p_{sc}}{\partial A_{sc}}$, and recalling the definitions of distensibility and compliance, respectively: $D=(1/A_{sc})\partial A_{sc}/\partial p_{sc}$ and $C_{sc}=\partial A_{sc}/\partial p_{sc}$. The above equation can be rewritten as

$$1/C_{sc} = R_{sc}V_F + (V_F/D)\frac{\partial R_{sc}}{\partial p_{sc}} \tag{6}$$

If we assume that VSVR is a weak function of the pressure in the systemic circuit and yet depends on distensibility "D", we can neglect $\frac{\partial R_{sc}}{\partial p_{sc}}$ and model the distensibility "$D=C_{sc}/A_{sc}$" contribution to the variable systemic resistance using the pulse wave velocity (V_p) via the water-hammer equation. Therefore, the above equation can be simplified to

$$V_F = 1/R_{sc}C_{sc} \tag{7}$$

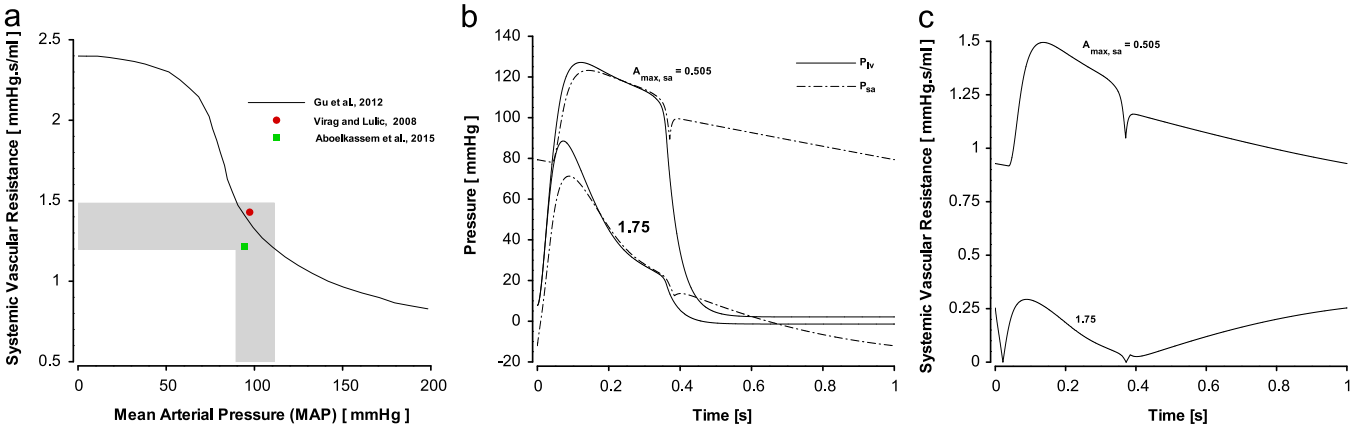

Fig. 1. (a) Averaged value of systemic resistance. The effect of varying A_{max} at $P_o=46.5$ mmHg, $P_1=35.8$ mmHg on both (b) left ventricular and aortic pressure waves, (c) variable systemic vascular resistance.