**A multiscale model of the human cardiovascular system can account for the Frank-Starling effect on vascular filling therapy**

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Introduction

Vascular filling therapy consists in intravenous administration of fluid to a patient in order to increase the stroke volume (= the amount of blood ejected by the ventricles). This therapy was proposed because of the Frank-Starling (FS) law of the heart, which states that an increase in ventricular preload (= initial stretch of cardiac fibers prior to contraction) leads to an increase in stroke volume (SV).The injected fluid increases the circulating blood volume and thus preload. A patient will be “fluid responsive” if the increase in circulating blood substantially increases SV, as expected by the FS mechanism.

Methods

Simulations of vascular filling experiments are performed with a 6-chamber multiscale model of the human cardiovascular system [1]. Ventricular contraction is described at the cellular scale where the FS mechanism originates from. Vascular filling is modeled with an increase in stressed blood volume (SBV), which is a parameter of the model. SV is then calculated for different values of SBV.

Results

The increase in SBV leads to an increase in preload, which leads to an increase in the maximal left ventricular pressure. This is a consequence of the FS mechanism. Since the pressure increases, SV increases. If the FS mechanism is removed from the cell model, the system does not present fluid-responsiveness anymore and SV monotically decreases with SBV.

Afterload, which can be defined as the resistance to blood ejection by the ventricle, is also affected by vascular filling. Our model shows that the aortic pressure at the opening of the aortic valve, a component of the afterload, increases with SBV.

The preload and afterload effects are actually competing: for low SBV values, the preload increases enough to counterbalance the afterload increase and vascular therapy may be considered. This is not the case for high SBV values where the fluid responsiveness is lost.

Conclusion

Our model corroborates the significance of the FS mechanism for fluid responsiveness. However, other factors such as afterload should also be taken into account when considering vascular therapy. It is worth noticing that the loss of fluid responsiveness for high SBV values is not the consequence of the saturating FS mechanism, but rather the result of the sharper afterload increase, which counterbalances the FS mechanism.

References

[1] Kosta, S., Negroni, J., Lascano, E., & Dauby, P. C. (2016). Multiscale model of the human cardiovascular system: Description of heart failure and comparison of contractility indices. *Mathematical Biosciences*.

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