Investigating cardiovascular aging through closed-loop multiscale hemodynamic modeling

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Aging of the cardiovascular system is one of the most impacting factors on quality of life and, currently, is a central topic in cardiovascular research because of its link with several debilitating conditions, such as dementia and kidney failure[1]. An aged human cardiovascular system is marked by stiffer large arteries that, losing their buffer capacity, increase pulse wave velocity (PWV) resulting in the early return of reflected pressure waves and the increase in the pressure pulsation. The pulsation increase causes a vicious mechanism which in turn leads to arterial geometry changes, ventricular remodeling, and microvascular damage on the organs more exposed to highly pulsatile pressure such as the brain[2]. Differently from the heart-arterial open-loop modeling typically adopted in current literature, here we propose a validated 1D-0D closed-loop multiscale cardiovascular model[3] to simulate the effects of aging on the entire cardiovascular system. Figure 1 schematically shows the main cardiovascular age-mediated changes clinically observed and their implementation in the model[4]. Aged main arteries undergo two main alterations: increased stiffness – taken into account by increasing the PWV – and geometric modifications, which translate into increased vessel length and diameter. Ventricular remodeling comprises both diastolic dysfunctions and enhanced contractility, represented with an increase in left ventricular minimum and maximum elastances, respectively. Moreover, aged hearts typically show slower contractions, which are modeled by imposing a slower heart rate. Finally, a reduction of venous peripheral compliance combined with an increase in small artery resistance is applied to capture modifications in the microvascular and venous circulations. The age-specific model serves as a foundation for studying the effect of cardiovascular diseases, such as arrhythmias, on the elderly population. In fact, by accounting for both aging and cardiovascular dysfunctions – as the effects of these conditions are commonly overlaid – it is possible to achieve a more faithful representation of a subject's hemodynamics.

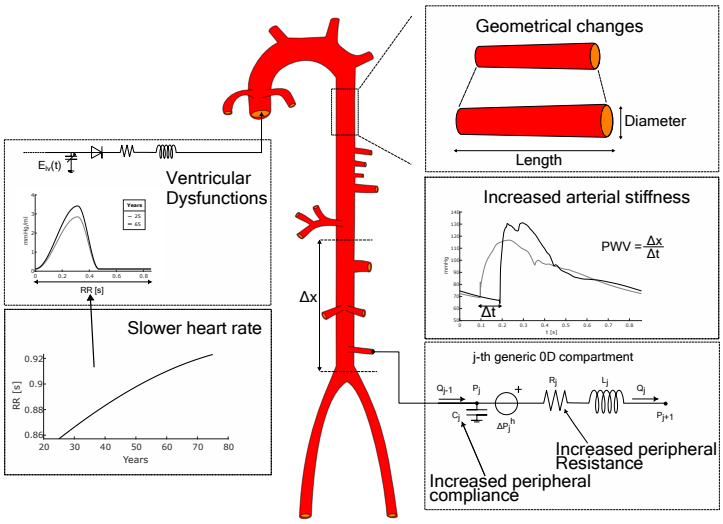

Figure 1: Schematic of the main changes observed in vascular aging: increased arterial vessel length and diameter, increased peripheral compliance and resistance, increased arterial stiffness, increased ventricular contractility, ventricular diastolic dysfunctions and slower heart rate.

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[1]O'Rourke et al., *Artery Research* **26**, 197 (2020)
[2]Chirinos et al, *Journal of the American College of Cardiology* **74**, 1237-1263 (2019)
[3]Fois et al., *npj Microgravity* **10**, 22 (2024)
[4]Charlton et al., *American Journal of Physiology-Heart and Circulatory Physiology* **317**, H1062-H1085 (2019)