Identifying haemodynamic determinants of pulse pressure: An integrated numerical and physiological approach

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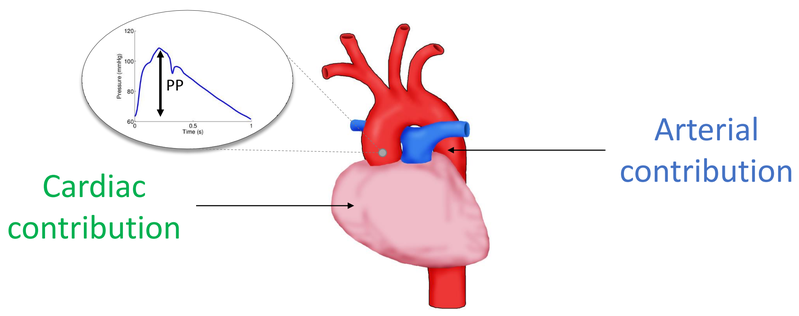
Background

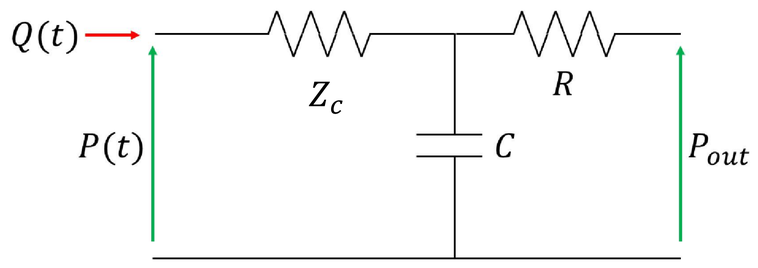
- Hypertension, the single most important cause of morbidity and mortality worldwide, arises mainly as a result of an increase in pulse pressure (PP).
- Haemodynamic basis of this increase in PP is still disputed



- We used a 3-element Windkessel (WK) model to identify cardiac and arterial contribution to PP

Method

- **Three-element Windkessel model**



$$P(t) = Z_c Q(t) + \frac{1}{C} e^{-\frac{t}{RC}} \int_0^t e^{\frac{t'}{RC}} Q(t')dt + (DBP - P_{out}) e^{-\frac{t}{RC}} + P_{out}$$

- ***In silico* data**

Following a similar approach to Willemet et al.[1], we created a virtual database of patients (n = 3,095) using a validated 1D model of the arterial network, with cardiac and arterial parameters varied within physiological healthy range.

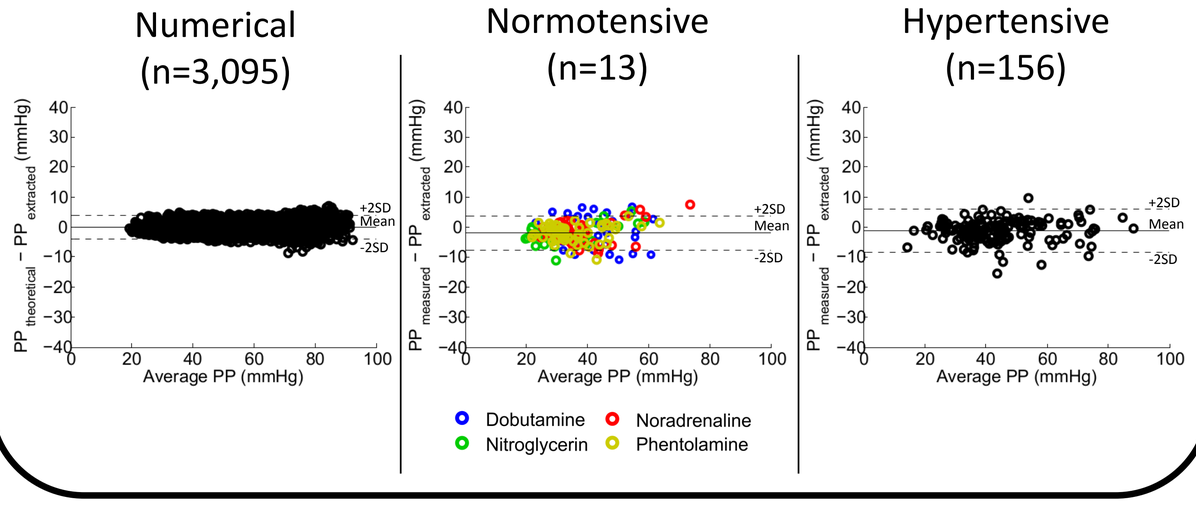
- ***In vivo* data**

Tonometric pressures and echo flows were acquired in normotensive healthy volunteers (n=13,10 men, age 49±8 yr, BP 110±16/69±10 mmHg, means±SD) and in hypertensive subjects (n=156, 83 men, age 46±17 yr, BP 130±23/83±13 mmHg). Healthy volunteers took part in cross-over studies to investigate the change in pulsatile haemodynamics during administration of drugs with different inotropic and vasopressor/vasodilator properties.

WK parameters were extracted from pressure and flow waveforms.

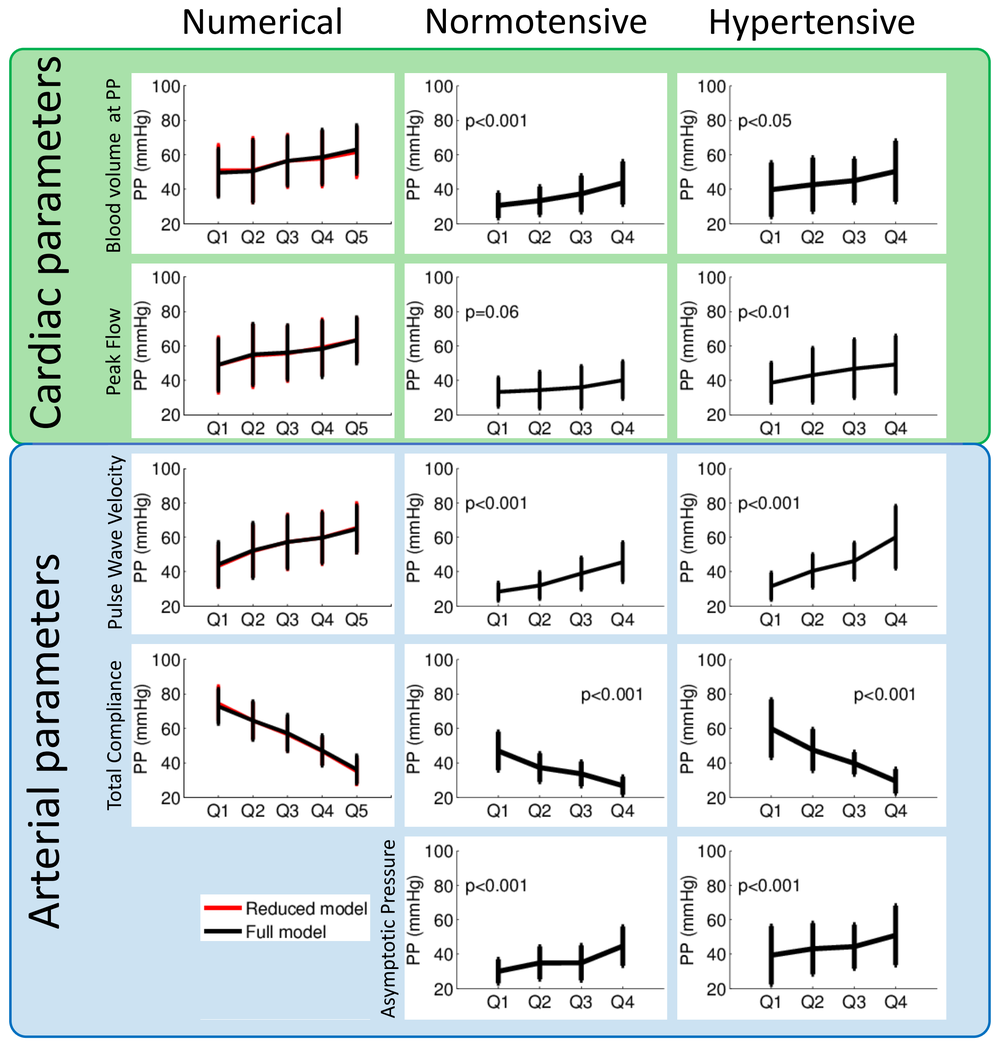
Results: Validation

Bland-Altman plots comparing the simulated/measured PP with the estimated PP

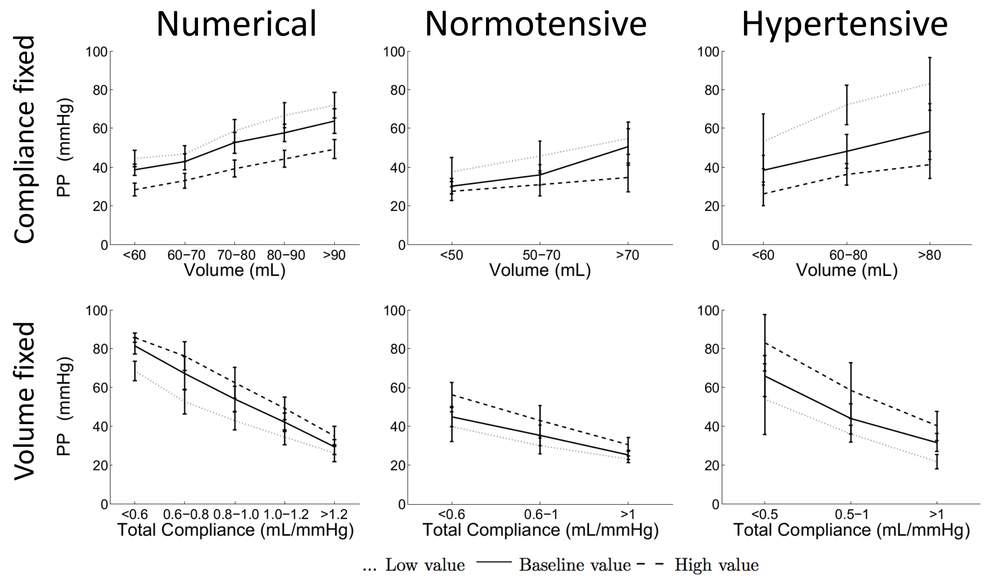


Results: Investigation

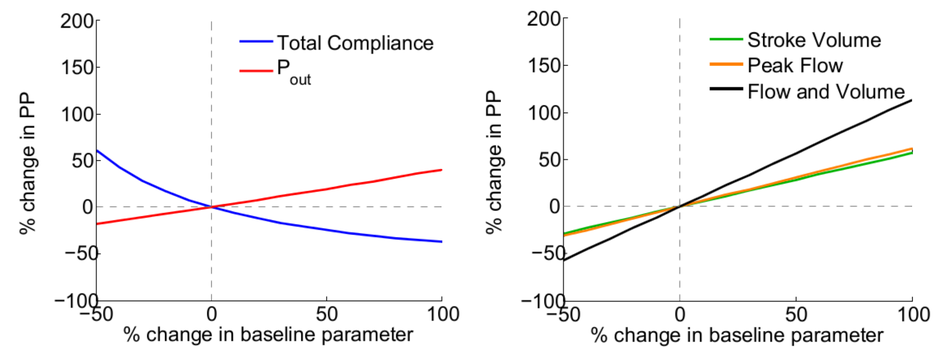
- **Impact of variations of the model parameters on PP**



- **Specific influence of Volume at time of PP and Total Compliance on PP**



- **Sensitivity analysis on the parameters of the model**



Implications

- The 3-element Windkessel model estimates accurately PP
- The main contributors to PP are the total arterial compliance (related to PWV) and the stroke volume
- Ventricular dynamics account for a relatively large proportion of the increased PP in hypertension (20.1 mmHg of the 39.0 mmHg difference in PP between upper and lower tertiles of the hypertensive subjects)[2]
- This approach can provide a haemodynamically orientated stratified approach to hypertension

[1] **Willemet et al. (2015)** "A database of virtual healthy subjects to assess the accuracy of foot-to-foot pulse wave velocities for estimation of aortic stiffness", *American Journal of Physiology-Heart and Circulatory Physiology*, 309(4), H663-H675.

[2] **Vennin et al. (2017)** "Identifying haemodynamic determinants of pulse pressure: an integrated numerical and physiological approach", *Hypertension*, 70(6), 1176-1182.