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Comparative Analysis of Porcine and Human Thoracic Aortic Stiffness

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WHAT THIS PAPER ADDS

This study uses a method to compare published data on porcine and human thoracic aortic stiffness from different studies consistently. The results of this analysis show that the stiffness of young porcine aortas is similar to that of human tissue aged under 60 years and less stiff than human tissue aged 60 years or more. This has implications for using the porcine aorta as a model for human aorta in research.

Objectives: To compare porcine and human thoracic aortic stiffness using the available literature.
Methods: The available literature was searched for studies reporting data on porcine or human thoracic aortic mechanical behaviour. A four fibre constitutive model was used to transform the data from included studies. Thus, equi-biaxial stress stretch curves were generated to calculate circumferential and longitudinal aortic stiffness. Analysis was performed separately for the ascending and descending thoracic aorta. Data on human aortic stiffness were divided by age <60 or ≥ 60 years. Porcine and human aortic stiffness were compared.
Results: Eleven studies were included, six reported on young porcine aortas, four on human aortas of various ages, and one reported on both. In the ascending aorta, circumferential and longitudinal stiffness were 0.42 ± 0.08 MPa and 0.37 ± 0.06 MPa for porcine aortas (4—9 months) versus 0.55 ± 0.15 MPa and 0.45 ± 0.08 MPa for humans <60 years, and 1.02 ± 0.59 MPa and 1.03 ± 0.54 MPa for humans ≥ 60 years. In the descending aorta, circumferential and longitudinal stiffness were 0.46 ± 0.03 MPa and 0.44 ± 0.01 MPa for porcine aortas (4—10 months) versus 1.04 ± 0.70 MPa and 1.24 ± 0.76 MPa for humans <60 years, and 3.15 ± 3.31 MPa and 1.17 ± 0.31 MPa for humans ≥ 60 years.
Conclusions: The stiffness of young porcine aortic tissue shows good correspondence with human tissue aged <60 years, especially in the ascending aorta. Young porcine aortic tissue is less stiff than human aortic tissue aged ≥ 60 years.

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INTRODUCTION

The porcine aorta is used as a model for the human aorta in various fields of cardiovascular research.[1—4] Differences and similarities between pigs and humans in terms of anatomy and physiology have been investigated to define the translational value of porcine models.[1] Part of the translational value of porcine models depends on the agreement between human and porcine aortic mechanical behaviour, specifically stiffness.

Aortic stiffness is determined by its structural constituents in the tunica media and adventitia. Elastin and collagen fibres, and the degree of activation of vascular smooth muscle cells together determine the active mechanical behaviour of the aortic wall.[5] The passive mechanical behaviour is determined mainly by the elastin and collagen fibres; the extent of the contribution of smooth muscle on passive mechanical behaviour is not yet known.[5] The presence and orientation of collagen fibre endows the aortic wall with an anisotropic (directionally dependent) material response. In the media, the diagonal orientation of collagen fibres is closer to circumferential alignment, while in the adventitia it is closer to axial alignment.[6] Histological evaluation of the thoracic aorta shows that elastin and

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collagen fibres are organised in the same functional unit in different mammals, and that the difference in size between the thoracic aorta of smaller and larger mammals is directly proportional to the number of these functional units.[7]

Numerous experimental protocols have been used to characterise the mechanical properties of human aortas.[8–13] The results of these experiments have been used to formulate mathematical models that describe aortic mechanical behaviour, specifically the relationship between stress and strain over a wide range of strains. In general, these mathematical formulations are called constitutive models, and their main goal is to be general enough to reproduce the measured experimental data and in doing so, to provide a description of the tissue stiffness. Ferruzzi et al. proposed a complex four fibre constitutive model for aortic mechanical behaviour based on the histological structure of the aortic wall.[14] This model was used by Roccabianca et al. to calculate regional human aortic stiffness for different age groups based on data from the available literature.[12] Such a comparison has limitations, because the included datasets originate from studies with different testing protocols, and cannot fully account for these differences. Nevertheless, it can be used to evaluate the available literature in a consistent manner. Even though it is not straightforward to compare porcine and human aortic stiffness based on literature, the current study uses the same analysis for available data on porcine aortic tissue.

MATERIALS AND METHODS

Selection of data on human and porcine aortas

A search was performed of Medline, EMBASE, and Cochrane databases to obtain data on porcine aortic tissue, using the following search terms: "aorta," "endovascular repair," "pig," "porcine," "ex vivo," "in vitro," "experimental," "isolated," "biomechanics," "haemodynamics," and synonyms. The search was last updated on June 29, 2016. Studies were included if they performed assessment of the stiffness of a specified region of the porcine aorta, and reported the results using either a plot or a non-linear constitutive model with associated best fit values of the material parameters. Studies reporting data only on purified elastic tissue, after other tissue engineering processes or after *in vivo* medical or surgical treatment of the pigs were excluded. The reference lists of the studies that remained after applying in- and exclusion criteria were checked for additional relevant articles. For data on human aortas, data were included from the article by Roccabianca et al., who included four studies after a comprehensive literature search for studies on mechanical testing of human aortic tissue without aneurysm or dissection.[8–12] Although a comparison between porcine tissue and diseased human tissue would be of interest, it was considered beyond the scope of the current study.

Data analysis

The procedure for creating consistent sets of data with associated stress strain curves for the included studies was the same in the present analysis as the one previously adopted by Roccabianca et al.[12] Such a procedure represents a consistent means for comparing results from different studies, regardless of the original testing protocols or constitutive relations used in each individual study. In particular, it was aimed to compare equi-biaxial stress strain curves for each individual article that was included in the study. However, the data as reported in the considered articles were not immediately comparable. Therefore, it was necessary to perform additional computations to homogenise these data.

In short, either the strain energy function with the corresponding material coefficients or the stress stretch curves as reported in the corresponding paper were used as input data to simulate five loading protocols (i.e. biaxial tests with stress ratio σ_{11}: $\sigma_{22} = 0.5$:1, 0.75:1, 1:1, 1:0.75, and 1:0.5, where σ_{11} and σ_{22} are the circumferential and longitudinal stresses, respectively).

Then, the obtained stress stretch curves were fitted using the four fibre constitutive model as reported in Roccabianca et al.

$$W = \frac{c}{2}(I_1 - 3) + \sum_{k=1}^{4} \frac{c_1^k}{4c_2^k}\left(\exp\left[c_2^k\left(\left(\lambda^k\right)^2 - 1\right)^2\right] - 1\right) \quad (1)$$

where c, c_1^k, and c_2^k are positive material parameters, I_1 is the first invariant of the right Cauchy-Green tensor C, and λ^k is the stretch in the direction of the k-th collagen fibre family and defined in the reference configuration by the unit vector $M^k = [0, \sin\alpha_0^k, \cos\alpha_0^k]$, with α_0^k the angle between the k-th fibre family (arranged in symmetrical spirals) and the axial direction of the arterial wall (blood flow direction). In particular, $\alpha_0^1 = 0°$ denotes the axially arranged fibre family, $\alpha_0^2 = 90°$ the circumferentially arranged fibre family, and $\alpha_0^3 = -\alpha_0^4 = \alpha$ the two -fibre families symmetrically oriented.

The Cauchy stresses in the circumferential and axial direction, σ_{11} and σ_{22}, are given by:

$$\sigma_{ii} = \lambda_i \frac{\partial W}{\partial \lambda_i} - p, \quad i = 1, 2 \quad (2)$$

with p a Lagrange multiplier to enforce the incompressibility constraint and computed through the known zero stress in the radial direction, $\sigma_{33} = 0$.

To generate the best fit values of material parameters for the four fibre constitutive model, the following objective function was minimised:

$$\chi = \sum_{i=1}^{N}\left(\sigma_{11}^{exp} - \sigma_{11}^{mod}\right) + \left(\sigma_{22}^{exp} - \sigma_{22}^{mod}\right) \quad (3)$$

with N the total number of data points, σ^{exp} the experimental stress data, and σ^{mod} the corresponding model prediction values computed in Eq. (2).

The minimisation was performed with a non-linear trust region reflective algorithm implemented in MATLAB, and multiple, randomly generated starting points were considered to find the global best fit solution.