Scaling Cardiovascular Parameters for Population Simulations

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Abstract

Computational models of cardiovascular function depend on the specification of parameters, whose values can depend quite strongly on particular subject characteristics (e.g., age, height, weight, disease state). In this study, we present a scaling scheme, based on the principle of elastic similarity, that allows for referencing of cardiovascular parameters to different anthropometric profiles. Combined with a sampling procedure, this scaling scheme allows for simulations of subjects of different body size. Simulated steady-state mean values, standard deviations, and ranges of important hemodynamic variables match their experimental analogs of the normal healthy adult population quite well. We conclude that scaling of cardiovascular parameters on the basis of elastic similarity provides a valid basis for incorporating the effects of size in population simulations.

1. Introduction

Lumped-parameter models of physiological systems have been used extensively in the past to quantify and to test our understanding of physiological systems, both in the realm of research and in teaching environments. Such models depend on parameters whose values can depend quite strongly on particular subject characteristics, such as age, height, weight, or disease state. Frequently, one is interested in modeling the behavior of a population of subjects and thus the parameter values need to be referenced to the mean characteristics of the subject population one is interested in representing. Identifying such a nominal (or referenced) parameter profile can be quite challenging and usually involves significant review of the pertinent medical and physiological literature. Once such a set of parameters has been identified, however, the model can be executed to generate a simulation that in some sense represents the *average response* of the subject population. In order to simulate the response of a population with different mean characteristics, a different set of parameters need to be specified.

In cardiovascular physiology, for example, blood volume is known to exhibit a strong dependence on body weight, as displayed in Figure 1. Cardiovascular parameters therefore need to be selected with particular anthropometric measures in mind.

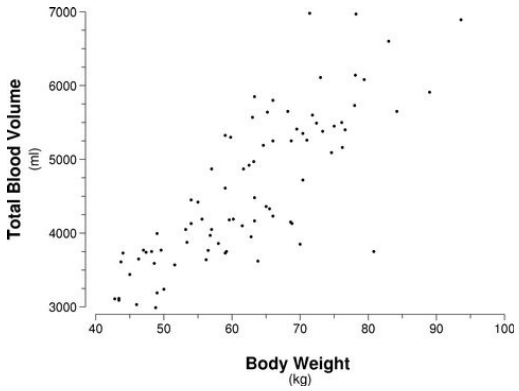

Figure 1. Correlation of total blood volume and body weight. Data adapted from [1].

The purpose of this study is to combine a set of nominal parameter values and their standard errors with general allometric scaling laws to allow for sampling of parameter profiles of subjects with different anthropometric and cardiovascular characteristics. This sampling will enable us to repeat simulations for different subject characteristics and therefore simulate individual members of a population rather than a single subject whose characteristics are chosen to be representative of the mean of the population.

We examine two commonly used allometric scaling laws, based on the principles of geometric and elastic similarity, respectively, as the basis for scaling of cardiovascular parameters. After establishing the details of the sampling scheme, we simulate steady-state values of cardiovascular variables and compare the model's predictions to hemodynamic data from healthy subjects.

2. Scaling laws

Scaling of physiological parameters is commonly described by allometric scaling laws, which take the form of power-law monomials

$$Y_i = a_i \cdot W^{k_i}$$

where Y_i is a physiological variable of interest, and W is the weight of a member of the population under consideration.

Theoretical frameworks have been developed to predict the scaling exponents for different physiological parameters, given a set of fundamental assumptions [2, 3]. Geometric similarity is based on the assumption that a set of individuals have the same general shape but differ in size. Mathematically, geometric similarity is based on proportional scaling of all variables of linear dimension. In particular, $\mathrm{L} \propto \mathrm{D}$, where L is the dimension of a characteristic length variable (such as the length of the femur), and D is the associated transverse dimension (such as the diameter of the femur neck)[1]. Elastic similarity, on the other hand, asserts that larger individuals are more strongly built than smaller ones [4]. In particular, it states that two variables are scaled in proportion to their characteristic elastic properties. Mathematically, elastic similarity is described by an affine transformation that scales the transverse dimensions relatively more than the longitudinal dimensions ($\mathrm{L} \propto \mathrm{D}^{\frac{2}{3}}$).

If one assumes constant tissue density, weight scales according to volume, $\mathrm{W} \propto \mathrm{L} \cdot \mathrm{D}^2$, so $\mathrm{L} \propto \mathrm{W}^{\frac{1}{3}}$ assuming geometric similarity and $\mathrm{L} \propto \mathrm{W}^{\frac{1}{4}}$ when the model of elastic similarity is employed. Alternatively, $\mathrm{D} \propto \mathrm{W}^{\frac{1}{3}}$ and $\mathrm{D} \propto \mathrm{W}^{\frac{3}{8}}$ under the geometric and elastic model, respectively. By computing the exponents k_i for various anthropometric and cardiovascular variables, we can decide which of the two models is more appropriate in describing the scaling behavior of the human body. Table 1 summarizes the results of such regression analyses as applied to data taken from the literature [1, 5, 6]. The results suggest that the data favor elastic over geometric similarity.

In healthy non-obese individuals, blood pressure does not scale with body size, that is $\mathrm{P} \propto \mathrm{W}^0$. Combining this information with the fact that blood volume scales proportional to body size, we can determine that vascular compliance scales according to $\mathrm{C} \propto \mathrm{W}$. We need to understand how blood flow scales in order to understand the scaling behavior of flow resistance. McMahon [4] argues and presents experimental confirmation that dynamic variables of metabolic importance such as blood flow, minute respiration, and metabolic oxygen consumption all scale according to $\mathrm{W}^{\frac{3}{4}}$ under the elastic similarity assumption. Resistance therefore scales as $\mathrm{R} \propto \mathrm{W}^{-\frac{3}{4}}$ and physiological time scales according to $\mathrm{T} \propto \mathrm{W}^{\frac{1}{4}}$.

3. Sampling scheme

Having established the scaling behavior of cardiovascular parameters, we can employ the following sampling scheme to sample parameter profiles corresponding to different anthropometric and cardiovascular characteristics. We assume that a nominal parameter profile has been established for a reference weight W_0.

1. Sample from an empirical distribution function of body weights to obtain a new weight W_1.
2. Sample a new parameter value θ_1^i from some appropriately chosen probability distribution function F_i:

$$\theta_1^i \sim F_i(\theta_0^i, \triangle\theta_0^i).$$

Here θ_0^i and $\triangle\theta_0^i$ represent the i-th nominal parameter value and standard error, respectively.
3. Scale the new parameter value by the appropriate power law to obtain the new nominal value $\hat{\theta}_1^i$:

$$\hat{\theta}_1^i = \theta_1^i \cdot \left(\frac{W_1}{W_0}\right)^{k_i}$$

We chose the normal distribution for the sampling step (Step 2), but constrained the samples to lie between predefined minima and maxima to account for the fact that under normal conditions, most cardiovascular variables do not assume extremely large or negative values.

Table 1. Allometric exponents of the human cardiovascular system.

	Exponent k		
	Predicted		Observed[†]
Variable	Geometric similarity	Elastic similarity	
Body height	0.333	0.250	(0.223 ± 0.003)
	0.333	0.250	(0.221 ± 0.026)
Leg height	0.333	0.250	(0.228 ± 0.004)
Calf girth	0.333	0.375	(0.347 ± 0.004)
Thigh girth	0.333	0.375	(0.350 ± 0.005)
Body surface area	0.667	0.625	(0.602 ± 0.019)
Cardiac output	0.667	0.75	0.71
Blood volume	1.0	1.0	(0.936 ± 0.074)

[†]Mean $\pm$ standard error.

4. Results

In Table 2, we summarize the steady-state mean values, standard deviations, and ranges of certain hemodynamic variables in the normal healthy adult population [7, 8, 9] and the results of our sampling-based population simulations using a lumped-parameter model of the cardiovascular system [10]. The simulations are based on 500 realizations of the sampling scheme outlined in the previous section. The data demonstrate that in addition to the mean values, the degrees of variability and the ranges of the population-based simulations generally match their experimental analogs quite well. Two exceptions are the systolic and the diastolic radial artery pressure, which will be discussed in the following section.

[1]The sign $\propto$ signifies proportionality.

Table 2. Comparison of population simulations to steady-state hemodynamic variables of recumbent adults.

Variable	Simulations		Measurements	
	Mean†	Range‡	Mean†	Range
Pressures, $\mathrm{mm\,Hg}$				
Radial artery*				
Systolic	(107 ± 7.5)	(97–120)	(135 ± 15.7)	(106–164)
Mean	(94 ± 5.1)	(86–103)	(91 ± 8.7)	(75–110)
Diastolic	(79 ± 3.4)	(74–85)	(71 ± 7.4)	(64–86)
Peripheral vein				
Mean	(10 ± 2.8)	(6–15)	(8 ± 2.5)	(4–13)
Right atrium				
Mean	(2 ± 1.7)	(0–5)	(0 ± 1.6)	(-2–2)
Right ventricle				
Systolic	(24 ± 5.9)	(15–35)	(25 ± 3.4)	(18–30)
End-diastolic	(1 ± 2.0)	(-1–4)	(2.6 ± 1.4)	(-0.5–4.5)
Pulmonary artery				
Systolic	(23 ± 6.0)	(13–34)	(22 ± 3.7)	(13–30)
Mean	(17 ± 4.4)	(10–24)	(17 ± 3.1)	(10–21)
Diastolic	(11 ± 3.5)	(8–17)	(12 ± 2.6)	(3–15)
Pulmonary capillary wedge⋆				
Maximum	(13 ± 3.4)	(8–20)	(15 ± 2.9)	(8–23)
Mean	(10 ± 2.8)	(7–16)	(12 ± 2.0)	(8–15)
Minimum	(9 ± 2.6)	(5–13)	(9 ± 2.2)	(5–14)
Left atrium				
Mean	(5 ± 2.5)	(2–8)	(7.9 ± 3.0)	(2–12)
Left ventricle				
Systolic	(108 ± 7.7)	(98-122)	(118 ± 16)	(90–140)
End-diastolic	(8 ± 2.8)	(5-13)	(8.7 ± 2.3)	(5–12)
Left ventricular end-diastolic volume index, $\mathrm{ml/m^2}$	(72 ± 14.7)	(52–96)	(70±20)	(54–120)
Left ventricular end-systolic volume index, $\mathrm{ml/m^2}$	(34 ± 9.8)	(18–50)	(24±10)	(14–45)
Cardiac index, $\mathrm{l/min/m^2}$	(2.7 ± 0.4)	(2.3–3.4)	(3.5 ± 0.7)	(2.5–5.3)
Stroke index, $\mathrm{ml/beat/m^2}$	(38 ± 8.4)	(27–51)	(46 ± 8.1)	(37–72)
Heart rate, $\mathrm{beats/min}$	(74 ± 7.8)	(61–87)	(79 ± 13.8)	(59–113)
Systemic resistance, PRU	(1.13 ± 0.19)	(0.84–1.48)	(0.85 ± 0.17)	(0.56–1.18)

†Mean ± population standard deviation. ‡(0.05–0.95) inter-quantile range.
*Compared to aortic root pressure. ⋆Compared to pulmonary venous pressure.

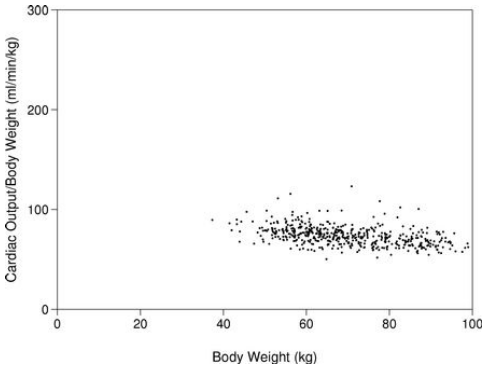

Figure 2. Normalized cardiac output as a function of body weight.

In Figure 2, we report normalized cardiac output similar to the data reported by de Simone and co-workers [6], who studied normalized cardiac output as a function of body weight in children and adult subjects. The distribution of simulated normalized cardiac output compares quite favorably to the part of the experimental observations in adult subjects.

5. Discussion and conclusions

Numerical values of most cardiovascular parameters depend quite strongly on the average size (weight or height) of the population one is interested in representing. In this study, we presented a sampling scheme, based on the principle of elastic similarity, that allowed for sampling of parameter profiles referenced to different anthropometric measures.

The observed discrepancies between systolic and diastolic radial artery pressure measurements and their simulated equivalents are a limitation of the lumped-parameter model rather than a limitation of the sampling scheme. The model is incapable of reproducing phenomena that arise as a result of the distributed nature of the cardiovascular system. The arterial pressure in our model represents aortic root pressure, yet it is well known that peak-systolic pressure increases and diastolic pressure decreases the further distal from the heart the pressure is being measured [11].

Yet despite these minor discrepancies, the resultant population simulations represent steady-state hemodynamic variables quite well. More detailed statistical testing can be performed when more hemodynamic data becomes available for the normal general population.

Acknowledgments

This work was partially supported by the National Aeronautics and Space Administration through the NASA Cooperative Agreement NC 9-58 with the National Space Biomedical Research Institute and by Grant Number RO1 EB001659 from the National Institute of Biomedical Imaging and Bioengineering (NIBIB). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIBIB or the National Institutes of Health.

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