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REVIEW ARTICLE

Indexing cardiovascular and respiratory variables: allometric scaling principles

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Abstract

Objectives To describe the allometric scaling principles underlying appropriate indexing of cardiovascular and respiratory measurements obtained in adult mammals, and to propose guidelines for indexing experimental cardiovascular and respiratory data.

Database used PubMed, using the terms 'allometry', 'allometric', 'indexing', 'cardiovascular' and 'respiratory'.

Conclusions Indexing of cardiopulmonary variables is commonly used in attempts to account for the effects of body size on measurements and to standardize them. Some cardiopulmonary variables have been indexed using various functions of body mass in a process that often ignores the underlying relationship between the variable of interest and body size, as described in the allometry literature. This can result in a failure to ideally reduce the effect of body size on measurements in a manner that highlights differences. We review how commonly measured cardiopulmonary variables are related to body mass in mammalian species according to the allometry literature, and offer suggestions on how this information can be used to appropriately index cardiopulmonary variables in a simple and informative manner.

Keywords cardiac index, cardiovascular, respiratory.

Introduction

Numerous variables of interest to the anesthesiologist are known to vary as a function of body size. Many variables increase as body size increases (e.g. cardiac output, minute ventilation), whereas others decrease as body size increases (e.g. heart rate, respiratory rate) and some do not vary systematically with body size (e.g. blood pressure, hematocrit). Many researchers have recognized the utility of expressing cardiopulmonary variables known to vary with body size as values indexed to another size-related variable; for example, cardiac index may be calculated as the quotient of cardiac output and body surface area (BSA). Such expressions reduce the variability of measurements, may artificially eliminate the effect of body size on the variable and give a clearer indication of how an individual animal's values compare with those expected for a typical animal of its body size. However, a variety of methods for such indexing are found in the literature. The simplest, and possibly most common adjustment, is to divide the measurement by body mass and present it mass-specifically. Although this is appropriate for some variables, as will be described, many cardiopulmonary variables increase or decrease in a manner that is not directly proportional to body mass, and indexing them to body mass will under- or overestimate, respectively, the true size-adjusted value; this error will be amplified as body size difference increases (Table 1). Therefore, the actual function of body mass with

Table 1 Effect of indexing a hypothetical variable specifically to body mass (M), or to a function of body mass related to metabolic rate [$M^{3/4}$ (interspecific) or $M^{2/3}$ (intraspecific)]. The effect of body size on this hypothetical variable is described by $100 \times M^{0.75}$

M (kg)	Measurement	Measurement indexed to *M*	Measurement indexed to $M^{3/4}$	Measurement indexed to $M^{2/3}$
1	100	100	100	100
2	168	84	100	106
5	334	67	100	114
10	562	56	100	120
20	946	47	100	127
50	1880	38	100	137
100	3162	32	100	145
500	10,574	21	100	164
1000	17,783	18	100	174

which the variable changes should be used for indexing. Examining the veterinary anesthesia literature confirms that incorrect indexing of cardiopulmonary measurements is common; for example, of 10 articles recently published in this journal that reported both cardiac index and stroke index, four used methods of indexing unsupported by allometric principles. In addition, in these four manuscripts, cardiac output and stroke volume were incorrectly indexed using the same function of body mass, which suggests that heart rate is not expected to be affected by body size (see below), a supposition known to be incorrect.

Scaling describes the structural and functional consequences of changes in size or scale among otherwise similar organisms (Schmidt-Nielsen 1984). Allometric scaling refers to the scaling of bodies or functions that do not vary in direct proportion to their size (Schmidt-Nielsen 1984). Many morphological and physiological variables have been shown to depend on body mass according to the general allometric equation $Y = Y_0 \times M^b$, where Y_0 is a constant, characteristic of the type of organism and equal to the value of the variable of interest in a 1 kg (assuming that M is expressed in kg) animal, b is the allometric exponent, and M is body mass (West et al. 1997). The value of b usually ranges from -1 to 1 for cardiopulmonary variables; negative values indicate that the variable decreases as body size increases, and positive values indicate that the variable increases as body size increases. When the exponent is 0, the variable is 'size-independent': it does not vary as a function of body size (see below). A simplified interpretation of the effects of different exponents in allometric equations is to consider the magnitude of the effect of changes in size, based on the logarithms of the exponent. For instance, if a variable scales as $M^{1/4}$, the variable will change by a factor of 10^1 (=10-fold) whenever body mass changes by 10^4. Because mammals span a size range of 10^8, this indicates that variables that scale with mass exponents of 1/4 (e.g. circulation time) or $-1/4$ (e.g. resting heart rate) differ by approximately 100-fold (10×10) between the smallest and largest mammals (Fig. 1). The theoretical basis for the allometric equation $Y = Y_0 \times M^b$ and the common allometric exponents has been discussed (West et al. 1997; Dodds et al. 2001; Glazier 2005, 2010; Chaui-Berlinck 2006; Clemente 2007; West & West 2013; White & Kearney 2014), but is beyond the scope of this review.

Kleiber's law

In 1883, the German physiologist Max Rubner demonstrated that in dogs spanning an order of magnitude difference in body size, metabolic heat production varied in proportion to BSA, or $M^{2/3}$ (Rubner 1883). In 1932, the distinguished physiologist Max Kleiber reported that metabolic rates (in kcal per day) for mammals and birds spanning a body mass range of 0.15 kg to 679 kg were best described by a relationship proportional to $M^{0.74}$, usually expressed rounded off to $M^{3/4}$ (Kleiber 1932). It should be noted that in the allometry literature, mass exponents derived from empirical data are typically expressed as decimal values (e.g. 0.74), whereas those denoting a generalized underlying relationship are expressed as fractions (e.g. 3/4). A few years later, studies using an even larger