Assessing the Sensitivity of Spontaneous Baroreflex Control of the Heart: Deeper Insight Into Complex Physiology

To the Editor:

While several papers support the physiological and clinical relevance of indices quantifying the sensitivity of spontaneous baroreflex control of heart rate (BRS), Lipman et al claim that they are unable to properly explore baroreflex function because spontaneous BRS was found to be quantitatively different from BRS values provided by the vasoactive drug injection technique and is unrelated to common carotid artery distensibility. We believe that this conclusion is not supported by Lipman’s data, for the following reasons.

1. The time honored (and still valuable) method for assessing BRS through vasoactive drugs injection cannot be a “gold standard” due to pharmacological alteration of baroreceptor activity through both changes in blood pressure (BP) and unquantifiable mechanical distortion of the vessel; direct drug effect on the sinus node; simultaneous stimulation of cardiopulmonary stretch receptors; and limited reproducibility of the few spot BRS estimates obtainable.

2. Pharmacological and spontaneous BRS values are significantly correlated in most instances, as demonstrated by Parlow et al in a study not cited by Lipman et al. Moreover, spontaneous and drug-related BRS values display directionally similar changes under different conditions, thus reflecting virtually superimposable baroreflex physiology.

3. Both the drug injection and the spontaneous sequence technique focus on the slope of the RR interval response to progressive Systolic (S) BP changes. Whether the origin of SBP ramps is spontaneous or by pharmacological means must be immaterial to the baroreceptors, with the partial physiological exception of spontaneous BP changes due to central influences simultaneously responsible also for arterial baroreflex resetting.

4. Spontaneous BRS assessment by the sequence and spectral method was validated not only by the drug injection approach, but also by surrogate data analysis and for baroreceptor denervation in animals, which led to disappearance of baroreflex sequences and to a marked reduction in the coefficient values.

5. The relation between carotid distensibility and BRS should be assessed in absence of diseases altering the baroreflex arch, while in some patients recruited in Lipman’s study normal carotid distensibility coexisted with disease-induced alterations of BRS. Moreover, there is evidence, in absence of drug injection, of spontaneous low frequency oscillations in carotid diameter that are related with low-frequency heart rate oscillations, further supporting the relevance of spontaneous methods to baroreflex physiology.

6. No BRS estimation technique, including drug injections, can produce stable numbers due to the physiological variability in BRS. Thus BRS estimates provided by only a few drug injections may be less reliable than spontaneous estimates assessed by averaging data over a sufficiently long time period.

7. Lipman et al’s paper also faces other methodological problems: patients selection criteria, excessive focus on subjects with low baroreflex gain in whom a decrease in the between-method correlation is mathematically expected given the larger bias of low BRS estimates; sequential performance of drug injections with insufficient time to resume baseline conditions; use of different algorithms to derive pharmacological and spontaneous BRS values; and improper use of the Bland-Altman approach to assess between-method discrepancies.

The conclusions of Lipman et al should thus be carefully reconsidered and the finding of quantitative discrepancies between pharmacological and spontaneous BRS values should not be interpreted as a difference between “real” and “biased” BRS estimates but rather as the expected difference in result of methods that explore baroreflex function from different but complementary perspectives.

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