Correlation analysis in repeated measures design

Sir,

We read with interest the article by Arimanickam and Manikandan detailing the correlation of changes in systolic pressure variation (SPV), pulse pressure variation (PPV) and trans-oesophageal echocardiography-derived stroke volume variation (SVV), at multiple time points, after a 1 gm/kg intravenous infusion of mannitol in neurosurgical patients undergoing elective supratentorial craniotomies.[1]

Within the context of the primary aim of the article to study correlation of the three variables over time, the statistical analysis used appears flawed at multiple levels. First, the authors demonstrated a significant change of the parameters over time for all the variables studied, which is basically a repeated measures design. The test used herein has been described as one-way ANOVA in the Table 2, which is an incorrect method for this design.[1] The correct method should have been a one-way repeated measures ANOVA, which partitions the error sum of squares (of one-way ANOVA) to have a separate between-subjects error term. The degrees of freedom for calculation of the F-statistic are also calculated differently.

Second, the authors describe the correlation between variables separately at each time point by applying Pearson's product–moment correlation. The first analysis is incorrect in that it ignores the dependencies between each pair of time points (i.e., finding a significant correlation in the previous time point increases the chances of finding the same in the next time point) and also ends up conducting multiple tests on the same patient data set, which potentially inflates alpha error. Third, they conduct a similar analysis of the pooled data of all patients, which basically violates the independence of observation assumption which is integral to conducting a Pearson's correlation.

The correct method of conducting correlation analysis in repeated measures design has not been rigorously described till date. One potential method includes creation of summary statistic for each variable in each patient, which incorporates the information regarding change of the variable over time, and which may be used to conduct the correlation analyses. Such summary statistics may include peak value, trough value, mean of values of all time points, duration of time during which the variable was above or below a specific threshold, an area under curve calculation for variable over time using the sum of trapezoidal rule or using slope of change of variable over time in each patient. The choice of the summary statistic must be commensurate with the information needed to be gleaned from the data.[2] For example, in this specific study, area under curve or the slope of change of variable over time may have worked out quite well.

Another potential method would be using a linear mixed-effects model design, which essentially models the variability in dependent variable (here SVV) as a sum of fixed-effects (variability in PPV/SPV) and random-effects (inter-subject variability, due to differing baseline values – random intercept, and differing changes in dependent variables over time – random slope) models. If the fixed-effects model is found to be significant after accounting for the random-effects model, the correlation may be said to be significant, while using the fixed-effect estimates *in lieu* of coefficient to describe change in dependent variable with unit change in the independent variable.[3]

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Deepti Srinivas, Dhritiman Chakrabarti

Department of Neuroanaesthesia and Neurocritical Care, National Institute of Mental Health and Neuro Sciences, Bengaluru, Karnataka, India

Address for correspondence:
Dr. Deepti Srinivas,
Department of Neuroanaesthesia and Neurocritical Care, 3rd Floor, Faculty Block, National Institute of Mental Health and Neuro Sciences, Hosur Road, Bengaluru - 560 029, Karnataka, India.
E-mail: bsdeepti@gmail.com

REFERENCES

1. Arimanickam G, Manikandan S. Correlation of systolic pressure variation, pulse pressure variation and stroke volume variation in different preload conditions following a single dose mannitol infusion in elective neurosurgical patients. J Neuroanaesth Crit Care 2016;3:219-26.
2. Matthews JN, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. BMJ 1990;300:230-5.
3. Roy A. Estimating correlation coefficient between two variables with repeated observations using mixed effects model. Biom J 2006;48:286-301.

Access this article online	
Quick Response Code:	Website: www.jnaccjournal.org
	DOI: 10.4103/jnacc.jnacc_38_17

How to cite this article: Srinivas D, Chakrabarti D. Correlation analysis in repeated measures design. J Neuroanaesthesiol Crit Care 2017;4:185-6.