Forearm plethysmography: does the right arm know what the left is doing?

John R. PETRIE*, Colin PERRY, Stephen J. CLELAND, Lilian S. MURRAY, Henry L. ELLIOTT and John M. C. CONNELL
University Department of Medicine and Therapeutics, Western Infirmary, Glasgow G11 6NT, U.K.

We read with interest the recent Comment by Chin-Dusting et al. [1] entitled ‘Human forearm plethysmography: methodology, presentation and analysis’ which addresses some important issues in the interpretation of studies using this technique. As the authors acknowledge, even when experimental conditions are carefully controlled, forearm blood flow (FBF) varies constantly in response to changes in sympathetic nervous system activity, mental arousal and ambient temperature, as well as in response to any intra-arterially infused test substance. They state that error is minimized when FBF is measured bilaterally (rather than unilaterally), with results expressed as percentage change in FBF ratio (infused/control arm). However, they appear to imply that this method is preferred on purely theoretical grounds and that it was described by Benjamin et al. [2] in 1995, when in fact it is supported by experimental evidence and was advocated much earlier. We note that FBF is measured unilaterally in their own studies [3].

Use of the contralateral arm as a concurrent control was first described in elegant experiments by Greenfield and Patterson in 1954 [4]. To our knowledge the only published evidence of the superiority of this technique is a study in which we examined the reproducibility (between-day intra-subject variability) of FBF in nine healthy, unselected male volunteers attending on three separate study days for identical protocols [5]. Coefficients of variation were derived from two-way analysis of variance (ANOVA) using terms for subject and day (MINITAB INC, State College, PA, U.S.A.). The square root of the error term of the adjusted mean squares from the ANOVA table (MSE_{TOTAL}) was divided by the mean of the observations and expressed as a percentage [6]. The Shapiro–Wilks test was used in order to check that residuals from ANOVA were Normally distributed.

Using these methods, we demonstrated (for example) that while FBF measured at rest in one arm on three separate occasions in nine individuals had a coefficient of variation (CV) of 31–39%, the CV for the FBF ratio was 19%. The corresponding values for forearm vascular resistance (FVR) and the FVR ratio were 27–29% and 14% respectively [5].

In response to requests from other workers in the field, we have recently completed ‘simulation’ analyses of these data in order to determine whether this apparent improvement in reproducibility is statistically significant. For each CV, 100 mean values [from N(mean, S.E.M.)] and 100 S.D.s were simulated (MINITAB) where N denotes a normal distribution. Each S.D. was simulated by first of all simulating n observations from an N(0, MSE_{TOTAL}) distribution and calculating the S.D. where n = 27. This allowed 100 simulated CVs to be calculated for each actual CV and hence a mean, S.D. and reference range (mean ± 2 S.D.) for the mean CV. Assuming (conservatively) that CVs to be compared are independent, then the S.D. of the difference (S.D.D.) of two observations is equal to the square root of the sum of the variance of the observations. This statistic was therefore calculated for each comparison between unilateral (left) and bilateral (ratio) CVs, and used to generate 95% confidence intervals for the differences (by multiplying each S.D.D. by 1.96 and adding and subtracting the resulting value from the difference between the CVs). Using this method, both the FBF ratio and the FVR ratio were more reproducible than unilateral FBF and FVR (P < 0.05).

Thus the longstanding method of using the contralateral arm as a concurrent control in studies using forearm plethysmography combined with intra-arterial infusions can now be recommended on the basis of experimental evidence (although data should also be plotted for individual arms to check for systematic bias). We agree with Chin-Dusting et al. [1] that plethysmography is an extremely useful technique in clinical investigation (provided that its limitations are taken into account).

Key words: bilateral, forearm blood flow, forearm vascular resistance, plethysmography, reproducibility.

Abbreviations: ANOVA, analysis of variance; CV, coefficient of variation; FBF, forearm blood flow, FVR, forearm vascular resistance; MSE_{TOTAL}, error term of the adjusted mean squares; S.D.D., S.D. of the difference.

Correspondence: Dr J. R. Petrie (e-mail jrp1s@clinmed.gla.ac.uk).
account in the experimental design), and we are pleased that they now recognize the merits of the bilateral technique.

REFERENCES


Received 10 June 1999