# On-line Supplement

# Relative plasma volume monitoring during hemodialysis aids the assessment of dry-weight

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## *Statistical Methods*

### *Relative Plasma Volume*

In the mixed model, the random effects were subject and time elapsed. An unstructured covariance matrix allowed the slopes and intercepts to vary independently of each other and maximal likelihood estimation was obtained. The visits were also modeled as random effects to account for the study participation effect. Since the RPV was log transformed, the coefficients on the slope terms in this model were converted back to percent change in RPV per hour by using the following formula: $100 \times (1-\exp(\beta))$ where $\beta$ is the coefficient on the reading time.

Most dialysis patients have measurement of volume through sequential changes in post-dialysis weight. The change from baseline to final visit in post-dialysis weight was calculated for each patient. To ascertain the effect of change from baseline in weight over 8 weeks on the RPV slopes we incorporated the change in weight from baseline in the above statistical model. We did so by forming this change from baseline in weight into quartiles. Whether the patient was in the control group or ultrafiltration group, each patient was classified into quartiles of body-weight change. We then tested the significance of quartiles on relative plasma volume slopes. If body weight change was the sole mediator of changes in RPV slopes, we reasoned that adjustment for quartiles of change in body weight will remove the relationship between RPV slope and probing dry-weight.

We next tested the effect of RPV slopes at baseline on subsequent change in RPV slopes. RPV slopes at baseline were calculated for each patient by ordinary least squares regression and this value was used to generate quartiles from the steepest RPV slope (quartile 1) to flattest RPV slope (quartile 4). The effect of these quartiles was then tested in a mixed model with the dependent variable being the RPV slope.

To test the combined effect of baseline RPV slopes and subsequent weight loss on RPV slopes we first dichotomized the RPV slopes and weight loss above and below median. Those above the median had flatter RPV slopes and greater weight loss. To predict RPV slopes, we created a model that included all main effects up to four-way interaction between 4 independent factors: groups (control vs ultrafiltration), visits (baseline vs final), median RPV slope (steeper vs flatter), and median weight loss (less vs more). A mixed effects model was used to calculate the slopes. The random effect part of the equation was the one described earlier. To test the significance of the two factors, RPV slope and weight loss, we first created models without either of these factors and then a model with one of these factors. The model fit of the two nested models were evaluated using the likelihood ratio test. We similarly compared the 2 models with 3 factors (group, visits, and weight; or group, visits and RPV slopes) with a model with all 4 factors using the likelihood ratio test.

### *Relationship between Relative Plasma Volume and Ambulatory BP*

Next we calculated the RPV slopes with ordinary least squares regression for each individual at baseline. These RPV slopes were divided into quartiles. These slope quartiles were used as independent variables to predict 44-hour interdialytic ambulatory systolic BP and changes in ambulatory systolic BP on probing dry-weight. Since RPV

monitoring was performed at baseline at 8 weeks, the corresponding ambulatory BP was used for these analyses. The changes in ambulatory BP were modeled using a mixed model. In this mixed model, ambulatory systolic BP was the dependent variable. Independent variables were the following: 1) indicator variables for group (ultrafiltration and control), visits (baseline and 8 weeks), and their interaction; and 2) interactions of these indicator variables with quartiles of RPV slope. The random effects were subjects and visits and an unstructured covariance matrix was used.

To explore the combined effect of baseline RPV slopes and change in RPV slopes on BP we dichotomized the RPV slopes at baseline about the median. We then calculated the RPV slopes at end of trial and dichotomized them about the median. We produced a 4 way interaction model with group, visits, baseline RPV slopes, and end of study RPV slopes as independent variables to predict 44-hour interdialytic ambulatory systolic BP.

**Table S1: Relative plasma volume (RPV) slopes (%/hr) by quartiles of RPV at baseline.**

| Group/Time | Q1 | Q2 | Q3 | Q4 | Heterogeneity between quartiles (p) |
|---|---|---|---|---|---|
| Control Baseline | 2.84 (0.16) | 1.94 (0.27) | 1.04 (0.16) | 0.31 (0.15) | <0.0001 |
| CFB control | -0.54 (0.02) | 0.01 (0.03) | -0.08 (0.01) | 0.67 (0.02) | <0.0001 |
| pairwise p for change | <0.0001 | >0.2 | <0.0001 | <0.001 | |
| UF Baseline | 2.99 (0.12) | 1.69 (0.11) | 0.98 (0.13) | 0.2 (0.14) | <0.0001 |
| CFB UF | -0.17 (0.01) | 0.13 (0.02) | 0.2 (0.02) | 1.19 (0.02) | <0.0001 |
| pairwise p for change | <0.0001 | <0.0001 | <0.0001 | <0.0001 | |
| CFB UF- CFB control | 0.37 (0.02) | 0.12 (0.03) | 0.28 (0.03) | 0.52 (0.03) | <0.0001 |
| p for delta-delta | <0.0001 | <0.001 | <0.0001 | <0.0001 | |

Q1-Q4 represent quartiles of RPV at baseline. Q1 represents the steepest RPV slope. CFB = change from baseline, UF = ultrafiltration, RPV = Relative plasma volume.

**Table S2: 44 hour ambulatory systolic BP by quartiles of RPV at baseline.**

| Group/Time | Q1 | Q2 | Q3 | Q4 | Heterogeneity between quartiles (p) |
|---|---|---|---|---|---|
| Control Baseline | 145.1 (2.8) | 138.8 (4.5) | 150.6 (2.6) | 145.8 (2.5) | 0.12 |
| CFB control | -10.1 (4.8) | -10.5 (7.6) | -4 (4.1) | -9.7 (4.4) | >0.20 |
| pairwise p for change | 0.017 | 0.082 | 0.16 | 0.013 | |
| UF Baseline | 142.6 (2.1) | 145.6 (1.8) | 148.4 (2.2) | 148.3 (2.2) | 0.17 |
| CFB UF | -9.6 (3.4) | -13.8 (3) | -15.1 (3.6) | -22.3 (3.8) | 0.09 |
| pairwise p for change | 0.002 | <0.0001 | <0.0001 | <0.0001 | |
| CFB UF- CFB control | 0.5 (5.9) | -3.2 (8.1) | -11.1 (5.4) | -12.6 (5.8) | * |
| p for delta-delta | >0.2 | >0.2 | 0.02 | 0.014 | |

Q1-Q4 represent quartiles of RPV at baseline. Q1 represents the steepest RPV slope. CFB = change from baseline, UF = ultrafiltration, RPV = Relative plasma volume. * Test of linear trend <0.05 in combined control and UF groups