Supplemental Digital Content

**How to perform indexing of Extravascular Lung Water? A validation study**

Stefan Wolf, Alexander Riess, Julia F. Landscheidt, Christiano B. Lumenta, Ludwig Schürer and Patrick Friederich

This online supplement provides the results of additional statistical analyses and contains three figures (E1 to E3).

1. **EVLWI\textsubscript{PBW} data per patient**
2. **EVLW raw data**
3. **EVLW indexed to body surface area, calculated either with actual or predicted body weight** (EVLWI\textsubscript{BSA(Act\textsubscript{BW})} and EVLWI\textsubscript{BSA(PBW)}, respectively)
1. **EVLWI\textsubscript{PBW} data per patient**

EVLWI\textsubscript{PBW} data showed no Gaussian distribution. The scatter increased with increasing mean of EVLWI\textsubscript{PBW}, calculated from a series of seven measurements per patient at predefined time points. In analogy to the repeatability coefficient, the scatter of the measurements in a single patient may be described by dividing their standard deviation by their mean. The median scatter of a measurement series was 13.7\% (IQR 9.5\% to 21.3\%, range 2.4\% to 49.4\%).

**Figure E1: All EVLWI\textsubscript{PBW} measurements, ordered by mean EVLWI\textsubscript{PBW} per patient**

![Figure E1](image)

The X axis represents single patients. Females are shown with yellow and males with blue dots. The dashed horizontal line represents the mean of all EVLWI\textsubscript{PBW} measurements in males, the dotted horizontal line the mean in females.
2. *EVLW raw data*

Females had a median EVLW of 483 ml (interquartile range 408 to 576 ml, range 272 to 1349 ml). Males had a median EVLW of 544 ml (interquartile range 486 to 620 ml, range 304 to 1367 ml). Mean EVLW was 516 (SD 165) ml in females and 572 (SD 139) ml in males. Univariate difference between genders was significant (P < 0.0001).

Multivariate analysis of EVLW showed no significant relationship for age and actual body weight (P = 0.56 and P = 0.29, respectively). Both body height and gender showed trends related to EVLW (P = 0.14 and P = 0.15), without significant interaction (P = 0.7). After removal of either one of these two factors from multivariate analysis, the remaining term gained significance (P = 0.03 and P = 0.03, respectively), besides fluid balance. Therefore, both factors were used for calculation of confidence intervals of normal values (Figure E2).

Per liter fluid gain, EVLW increased linearly by a factor of 1.035 (95 % CI: 1.0 to 1.07, P = 0.034) or 3.5 %.
Both covariates combined show a significant relationship with EVLW. Female data are represented by yellow color and dotted lines, male data by blue color and dashed lines. Inner lines with shaded areas correspond to the regression mean for all data with its 95% confidence interval for males and females, respectively. The outer lines denote the 95% confidence interval for multiple measurements in a single patient.
3. *EVLW indexed to body surface area*

By currently used convention, BSA calculated with actual body weight is used for indexing cardiac output data, while BSA based on predicted body weight is used for indexing the preload parameter global end-diastolic volume. Therefore, both methods of indexing may be considered for EVLW data as well.

Body surface area was computed using predicted body weight and the Du Bois equation (E1):

\[ BSA = 0.007184 \times \text{length}_{cm}^{0.725} \times \text{weight}_{kg}^{0.425}. \]

In this formula, weight was replaced with either actual or predicted body weight, yielding EVLWI_{BSA(ActBW)} or EVLWI_{BSA(PBW)}.

Analyzed multivariately, EVLWI_{BSA(PBW)} was inversely related to body height (P = 0.03). No significant relationships were found for age, sex or actual body weight (P = 0.53, P = 0.43, P = 0.26, respectively).

EVLWI_{BSA(ActBW)} was inversely related to actual body weight (P = 0.002) in multivariate analysis. No significant relationships were found for body height, age or sex (P = 0.49, P = 0.64, P = 0.22, respectively).

*Reference for the Supplemental Digital Content:*

Figure E3A: Statistically significant relationship of a patients’ measured body height to EVLW indexed to body surface area calculated with predicted body weight (EVLW_{BSA(PBW)}).

Female data are represented by yellow color and dotted lines, male data by blue color and dashed lines. Inner lines with shaded areas correspond to the regression mean for all data with its 95% confidence interval for males and females, respectively. The outer lines denote the 95% confidence interval for multiple measurements in a single patient.
Figure E3B: Statistically significant dependency of EVLW indexed to body surface area calculated with actual body weight (EVLWI_{BSA(ActBW)}) to a patients’ measured weight.

Female data are represented by yellow color and dotted lines, male data by blue color and dashed lines. Inner lines with shaded areas correspond to the regression mean for all data with its 95% confidence interval for males and females, respectively. The outer lines denote the 95% confidence interval for multiple measurements in a single patient.