Fluid Overload and Mortality: Comparison of Bioimpedance Spectroscopy-Derived Markers in a Large International Hemodialysis Population

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Introduction

Chronic fluid overload in hemodialysis patients is a risk factor for death. We aimed to determine which marker of fluid overload determined by bioimpedance spectroscopy (BIS) best predicts mortality.

Methods

- 31,955 patients treated by a large dialysis care organization (NephroCare) in 25 countries with at least one BIS-measurement using the Body Composition Monitor (BCM, Figure 1) within 90 days of initiating hemodialysis or hemodiafiltration were included.
- Mean follow-up period: 392 days
- Over this interval, BCM-derived measures of fluid overload (predialysis [FOpre], postdialysis [FOpost], averaged over the dialysis cycle [TAFO], Table 1) were averaged.
- Associations with all-cause mortality determined by Cox regression models.

Table 1. BCM-derived markers of fluid overload.

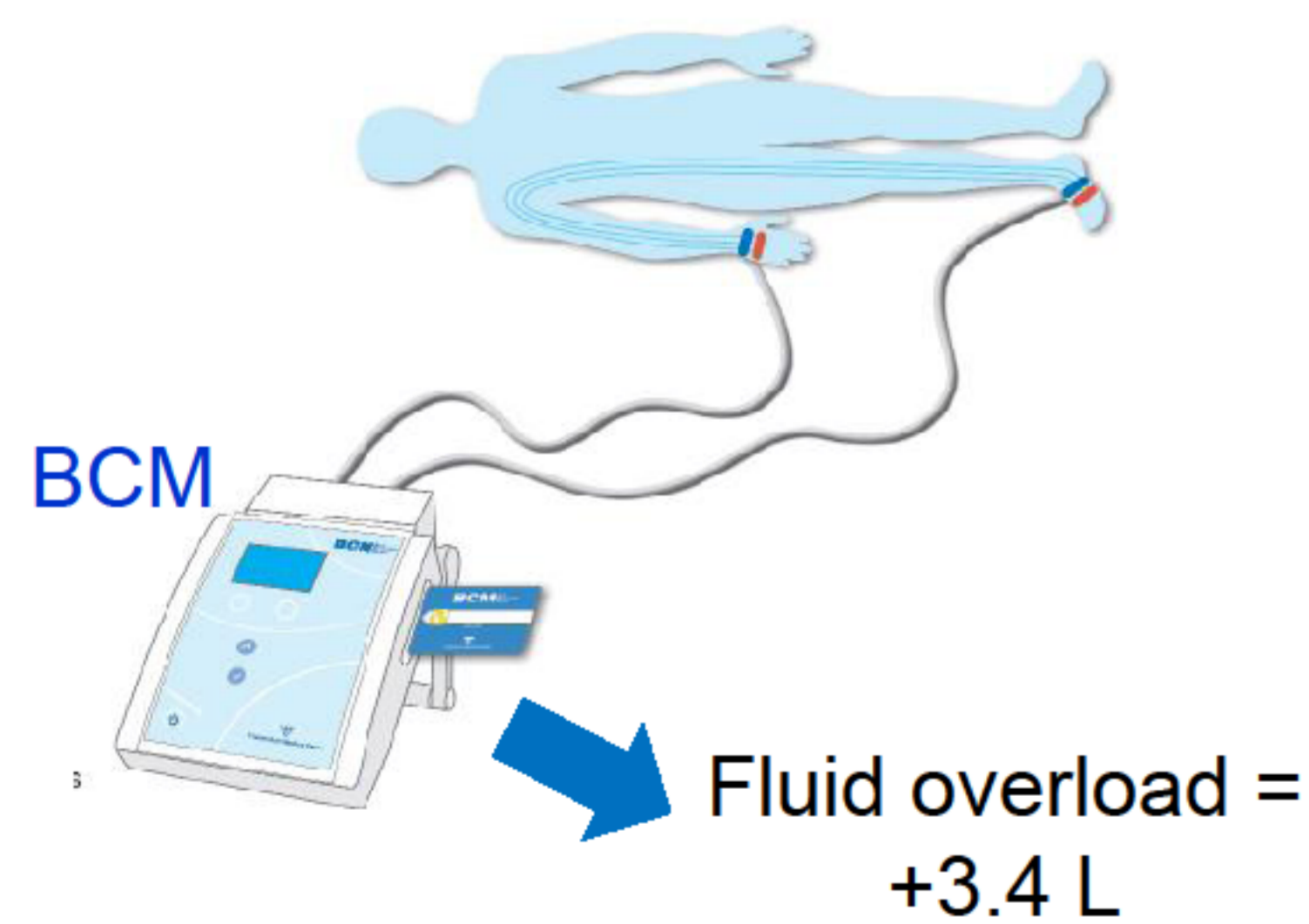| Fluid Overload predialysis	taken directly from the BCM device before the hemodialysis session
Time-averaged Fluid Overload	Average between FOpre and FOpost, using predialysis BCM-measurement and intradialytic weight loss (FOpre-([preweight-postweight]/2))
Fluid Overload postdialysis	fluid overload predialysis minus intradialytic weight loss (FOpre-[predialysis body weight-postdialysis body weight])

BCM

Fluid overload = +3.4 L

Figure 1. Measuring fluid overload with the Body Composition Monitor (BCM)

Table 2. Patient characteristics, by quartile of fluid overload.

Results

- Several risk factors, such as lower body mass index, age and comorbidities, increased from lower to higher fluid overload quartiles (Table 2).
- Patients in the third and fourth quartiles of all FO measurements (Figure 2) had higher mortality risk, which remained significant after extensive adjustments.
- Regarding the lowest quartile as the reference, the adjusted hazard ratio for mortality in the highest quartile was greater for FOpost (HR=4.45, 95% confidence interval [CI] 4.03-4.92) compared with TAFO (HR=3.86, 95% CI 3.50-4.27), FOpre (HR=3.24, 95% CI 2.94-3.57) and relative FO measures.
- The difference in mortality risk between the quartiles was best discriminated by Fopost (Figure 3).
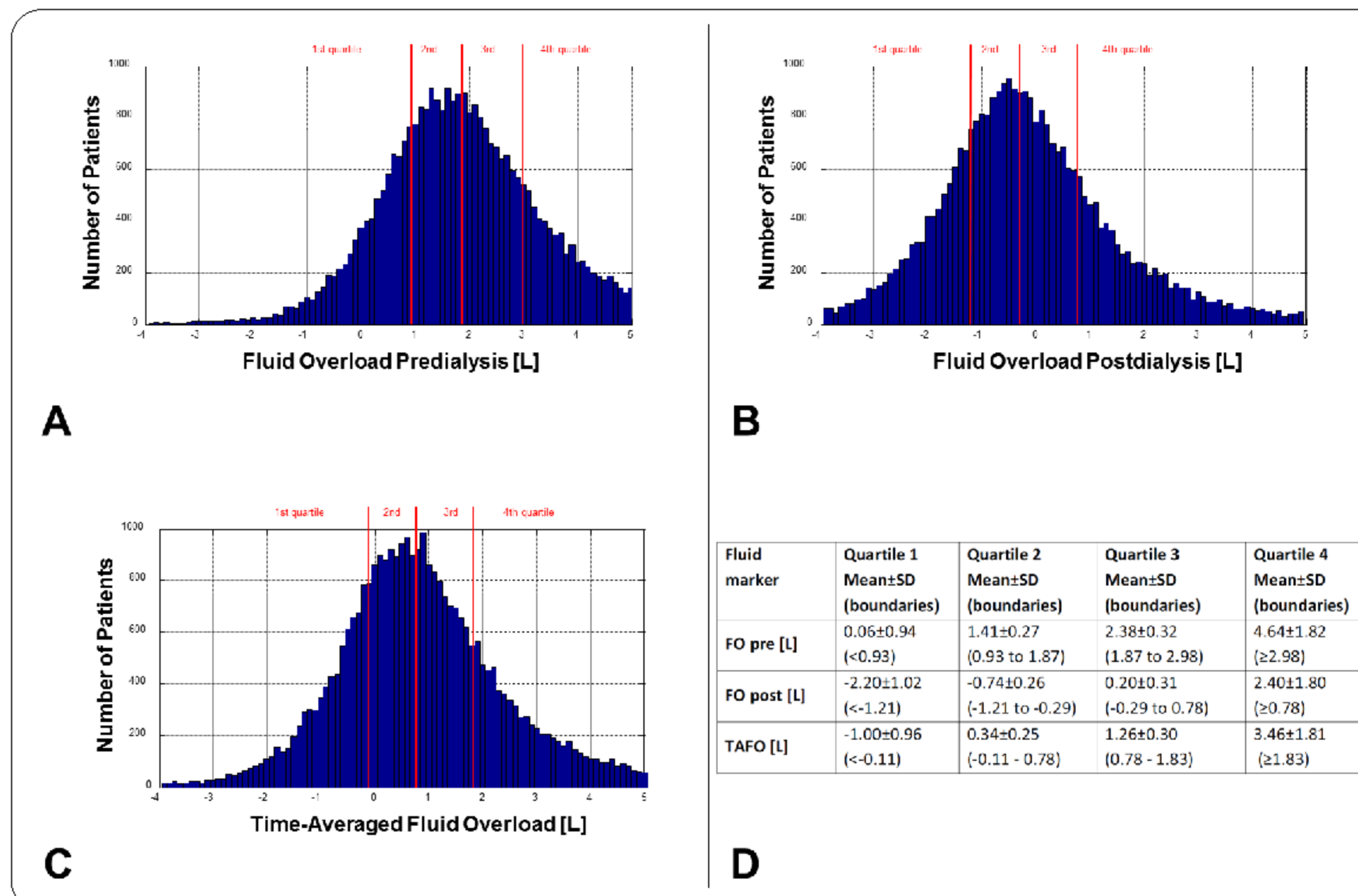

Figure 2: Distribution of fluid volume status

A-C: Three different markers of fluid volume status were used to depict the fluid distribution in the study population.
D: Means ± standard deviations and boundaries from lowest to highest fluid overload quartile, by the respective fluid marker.
Abbreviations: FO pre=fluid overload predialysis, FO post=fluid overload postdialysis, TAFO=time-averaged fluid overload, L=liter, SD=standard deviation.
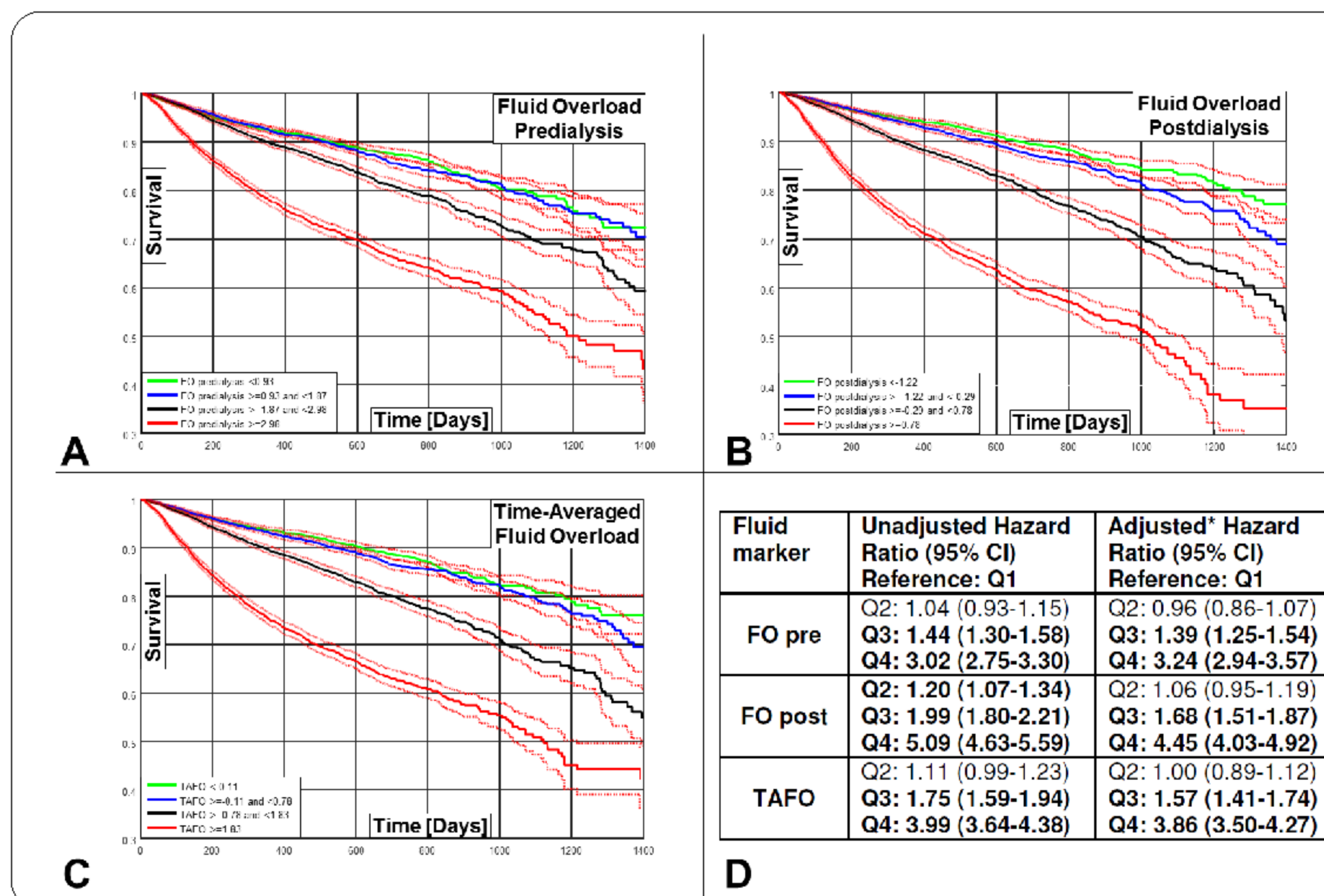
Fluid marker	Quartile 1 Mean±SD (boundaries)	Quartile 2 Mean±SD (boundaries)	Quartile 3 Mean±SD (boundaries)	Quartile 4 Mean±SD (boundaries)
FO pre [L]	0.06±0.94 (<0.93)	1.41±0.27 (0.93 to 1.87)	2.38±0.32 (1.87 to 2.98)	4.64±1.82 (≥2.98)
FO post [L]	-2.20±1.02 (<-1.21)	-0.74±0.26 (-1.21 to -0.29)	0.20±0.31 (-0.29 to 0.78)	2.40±1.80 (≥0.78)
TAFO [L]	-1.00±0.96 (<-0.11)	0.34±0.25 (-0.11 - 0.78)	1.26±0.30 (0.78 - 1.83)	3.46±1.81 (≥1.83)

Figure 3: Fluid overload and survival

A-C: Unadjusted Kaplan-Meier survival curves, by quartile of fluid overload. D: Mortality hazard ratios and 95% confidence intervals. Quartiles (Q) 2, 3 and 4 were compared with Q1 (reference).
*Adjusted for age, gender, Kt/V, diabetes status, peripheral vascular disease, coronary artery disease, chronic heart failure, systolic and diastolic blood pressure.
Abbreviations: FO pre=fluid overload predialysis, FO post=fluid overload postdialysis, TAFO=time-averaged fluid overload, CI=confidence interval.

Fluid marker	Unadjusted Hazard Ratio (95% CI) Reference: Q1	Adjusted* Hazard Ratio (95% CI) Reference: Q1
FO pre	Q2: 1.04 (0.93-1.15) **Q3: 1.44 (1.30-1.58)** **Q4: 3.02 (2.75-3.30)**	Q2: 0.96 (0.86-1.07) **Q3: 1.39 (1.25-1.54)** **Q4: 3.24 (2.94-3.57)**
FO post	**Q2: 1.20 (1.07-1.34)** **Q3: 1.99 (1.80-2.21)** **Q4: 5.09 (4.63-5.59)**	Q2: 1.06 (0.95-1.19) **Q3: 1.68 (1.51-1.87)** **Q4: 4.45 (4.03-4.92)**
TAFO	Q2: 1.11 (0.99-1.23) **Q3: 1.75 (1.59-1.94)** **Q4: 3.99 (3.64-4.38)**	Q2: 1.00 (0.89-1.12) **Q3: 1.57 (1.41-1.74)** **Q4: 3.86 (3.50-4.27)**

Parameter	Quartile 1	Quartile 2	Quartile 3	Quartile 4
FOpost [L] (cutoff)	-2.2±1.02 (<-1.21)	-0.74±0.26 (-1.21 – -0.29)	0.2±0.31 (-0.29-0.78)	2.4±1.8 (≥0.78)
# of meas./surv. time [days]	11.1/446.7 =0.0248	12.6/455.2 =0.0277	11.0/398.2 =0.0276	6.7/266.9 =0.0251
Age [years]	58.0±15.8	61.6±16.2	63.4±15.6	62.6±14.9
BMI [kg/m²]	28.6±5.9	26.4±5.1	25.5±4.8	25.2±5.0
Gender [%male]	52.1%	55.3%	60.3%	70.3%
Diabetes [%]	26.3%	28.5%	32.5%	38.8%
CHF [%]	11.2%	14.2%	16.5%	17.6%
PVD [%]	6.2%	9.7%	10.9%	9.8%
CAD [%]	4.0%	5.6%	6.0%	6.4%
Kt/V	1.6±1.3	1.6±1.3	1.5±0.5	1.4±1.1
BPsys [mmHg]	137.9±17.8	139.3±17.2	139.6±18.3	140.7±19.6
BPdia [mmHg]	73.5±10.9	72.6±11.0	72.3±10.9	73.4±10.8
Albumin [g/l]	3.9±0.4	3.9±0.4	3.8±0.4	3.5±0.5
Hemogl. [g/l]	11.0±1.2	10.9±1.2	10.6±1.3	10.0±1.5
IDWG [kg]	2.5±0.8	2.2±0.7	2.1±0.8	2.0±0.8

Conclusion

FOpost is the strongest and most sensitive BIS-based predictor of mortality and should be used clinically as well as in the design of interventional studies investigating fluid overload removal in hemodialysis patients.

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