

Dynamics of Fluid Status and Inflammation in an International Hemodialysis Patient Cohort

Marijke JE Dekker MD^{1,2}, Daniele Marcelli MD, PhD³, Bernard J Canaud MD, PhD³, Paola Carioni³, Yuedong Wang PhD⁴, Aileen Grassmann PhD³, Constantijn JAM Konings MD PhD², Peter Kotanko MD, FASN^{5,6}, Karel M Leunissen MD, PhD¹, Nathan W Levin MD^{5,7}, Frank M van der Sande MD, PhD¹, Xiaoling Ye⁵, Vaibhav Maheshwari, PhD⁵, Len A Usvyat PhD^{5,8}, Jeroen P Kooman MD, PhD¹ for the MONDO Initiative.

¹Department of Internal Medicine, Division of Nephrology, Maastricht University Medical Center, Maastricht, The Netherlands; ²Department of Internal Medicine, Division of Nephrology, Catharina Hospital Eindhoven, The Netherlands; ³Fresenius Medical Care, Bad Homburg, Germany; ⁴University of California, Santa Barbara, California, United States; ⁵Renal Research Institute, New York, United States; ⁶Department of Medicine, Division of Nephrology, The Mount Sinai Hospital, New York, United States; ⁷Icahn School of Medicine at Mount Sinai Health System; ⁸Fresenius Medical Care North America, Waltham, United States.

Introduction

- In hemodialysis patients fluid overload (FO) is a predictor of all-cause mortality and a relation with inflammation has been observed in previous studies.
- The magnitude and nature of this interaction and the effects of moderate FO and fluid depletion on survival are still unclear.

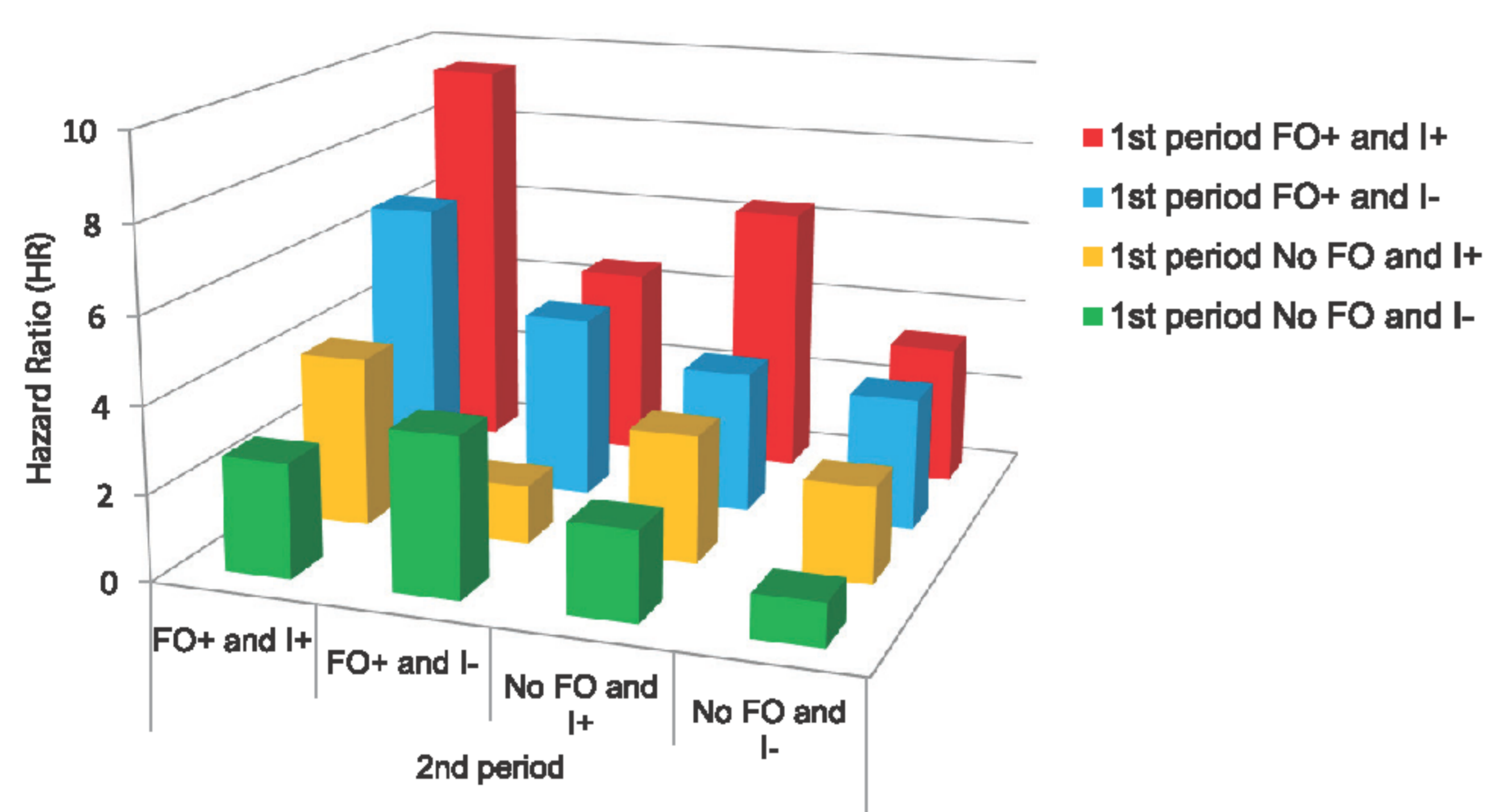
Methods

- We conducted a retrospective cohort study in the European subset of the MONDO-Initiative database.
- Fluid status was assessed using bioimpedance and inflammation by C-reactive protein (CRP) measurements.
- We included patients with at least one measurement each during baseline. All-cause mortality was recorded during 12 months follow-up.
- In a second analysis patients were divided into 4 groups based on average fluid and inflammation status during two consecutive 3 months periods, in which the change or persistency of both variables was observed and all-cause mortality was noted during a subsequent 6 months follow up period in this analysis.

Results

- We included 8883 patients (age 63 years, 57.2% male).
- FO was associated with risk of mortality, already apparent at moderate levels of pre- and post-dialysis FO (> +1.1L to +2.5L; hazard ratio (HR) 1.64 (95% confidence interval (CI) 1.35-1.98) and HR 1.72 (95% CI 1.45-2.05) respectively).
- Likewise, pre-dialysis FD ($\leq -1.1L$; HR 2.03 (95% CI 1.32-3.12)) was associated with increased mortality risk, whereas post-dialysis FD was associated with a survival benefit HR 0.74 (95% CI 0.62-0.90).
- In patients with severe pre-dialysis FO (> +2.5L to +5.0L) but without inflammation (CRP level ≤ 6.0 mg/L), the HR was 3.09 (95% CI 2.20-4.36) compared to an HR of 6.02 (95% CI 4.41-8.23) when inflammation was present.
- In the subset analysis the association with mortality was the highest in the groups of patients with persistent FO and inflammation (adjusted HR 9.44 (95% CI 5.67-15.72)), this increased risk of death remained elevated even after resolving both fluid overload and inflammation (HR 3.28 (95% CI 1.13-9.52)).
- The presence of inflammation was not significantly related with the occurrence of FO, also the reverse relation was not statistically significant.

Figure 1 Dynamics of fluid status and inflammation and survival during 6 months follow up



Legend: results of a cox proportional hazards model adjusted for age, gender, dialysis vintage, access type (arterio-venous versus catheter access), region, body mass index, normalized Protein Catabolic Rate (nPCR), ultrafiltration rate (mL/h/kg), diabetes mellitus, congestive heart failure, peripheral vascular disease and the presence of a malignancy. FO+: fluid overload (pre-dialysis OH >+2.5L), I+: inflammation (CRP levels above 6.0 mg/L). no FO: no fluid overload (pre-dialysis OH <+2.5L), I-: no inflammation (CRP levels below 6.0 mg/L)

Conclusions

- Both pre-dialysis and post-dialysis FO and FD are associated with an increased risk of death, whereas post-dialysis FD is associated with a survival benefit.
- The concurrent presence of FO and inflammation is associated with the highest risk of death.
- Both parameters remain significant predictors of outcome during a 6 months period even after improvement.