Medium Cut-Off Versus High-Flux Hemodialysis Membranes and Clinical Outcomes: A Cohort Study Using Inverse Probability Treatment Weighting

Molano AP, Hutchison CA, Sanchez R, et al. Medium Cut-Off Versus High-Flux Hemodialysis Membranes and Clinical Outcomes: A Cohort Study Using Inverse Probability Treatment Weighting. *Kidney Medicine*. 2022. In Press. doi: https://doi.org/10.1016/j.xkme.2022.100431.

BACKGROUND

Despite advances in the field of chronic hemodialysis (HD) and improvements in morbidity and mortality, outcomes for chronic HD patients are far from optimal. Improved clearance of uremic toxins may reduce their adverse effects on biological systems and lead to improved outcomes. Recent data suggest that increased removal of large middle molecules may improve clinical outcomes through impact on inflammation and atherosclerosis. Advances in bioengineering have allowed development of a novel medium cut-off (MCO) membrane (**Theranova**® 400/500, Baxter) that improves clearance of large middle-molecules 25 kDa and above.

OBJECTIVE

Determine whether there are differences in clinical outcomes when chronic HD patients are treated with MCO membranes compared to high-flux (HF) membranes.

METHODOLOGY

This was a retrospective, observational, multicenter, cohort study of patients undergoing HD (defined as received HD for 90 days) in Colombia. Patients were included from Baxter Renal Care Services network of renal between September 1, 2017 to November 30, 2017, with follow up to November 30, 2019. Enrollment occurred immediately for patients in the MCO cohort once switched to this new membrane type. Inclusion criteria included: age >18 years; receiving expanded hemodialysis (HDx) using an MCO membrane (**Theranova**®, Baxter, Deerfield, IL, USA) or conventional HD using HF membrane for a minimum of 4 hours 3 times per week. Patients in both cohorts were included from the same dialysis clinics and membrane allocation was not done by predetermined methods but rather by decisions by each individual clinician. Standard dialyzers available in renal clinics were used. Exclusion criteria were life expectancy of less than six months, active infection, metastatic disease, or a Charlson comorbidity index greater than eight.

Patients were divided into two cohorts according to the membrane used at the time of enrollment: 1) MCO group or 2) HF group. Once a patient had been included in one of the two cohorts, the clinical teams were instructed not to change the membrane type unless determined by a medical decision or patient request.

OUTCOMES AND ANALYSIS

Primary outcome: hospitalization rate from any cause and hospitalization days per patient-year.

Secondary outcomes: non-fatal cardiovascular events (any hospitalization event for causes predefined in the International Classification of Diseases 10 as cardiovascular); time to death survival analysis from any cause; changes in serum albumin levels during follow-up.

Inverse Probability of Treatment Weighting (IPTW) using a propensity score was used to control differences between groups. The propensity score for each subject was calculated from a logistic regression model that included clinical and demographic variables as predictors of the exposure status such as age, sex, race, dialysis duration, CKD cause, hypertension history, diabetes history, cardiovascular disease history, Charlson comorbidity index, Karnofsky scale, urine output ml/day, BMI, serum albumin, hemoglobin, parathormone intact, phosphorous, potassium, Kt/V single pool, and normalized protein catabolic rate and the research site location. The IPTW for each individual subject was then calculated and the balance between exposed and unexposed groups in the weighted sample was evaluated based on descriptive methods (standardized differences, with a target value of < 0.1, and variance ratios) and inferential methods (over identification test for covariate balance), and the effect of the exposure on each outcome was estimated using robust standard errors. For the outcome hospitalization rate and days, negative binomial regression models were used for violation of the over dispersion assumption and Akaike and Bayesian Information criteria were used to compare the models; the association was estimated with Incidence Rate Ratio (IRR). Survival time was estimated in the full sample, and the weighed population according to membrane use; the log-rank test was used to compare the equality of the survival functions in the full sample; for comparison in the weighed population, we used Cox regression. To confirm the direction of the effect, negative binomial regression models in full sample were performed.

RESULTS

Patients

A total of 1098 patients were enrolled (564 in the MCO group and 534 in the HF group); and 711 completed the total follow-up time (391 in the MCO group and 320 in the HF). Mean age was 60.3 ±14.9 years in the MCO group, and 60.8 ±15.0 years in the HF group, and 65.2% were male in the HF group and 59.6% in the HF group. The proportion of patients with diabetes mellitus was similar in the two groups, 43.6% for MCO vs. 40.1% for HF, p = 0.23. Baseline albumin levels were 4.0 g/dl for MCO vs. 4.0 g/dl for HF. After weighting using IPW, no statistically significant difference between groups in baseline characteristics was observed.

Clinical Outcomes

In the weighted sample, MCO was associated with fewer all-cause hospitalization events rate per patient-year, IR = 0.93 [95% CI 0.82–1.03] versus 1.13 [95% CI 0.96–1.30] for HF, corresponding to a significant IRR MCO/HF of 0.82 [95% CI 0.68-0.99]; p = 0.04.

There was no significant difference in hospital days; p = 0.73. Across both groups, cardiovascular events were the most frequent cause of hospitalization (28.5% MCO vs 31.1% HF).