M O N D O: MONitoring Dialysis Outcomes

Higher HDL cholesterol is associated with lower cardiovascular events while higher LDL cholesterol is associated with lower infectious events in a large international population of hemodialysis patients.

George A. Kaysen[1]; Len Usvyat [2]; Aileen Grassmann [3]; Daniele Marcelli [3]; Roberto Pecoits-Filho [4]; Cristina Marelli [5]; Frank van der Sande [6]; Yosef Haviv [7]; Albert Power [8]; Peter Kotanko [2] and the MONDO initiative.

[1] Department of Biochemistry and Molecular Medicine, UC Davis, Davis/USA; [2] Research Division, Renal Research Institute, New York/USA; [3] Fresenius Medical Care, Bad Homburg, Germany; [4] Medicina Renal, Pontificia Universidade Catolica do Parana, Curitiba/BR; [5] Fresenius Medical Care, Buenos Aires/RA; [6] Internal Medicine, Maastricht University Medical Centre,Maastricht/NL; [7] Hadassah-Hebrew University Medical Center, Jerusalem/IL; [8] Department of Medicine, Imperial College London, London/UK;

Background

The effect of lipid lowering agents on prevention of all-cause mortality decreases as renal function declines losing statistical significance in patients in End Stage Renal Disease (ESRD). Low density lipoprotein (LDL) is capable of absorbing and inactivating bacterial toxins (S Bhakdi, et.al. JBC. 1983) and human LDL can prevent endotoxin induced lethality in mice (Feingold, Infect. Immun. 1995). The second highest leading cause of death among ESRD patients after cardiovascular diseases (CVD) is infectious. We conducted this analysis to explore the relationship between blood lipid levels and both CVD and infectious outcomes.

Methods

Databases from Renal Research Institute (RRI) and Fresenius Medical Care (FMC) Europe [17 countries] were used to identify all patients with in-center treatments [1/2006-12/2012] who survived 12 months on hemodialysis (HD). Those with at least one record of high density lipoprotein (HDL), LDL and triglycerides in the first 12 months were selected (baseline).

We studied 22,746 patients. Mean clinical and laboratory parameters were computed for the first 12 months and hospitalizations and clinical events (deaths and hospitalizations) were observed in months 13 to 24 (follow up). Hospitalizations and mortality were classified as CVD or infectious. Poisson regression models were constructed to explore associations between baseline parameters and the number of CVD and infectious events in the follow up period. We adjusted for inflammation using either C-reactive protein (CRP) or neutrophil lymphocyte ration (NLR). Time to infectious death was analyzed using a Cox model.

Table 1: Risk of CVD-related events, with CRP (prediction of multiple events)

	Estimate	95% CI		p-value
Age (yrs)	0.022	0.017	0.027	<.0001
Male	0.057	-0.078	0.191	0.408
race_white	0.199	-0.459	0.858	0.553
BMI (kg/m^2)	-0.011	-0.023	0.002	0.106
Diabetes	0.584	0.454	0.715	<.0001
Albumin (g/dL)	-0.281	-0.443	-0.118	0.001
HDL (mg/dL)	-0.009	-0.015	-0.003	0.003
LDL (mg/dL)	0.001	-0.001	0.003	0.150
Triglycerides (mg/dL)	0.000	-0.001	0.001	0.982
Log CRP (mg/L)	0.011	0.007	0.014	<.0001

Table 2: Risk of CVD-related events, with NLR (prediction of multiple events)

	Estimate	95% CI		p-value
Age (yrs)	0.020	0.014	0.025	<.0001
Male	0.099	-0.040	0.238	0.163
Race White	0.352	-0.070	0.773	0.102
BMI (kg/m^2)	-0.017	-0.030	-0.003	0.014
Diabetes	0.507	0.372	0.642	<.0001
Albumin (g/dL)	-0.537	-0.695	-0.379	<.0001
HDL (mg/dL)	-0.013	-0.019	-0.007	<.0001
LDL (mg/dL)	0.001	-0.001	0.003	0.374
Triglycerides (mg/dL)	0.000	-0.001	0.001	0.926
NLR	0.034	0.015	0.053	0.000

Table 3: Risk of infection-related death (Cox model)

	Hazard Ratio	95% CI		p-value
Age (yrs)	1.043	1.026	1.059	<.0001
Male	0.796	0.555	1.142	0.216
BMI (kg/m^2)	0.963	0.928	1.001	0.054
Diabetes	1.362	0.929	1.997	0.113
Albumin (g/dL)	0.497	0.326	0.755	0.001
HDL (mg/dL)	1.001	0.987	1.016	0.860
LDL (mg/dL)	0.991	0.985	0.997	0.003
Triglycerides (mg/dL)	0.998	0.996	1.001	0.262
Log CRP (mg/L)	1.537	1.299	1.819	<.0001

Table 4: Risk of infection-related events (prediction of multiple events)

	Estimate	95% CI		p-value
Age (yrs)	0.019	0.012	0.025	<.0001
Male	-0.162	-0.327	0.004	0.056
Race_White	0.755	-0.247	1.757	0.140
BMI (kg/m^2)	-0.012	-0.028	0.004	0.153
Diabetes	0.279	0.108	0.449	0.001
Albumin (g/dL)	-0.473	-0.668	-0.277	<.0001
HDL (mg/dL)	0.001	-0.005	0.008	0.719
LDL (mg/dL)	-0.004	-0.007	-0.001	0.003
Triglycerides (mg/dL)	-0.001	-0.002	0.000	0.071
Log CRP (mg/L)	0.017	0.013	0.020	<.0001

Results:

Higher HDL was associated with fewer CVD events (deaths and hospitalizations) even after adjustment for markers of inflammation, CRP (**Table 1**) or NLR (**Table 2**). Adjustment for CRP eliminated the protective effect of HDL for cardiovascular death alone (data not shown). Higher LDL was associated with fewer infection-related deaths (**Table 3**) and infection-related events (**Table 4**), but had no relationship to CVD outcomes.

Conclusion

Higher HDL is associated with fewer CVD events, while higher LDL is associated with fewer infectious deaths and hospitalizations. These data suggests a mechanism accounting for the inverse association between LDL and mortality in the dialysis population and partially explains the lack of a decline in mortality among dialysis patients treated to reduce LDL. While both CRP and NLR, surrogates for inflammation, are associated with CVD, their interaction with the effect of HDL may differ.

51ERA-EDTA 643--SP

M) Dialysis. M8) Epidemiology, outcome research, health services research in CKD 5D.

Len Usvyat

DOI: 10.3252/pso.eu.51era.2014

Poster presented at: 51 ERA-EDTA CONGRESS AMSTERDAM 2014

PosterSessionOnline.com