Table S1. Dialysis Treatment Parameters According to Randomized Treatment Assignment

HD Characteristic	Placebo	Mannitol	P
Qb, mL/min			
$HD_{1\ (n=52)}$	200 [200, 200]	200 [200, 200]	0.30
$HD_{2\ (n=52)}$	300 [300, 300]	300 [250, 300]	0.18
$HD_{3\ (n=52)}$	400 [300, 400]	400 [350, 400]	0.74
Qd, mL/min			
$HD_{1\ (n=52)}$	400 [400, 400]	400 [400, 400]	0.35
$HD_{2\ (n=52)}$	600 [600, 600]	600 [600, 600]	0.07
$HD_{3\ (n=52)}$	800 [800, 800]	800 [800, 800]	0.34
Session length, mins			
$HD_{1\ (n=52)}$	120 [120, 120]	120 [120, 120]	0.68
$HD_{2\ (n=52)}$	180 [180, 180]	180 [180, 180]	0.69
$HD_{3\ (n=52)}$	240 [240, 240]	240 [240, 240]	0.56
Ultrafiltration Rate, ml/kg/hr			
$HD_{1\ (n=43)}$	3.6 [0.0, 6.3]	2.2 [0.0, 6.8]	0.94
$HD_{2\ (n=45)}$	5 [2.5, 7.5]	6.1 [2.7, 8.1]	0.31
$HD_{3\ (n=44)}$	4.2 [1.8, 8.0]	5.7 [3.4, 9.5]	0.28
Dialysate Temperature, °C			
$HD_{1\ (n=45)}$	36.5 [36, 37]	36.5 [36, 37]	0.99
$HD_{2\ (n=46)}$	36.5 [36, 37]	36.5 [36, 37]	0.91
$HD_{3\ (n=45)}$	36.5 [36, 37]	37 [36.5, 37]	0.25

P values refer to a test for difference using the Wilcoxon Rank Sum for non-normally distributed continuous variables, according to randomized treatment assignment
Qb, blood flow; Qd, dialysate flow

Table S2. Raw Biomarker Concentrations According to Randomized Treatment Assignment

		Placebo	Mannitol	P
HD Session				
HD_1 (n=51)	**Pre-HD BUN (mg/dL)**	102 ± 32	73 ± 26	0.001
HD_2 (n=50)	**Pre-HD BUN (mg/dL)**	70 ± 25	52 ± 20	0.01
HD_3 (n=49)	**Pre-HD BUN (mg/dL)**	45 ± 17	35 ± 15	0.04
HD_1 (n=51)	**Pre-HD Osmolality (mOsm/kg)**	336 ± 14	326 ± 16	0.02
HD_2 (n=50)	**Pre-HD Osmolality (mOsm/kg)**	325 ± 11	318 ± 11	0.02
HD_3 (n=49)	**Pre-HD Osmolality (mOsm/kg)**	315 ± 12	313 ± 10	0.49
HD_1 (n=49)	**Pre-HD Osmolality (mOsm/kg)**	323 ± 10	317 ± 10	0.03
HD_2 (n=45)	**Pre-HD Osmolality (mOsm/kg)**	308 ± 5	308 ± 7	0.95
HD_3 (n=46)	**Pre-HD Osmolality (mOsm/kg)**	305 ± 11	304 ± 9	0.8
HD_1 (n=51)	**Pre-HD hsTnT (ng/L)**	77 [52, 150]	85 [48, 192]	0.56
HD_2 (n=50)	**Pre-HD hsTnT (ng/L)**	79 [41, 149]	81 [53, 186]	0.70
HD_3 (n=49)	**Pre-HD hsTnT (ng/L)**	78 [62, 137]	80 [44, 210]	0.84
HD_1 (n=43)	**Pre-HD NTproBNP (pg/mL)**	5648 [1152, 10629]	5105 [2011, 18318]	0.47
HD_2 (n=N/A)	**Pre-HD NTproBNP (pg/mL)**	NA	NA	NA
HD_3 (n=44)	**Pre-HD NTproBNP (pg/mL)**	5763 [2707, 9384]	5498 [2147, 17682]	0.79

P values refer to a test for difference (t-test for normally distributed variables or Wilcoxon Rank Sum for non-normally distributed continuous variables) according to randomized treatment assignment

IDH, defined as SBP drop ≥25 mmHg, developed during 36% of the placebo arm sessions (29 of 81 sessions) versus 20% of the mannitol arm sessions (15 of 75 sessions; P-difference=0.03). When analyzed to account for intra-patient correlation, the use of mannitol was associated with a trend towards lower odds of developing IDH (OR 0.37; 95%CI 0.12 to 1.16; P=0.09).

IDH, defined as SBP drop ≥30 mmHg, developed during 22% of the placebo arm sessions (18 of 81 sessions) versus 13% of the mannitol arm sessions (10 of 75 sessions; P-difference=0.15). When analyzed to account for intra-patient correlation, the use of mannitol was not significantly associated with lower odds of developing IDH, but the magnitude of the effect estimate was consistent with other definitions (OR 0.41; 95%CI 0.12 to 2.04; P=0.31).

Table S3. Raw Pre-Dialysis Plasma and Urine Kidney Injury Biomarker Concentrations According to Randomized Treatment Assignment

		Placebo	Mannitol	P
HD Session				
HD_1 (n=29)	**Plasma MCP1 (pg/mL)**	217 [140, 264]	276 [138, 329]	0.46
HD_2 (n=27)	**Plasma MCP1 (pg/mL)**	233 [162, 408]	242 [164, 339]	0.73
HD_3 (n=27)	**Plasma MCP1 (pg/mL)**	246 [114, 327]	234 [164, 369]	1.00
HD_1 (n=31)	**Plasma hTNFr1 (pg/mL)**	6256 [4763, 8617]	6287 [5501, 10211]	0.53
HD_2 (n=30)	**Plasma hTNFr1 (pg/mL)**	6447 [4702, 7767]	6648 [5939, 10207]	0.35
HD_3 (n=29)	**Plasma hTNFr1 (pg/mL)**	6048 [4912, 7925]	8682 [6535, 11723]	0.06
HD_1 (n=31)	**Plasma KIM1 (pg/mL)**	747 [423, 1327]	948 [373, 2074]	0.72
HD_2 (n=30)	**Plasma KIM1 (pg/mL)**	747 [525, 1380]	739 [535, 1805]	0.88
HD_3 (n=29)	**Plasma KIM1 (pg/mL)**	783 [578, 1313]	868 [504, 2111]	0.79
HD_1 (n=31)	**Plasma IL-18 (pg/mL)**	474 [290, 822]	483 [269, 800]	0.91
HD_2 (n=30)	**Plasma IL-18 (pg/mL)**	408 [297, 929]	496 [283, 802]	0.72
HD_3 (n=29)	**Plasma IL-18 (pg/mL)**	390 [344, 704]	594 [378, 1072]	0.16
HD_1 (n=31)	**Plasma SuPAR (pg/mL)**	48908 [31747, 61884]	53304 [33313, 75263]	0.48
HD_2 (n=30)	**Plasma SuPAR (pg/mL)**	47730 [31317, 65493]	55094 [36334, 81399]	0.31
HD_3 (n=29)	**Plasma SuPAR (pg/mL)**	48123 [32638, 63555]	50559 [43957, 90821]	0.43
HD_1 (n=31)	**Plasma hTNFr2 (pg/mL)**	7951 [6493, 8944]	9225 [7644, 12137]	0.13
HD_2 (n=30)	**Plasma hTNFr2 (pg/mL)**	8110 [6533, 9015]	9368 [8622, 12530]	0.02
HD_3 (n=29)	**Plasma hTNFr2 (pg/mL)**	8045 [6866, 9913]	10173 [9090, 12756]	0.01
HD_1 (n=25)	**Urine MCP1/Creat (pg/mg)**	8 [5, 22]	17 [9, 24]	0.26
HD_2 (n=19)	**Urine MCP1/Creat (pg/mg)**	13 [8, 23]	16 [15, 28]	0.25
HD_3 (n=21)	**Urine MCP1/Creat (pg/mg)**	15 [8, 23]	24 [18, 65]	0.12
HD_1 (n=25)	**Urine hTNFr1/Creat**	129 [84, 172]	188 [98, 269]	0.21

	(pg/mg)			
HD_2 (n=19)	**Urine hTNFr1/Creat (pg/mg)**	149 [111, 212]	400 [234, 498]	0.01
HD_3 (n=21)	**Urine hTNFr1/Creat (pg/mg)**	194 [144, 289]	323 [201, 447]	0.12
HD_1 (n=25)	**Urine KIM1/Creat (pg/mg)**	23 [18, 39]	33 [23, 57]	0.14
HD_2 (n=19)	**Urine KIM1/Creat (pg/mg)**	27 [17, 42]	56 [48, 60]	0.03
HD_3 (n=21)	**Urine KIM1/Creat (pg/mg)**	29 [19, 58]	64 [46, 82]	0.07
HD_1 (n=25)	**Urine IL-18/Creat (pg/mg)**	0 [0, 1]	1 [0, 1]	0.51
HD_2 (n=19)	**Urine IL-18/Creat (pg/mg)**	1 [0, 1]	2 [1, 2]	0.01
HD_3 (n=21)	**Urine IL18/Creat (pg/mg)**	1 [0, 3]	2 [1, 3]	0.29
HD_1 (n=25)	**Urine SuPAR/Creat (pg/mg)**	3640 [2093, 5635]	4445 [3116, 6967]	0.37
HD_2 (n=19)	**Urine SuPAR/Creat (pg/mg)**	3868 [2990, 7408]	7369 [6496, 8130]	0.15
HD_3 (n=21)	**Urine SuPAR/Creat (pg/mg)**	7008 [4665, 9204]	7397 [5143, 9081]	0.67
HD_1 (n=25)	**Urine hTNFr2/Creat (pg/mg)**	103 [68, 162]	160 [115, 196]	0.07
HD_2 (n=19)	**Urine hTNFr2/Creat (pg/mg)**	114 [84, 172]	249 [214, 316]	0.01
HD_3 (n=21)	**Urine hTNFr2/Creat (pg/mg)**	172 [138, 226]	223 [173, 276]	0.20

P values refer to a test for difference (Wilcoxon Rank Sum for non-normally distributed continuous variables) according to randomized treatment assignment

Table S4. Difference in pre-HD Biomarkers According to Randomized Treatment Assignment

	Percent Change in Pre-Dialysis Biomarkers (from HD_1 to HD_3) for Mannitol versus Placebo	
	Ratio	**P***
Plasma MCP1 (n=26)	6% (-37% to 81%)	0.81
Plasma hTNFr1 (n=29)	20% (4% to 39%)	0.01
Plasma KIM1 (n=29)	-3% (-23% to 22%)	0.81
Plasma Urine IL-18 (n=29)	77% (3% to 304%)	0.04
Plasma huPAR (n=29)	13% (-2% to 31%)	0.09
Plasma hTNFr2 (n=29)	14% (3% to 25%)	0.01
Urine MCP1/Creatinine (n=19)	-3% (-42% to 61%)	0.89
Urine hTNFr1/Creatinine (n=19)	-11% (-44% to 42%)	0.62
Urine KIM1/Creatinine (n=19)	29% (-11% to 86%)	0.16
Urine Il-18/Creatinine (n=19)	206% (-29% to 600%)	0.17
Urine SuPAR/Creatinine (n=19)	-13% (-46% to 41%)	0.55
Urine hTNFr2/Creatinine (n=19)	-17% (-44% to 22%)	0.31

Effect estimates are calculated as the difference in log-transformed biomarkers between HD_3 and HD_1, adjusted for baseline pre-HD_1 biomarker concentrations.
*P values are not adjusted for multiple comparisons.

Table S5. Summary of adverse events

Adverse Event	Placebo (n=27)	Mannitol (n=25)	P
Number of participants (Number of events)			
Hypertension (>180mmHg)	10 (15)	9 (15)	1.0
Chest Pain	0 (0)	2 (2)	0.23
Tachycardia	0 (0)	1 (1)	0.48
Nausea	5 (5)	1 (1)	0.19
Cramps	2 (2)	1 (2)	1.0
Headache	2 (3)	1 (1)	1.0
Confusion	2 (2)	1 (1)	1.0
Oxygen Requirement	2 (2)	4 (7)	0.41
Access Dysfunction	2 (2)	2 (2)	1.0
Urinary Tract Infection	0 (0)	1 (1)	0.48

P-value for difference in number of participants between groups using Fisher's exact test