

Supplementary Data

Table of Contents

Supplementary Table s1 Modified Hachinski protocol of cognitive assessments used both on and off dialysis. All assessments could be completed in less than one hour. For assessments completed during dialysis all tests were completed within the first 2 hours of dialysis.

Supplementary Table s2 MAR and MCAR based results for weighted GEE with time as an ordinal variable.

Supplementary Table s3 Correlation of change in cognitive assessment and MFV as demonstrated in Table 3, with false detection rate and Bonferroni corrections. For comparison, FDR is calculated using an alpha of 0.1, where each p-value = rank/number of test multiplied by 0.1.

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Supplementary Figure 1 Flow chart demonstrating recruitment, follow-up and participant attendance to study visits and MRI. Abbreviations: CeVD, Cerebrovascular disease; MRI, Magnetic Resonance Imaging; HD, Hemodialysis

Supplementary Figure 2 Correlation plot of UF and % decline MFV, Spearman's rho -0.512, $p < 0.001$. More positive ultrafiltration volumes correlate with more negative %decline in MFV.

Supplementary Figure 3 Correlation plot of delta TMT-B (early visits) and % decline MFV - Spearman's rho -0.323, $p = 0.01$. Delta score is calculated as score during dialysis minus score off dialysis. Thus, for TMT-B, if time taken to complete on dialysis is longer then the delta score is positive. A more positive delta TMT-B denotes worsening of executive function during dialysis.

Supplementary Figure 4 Correlation plot of delta TMT-B (long term) and % decline MFV in those on continued HD - Spearman's rho -0.403, $p = 0.005$. Delta score is calculated as score at follow-up minus score at baseline. Thus, for TMT-B, if time taken to complete is longer at follow-up delta score is more positive. A more positive delta TMT-B denotes a worsening executive function at follow-up.

Supplementary Figure 5 Correlation plot of delta CES-D (long term) and delta WMH volume in those on continued HD - Spearman's rho 0.485, $p = 0.03$. Delta score is calculated as score at follow-up minus score at baseline. Thus, for CES-D, if depression scoring is greater at follow-up delta score is more positive. A more positive delta CES-D denotes a worsening in depressive symptoms at follow-up.

Supplementary Figure 6 Trajectory of MFV during dialysis, in those without cognitive impairment

Supplementary Figure 7 Trajectory of MFV during dialysis, in those with cognitive impairment

Supplementary Figure 8 Trajectory of MFV during dialysis, in those with and without cognitive impairment grouped

Screening Assessment	
Montreal Cognitive Assessment (MOCA)	Repeatable and validated tool, used to screen for cognitive impairment. Briefly assesses multiple cognitive domains, with greater sensitivity to vascular cognitive impairment than the mini-mental state exam. Maximal score 30. Score <26 indicative of mild cognitive impairment.
Verbal Fluency	
Phonemic Fluency	Participants are given 1 minute to produce as many unique words beginning with a specific letter, excluding pronouns. Three letters are used, FAS, and score totalled. Deficits in phonemic fluency are more commonly observed in those with deficits in executive function
Semantic Fluency	Participants are given 1 minute to produce as many different animals. Animals at different development stages, e.g. lamb and sheep, are only counted once. In contrast to phonemic fluency, deficits in semantic fluency are more commonly observed in those with degenerative disorders such as Alzheimer's' disease.
Executive function	
Trail Making Test A & B (TMTA & TMTB)	Assessment of visual attention and task switching. Participants are asked to connect a set of dots in ascending order as rapidly as possible, whilst maintaining accuracy. TMTA is purely numerical (1-2-3-...) whereas TMTB alternates between letters and numbers (1-A-2-B-3-C-...). The score provided is time taken to complete; therefore a higher score denotes worse cognitive function.
Letter Digit Substitution Test (LDST)	Assessment of processing speed. Participants are allowed one minute to accurately match numbers 1-9 to their randomly allocated paired letter, using a key situated at the top of the page.
Auditory-verbal memory	
Hopkins Verbal Learning Test (HVLT)	Participants are read a list of 12 words and asked to immediately as many as possible.
Total Recall	Related to the total number of recalled words after three trials
Delayed Recall	Without warning, participants are asked to recall the list following a 20-25 minute delay
Retention	Calculated percentage of retained words = delayed recall/highest score from trial 2 or 3
Discrimination Index	Finally, a second list, including the original words, is read. Participants must identify their original words. Discrimination index = number of true positives - number of false positives.
Mood	
Centre for Epidemiologic Studies Depression Scale (CES-D)	Self-ranking depression scale. Higher scores are associated with a greater likelihood of depression. All scoring ≥ 17 were assessed for core symptoms of depression and, if warranted, onward referral made.

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Time versus -15 minutes	MAR		MCAR	
	Estimate	P-value	Estimate	P-value
15	0.4072	0.4286	0.304	0.4792
30	-0.2094	0.6872	-0.3806	0.41
90	-1.6049	0.0167*	-1.7145	0.0063*
180	-5.7067	<.0001*	-5.7005	<.0001*
210	-5.8809	<.0001*	-5.8323	<.0001*

Note: MAR=missing at random; MCAR=missing completely at random; * $P < 0.05$.

Supplementary Table s2 MAR and MCAR based results for weighted GEE with time as an ordinal variable. MAR ($\beta = -0.0317$, $P < 0.0001$) and MCAR ($\beta = -0.0313$, $P < 0.0001$)

based results showed CBFV generally decreased with time as a continuous variable. Each data mechanism provided similar results and parameter estimates for missingness model show that missing values are likely not related to time ($\beta = 0.0030$, $P = 0.6133$) and so MCAR is a reasonable assumption in this case.

Cognitive Assessment	Correlation with % Δ MFV, Rho	Unadjusted p-value	Rank	FDR adjusted p-value	False detection rate	Bonferroni adjusted p-value significance	Bonferroni
HVLT: Retention	0.046	0.70	11	0.10	Non-significant	0.0045	Non-significant
HVLT: Discrimination	-0.057	0.63	10	0.09	Non-significant	0.0045	Non-significant
HVLT: Total Recall	-0.089	0.45	9	0.08	Non-significant	0.0045	Non-significant
HVLT: Delayed Recall	-0.098	0.41	8	0.07	Non-significant	0.0045	Non-significant
CES-D	-0.097	0.41	7	0.06	Non-significant	0.0045	Non-significant
LDST	0.17	0.15	6	0.05	Non-significant	0.0045	Non-significant
Semantic	-0.172	0.14	5	0.05	Non-significant	0.0045	Non-significant
MOCA	-0.27	0.02	4	0.04	Significant	0.0045	Non-significant
Phonemic	-0.302	0.01	3	0.03	Significant	0.0045	Non-significant
TMTB	0.323	0.01	2	0.02	Significant	0.0045	Non-significant
TMTA	0.454	0.001	1	0.009	Significant	0.0045	Significant

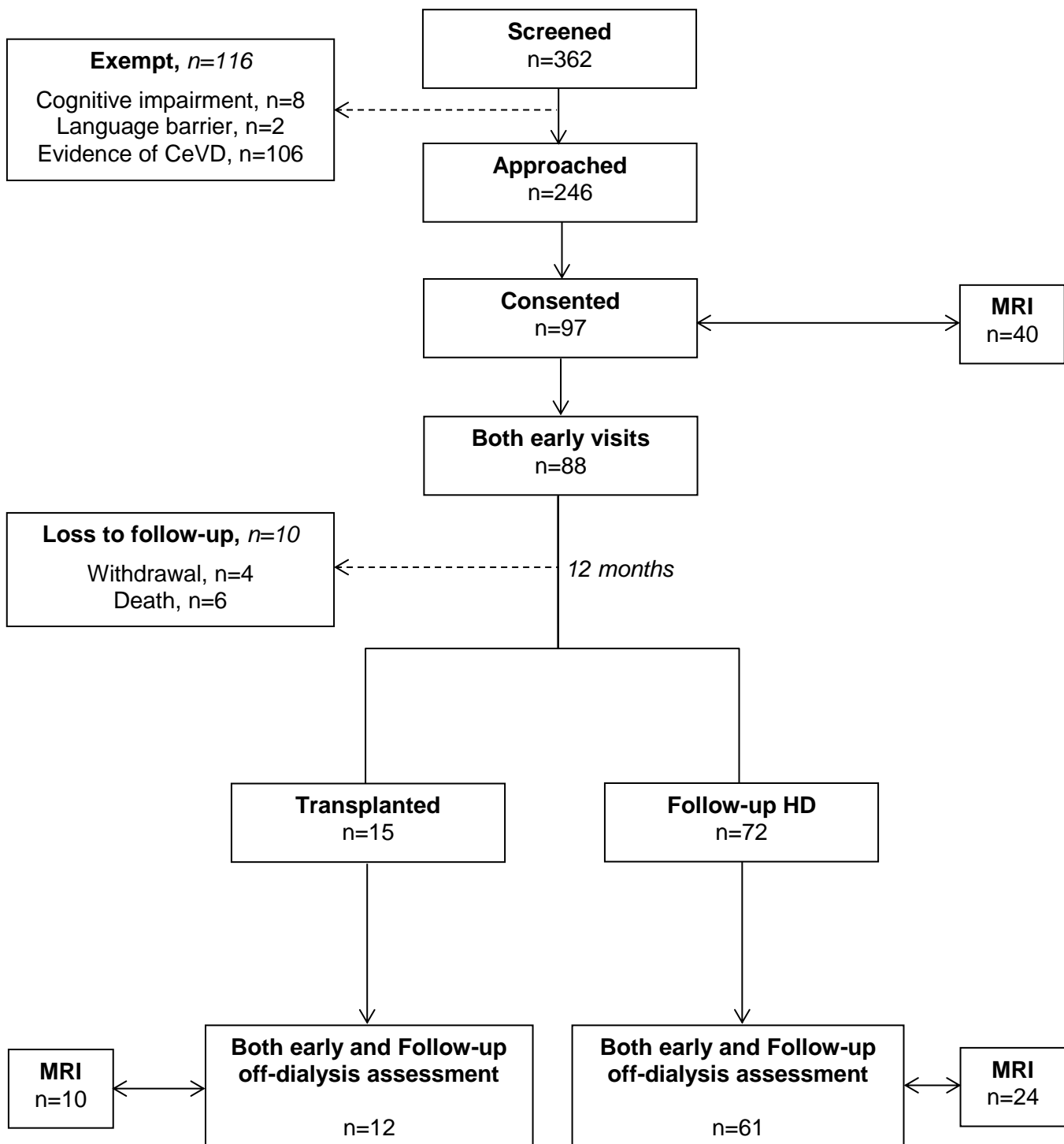
Supplementary Table s3 Correlation of change in cognitive assessment and MFV as demonstrated in Table 3, with false detection rate and Bonferroni corrections. For comparison, FDR is calculated using an alpha of 0.1, where each p-value = rank/number of tests multiplied by 0.1.

Cognitive Assessment	Correlation with % Δ MFV, Rho	Unadjusted p-value	Rank	FDR adjusted p-value	False detection rate	Bonferroni adjusted p-value significance	Bonferroni
Continued hemodialysis, n= 61							
LDST	-0.085	0.55	11	0.10	Non-significant	0.0045	Non-significant
Total Recall	0.098	0.48	10	0.09	Non-significant	0.0045	Non-significant
CES-D	0.139	0.32	9	0.08	Non-significant	0.0045	Non-significant
Discrimination	0.149	0.30	8	0.07	Non-significant	0.0045	Non-significant
Phonemic	0.15	0.28	7	0.06	Non-significant	0.0045	Non-significant
TMTA	-0.209	0.15	6	0.05	Non-significant	0.0045	Non-significant
Retention	0.219	0.15	5	0.05	Non-significant	0.0045	Non-significant
Semantic	0.201	0.15	4	0.04	Non-significant	0.0045	Non-significant
Delayed Recall	0.243	0.08	3	0.03	Non-significant	0.0045	Non-significant
MOCA	0.276	0.04	2	0.02	Non-significant	0.0045	Non-significant
TMTB	-0.403	0.005	1	0.009	Significant	0.0045	Non-significant
Transplanted at follow-up, n=12							
MOCA	0.086	0.81	11	0.10	Non-significant	0.0045	Non-significant
Delayed Recall	-0.123	0.75	10	0.09	Non-significant	0.0045	Non-significant
Discrimination	0.273	0.45	9	0.08	Non-significant	0.0045	Non-significant
TMTB	-0.317	0.41	8	0.07	Non-significant	0.0045	Non-significant
Total Recall	0.329	0.35	7	0.06	Non-significant	0.0045	Non-significant
CES-D	-0.334	0.35	6	0.05	Non-significant	0.0045	Non-significant
Retention	-0.358	0.31	5	0.05	Non-significant	0.0045	Non-significant
LDST	0.383	0.28	4	0.04	Non-significant	0.0045	Non-significant
TMTA	-0.5	0.17	3	0.03	Non-significant	0.0045	Non-significant
Semantic	0.609	0.06	2	0.02	Non-significant	0.0045	Non-significant
Phonemic	0.758	0.01	1	0.009	Non-significant	0.0045	Non-significant

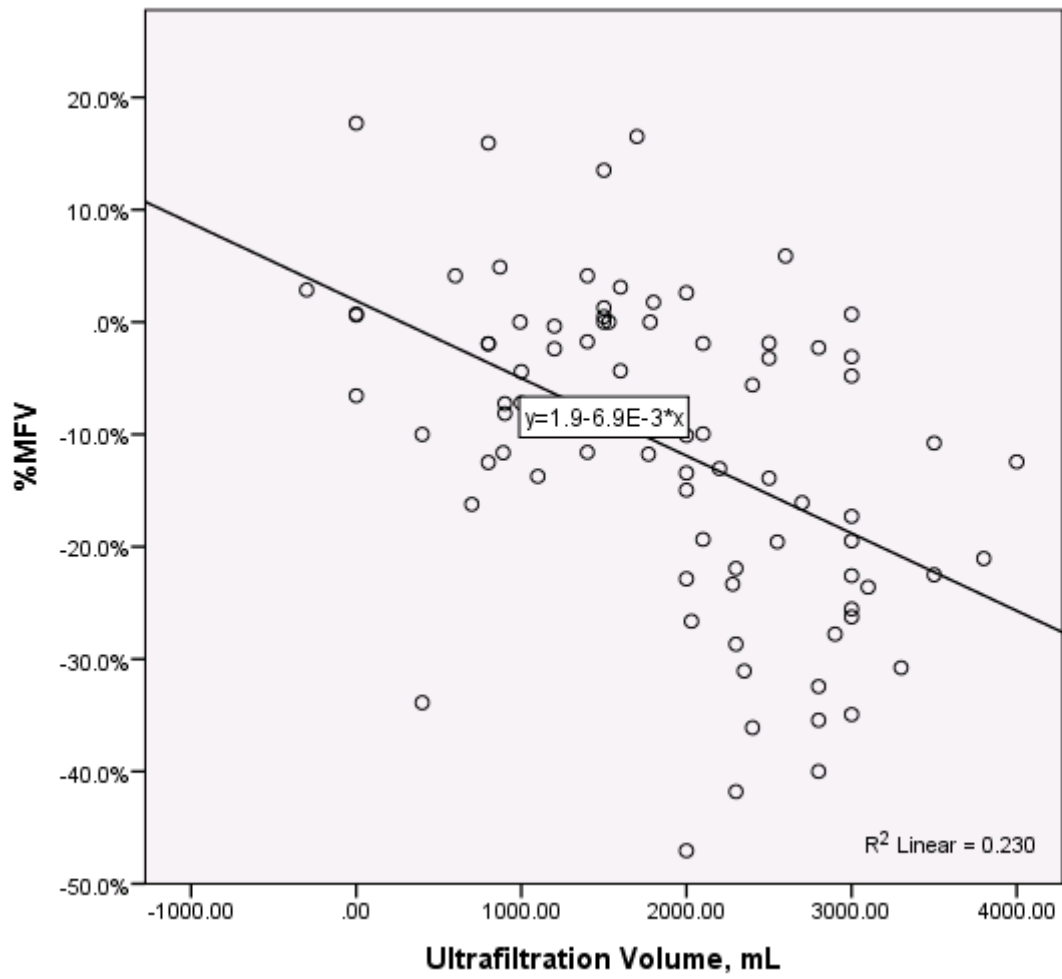
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	Continued Hemodialysis , n=72	Transplanted during study, n=15	p-value
Median Age [IQR]	60 [52,67]	51 [40,63]	0.02
Female, n [%]	34 [41.5]	6 [40]	0.92
Ethnicity, n [%]			
European	80 [97.6]	13 [86.7]	0.05
Asian	2 [2.4]	2 [13.3]	
Primary Renal Diagnosis, n [%]			
Diabetes	16 [19.5]	2 [13.3]	
Glomerulonephritis	20 [24.4]	0	
Interstitial	16 [19.5]	4 [26.7]	
Multisystem	16 [19.5]	4 [26.7]	
Other	14 [17.1]	5 [33.3]	0.18
Past Medical History, n [%]			
Hypertension	74 [90.2]	11 [73.3]	0.07
Diabetes mellitus	26 [35.4]	3 [20]	0.25
Ischemic heart disease	19 [23.2]	2 [13.3]	0.40
Congestive cardiac failure	11 [13.4]	0	0.13
Peripheral Vascular disease	7 [8.5]	0	0.24
Atrial Fibrillation	11 [13.4]	0	0.13
Depression	17 [20.7]	4 [26.7]	0.61
Duration of ESRD, median years [IQR]	2.09 [0.73,4.54]	0.6 [0.22,1.61]	<0.01
Dialysis Related Variables, median [IQR]			
Pre-SBP	143.4 [121.3,158.5]	142.5 [121.0,157.5]	0.85
Pre-DBP	72.3 [65.0,79.8]	78.5 [70.8,84.7]	0.08
Post-SBP	129.6 [112.7,148.3]	130.8 [121.8,135.7]	0.94
Post-DBP	68.4 [59.5,76.2]	73.7 [61,88.3]	0.15
UF Volume	2.07 [1.5,2.5]	1.73 [1.28,2.49]	0.34
Dialysis Access, n [%]			
AV access	59 [72]	10 [66.7]	
Central Venous Catheter	23 [28]	5 [33.3]	0.68
Laboratory Values, median [IQR]			
Serum Adjusted Calcium	2.39 [2.28,2.46]	2.34 [2.25,2.56]	0.89
Serum Phosphate	1.7 [1.47,2.01]	1.94 [1.71,2.05]	0.10
Hemoglobin	112.5 [102,122]	113.3 [96.7,118.7]	0.82
Serum Albumin	32.7 [30,35]	33.7 [31.7,35.0]	0.49
PTH	55.9 [36.4,92.5]	85.7 [59.1,156.7]	0.02
Urea Reduction Ratio	72.8 [70,77.5]	73.0 [68,78]	0.95
Years of Education, median [IQR]	12 [11,14]	13 [11,14]	0.61

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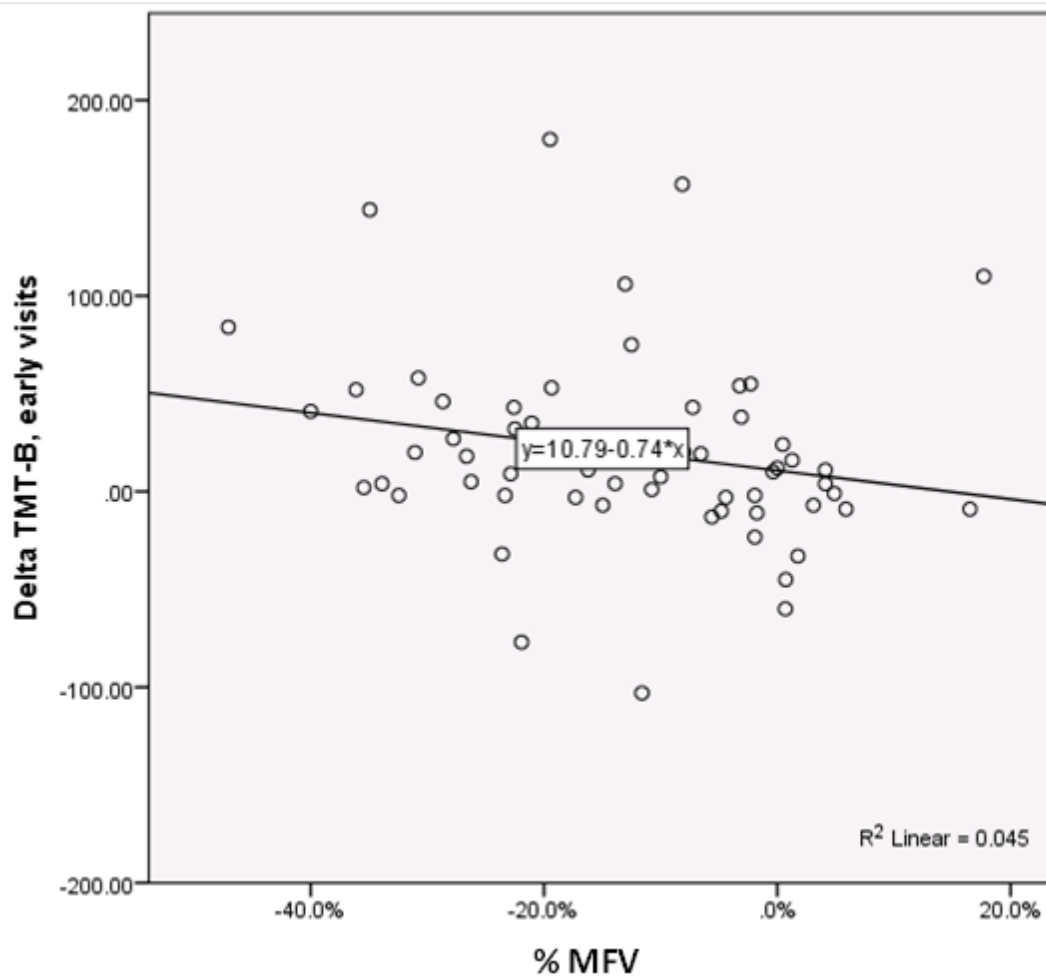


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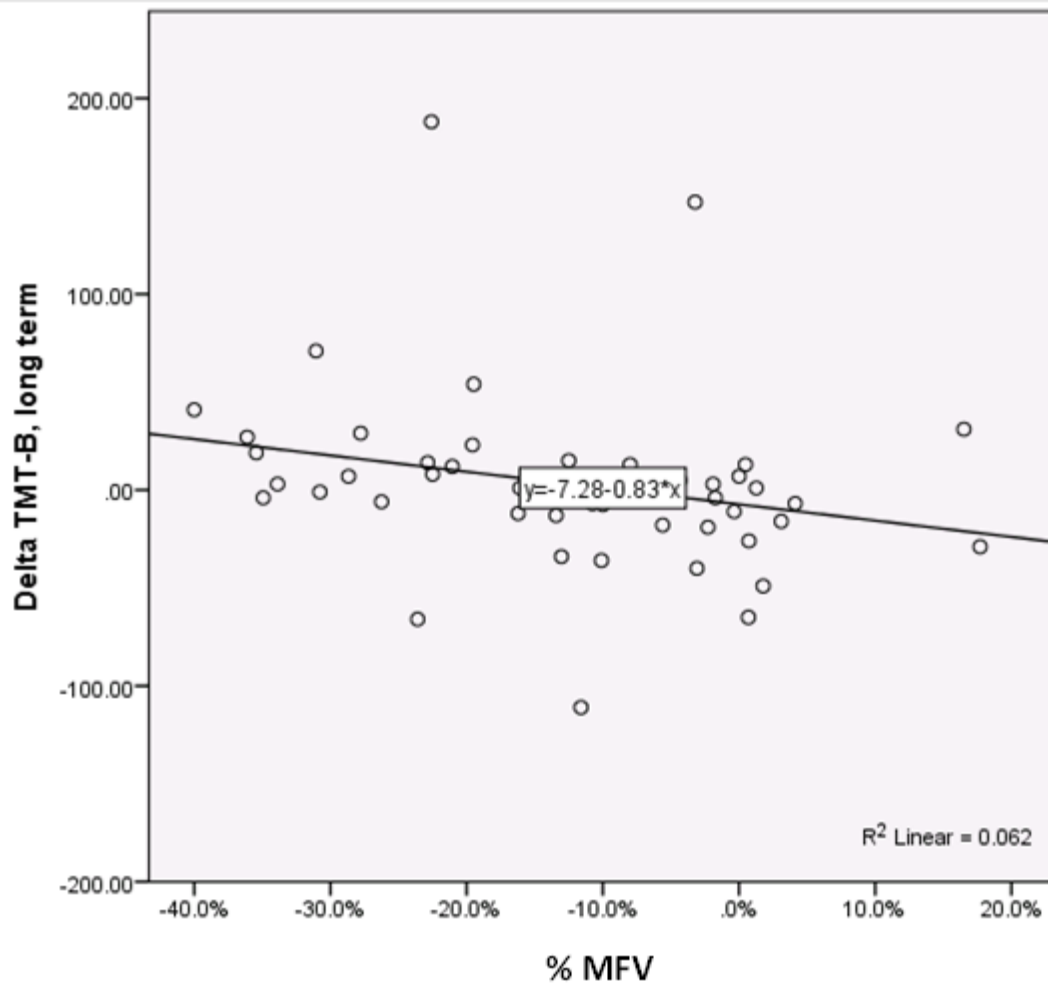


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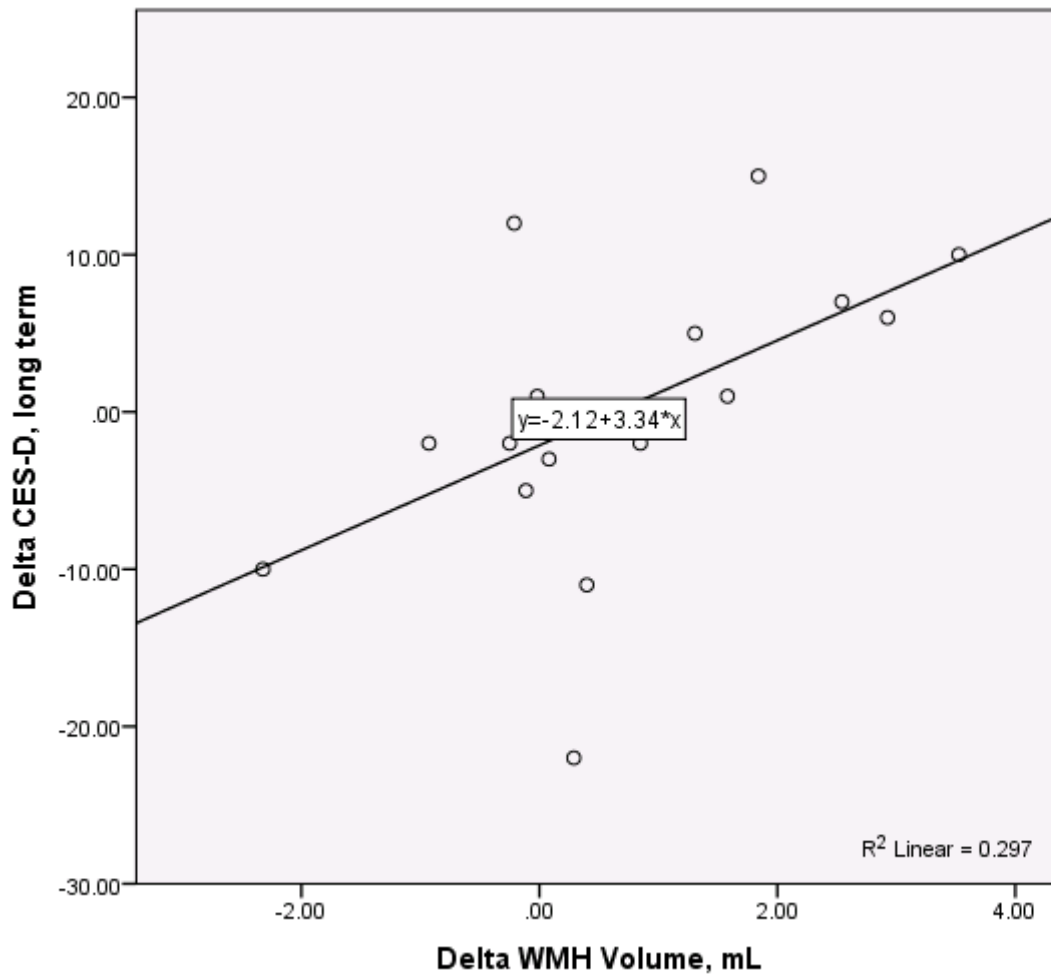
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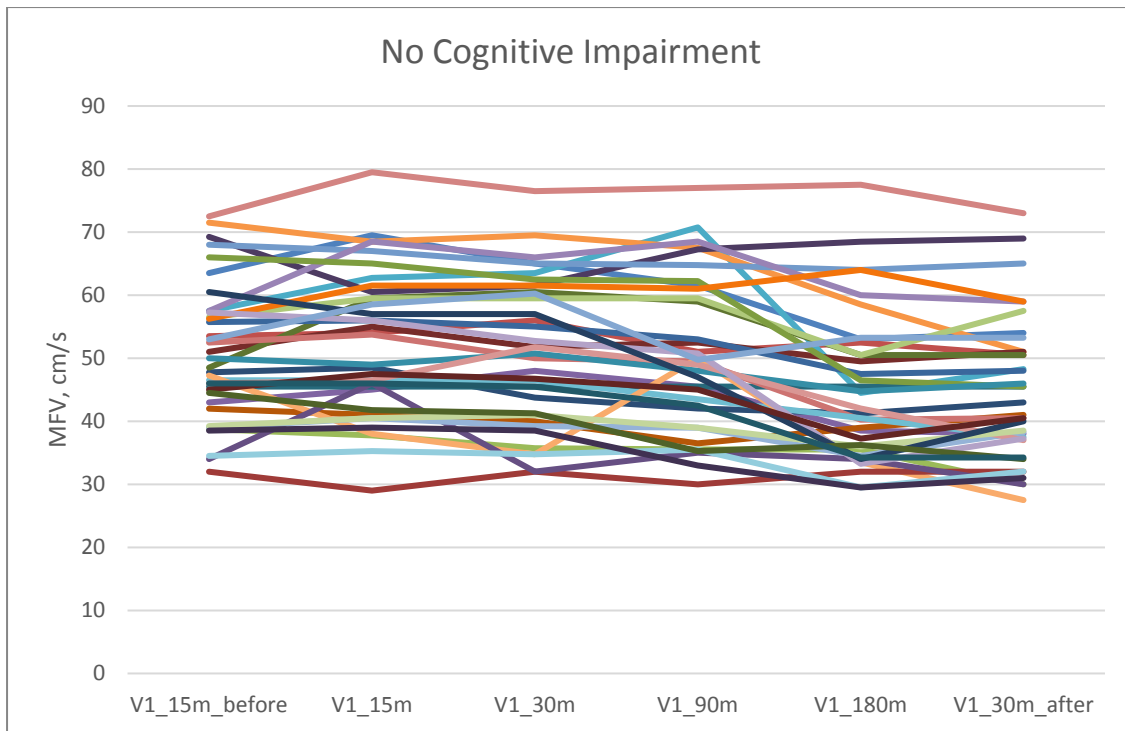
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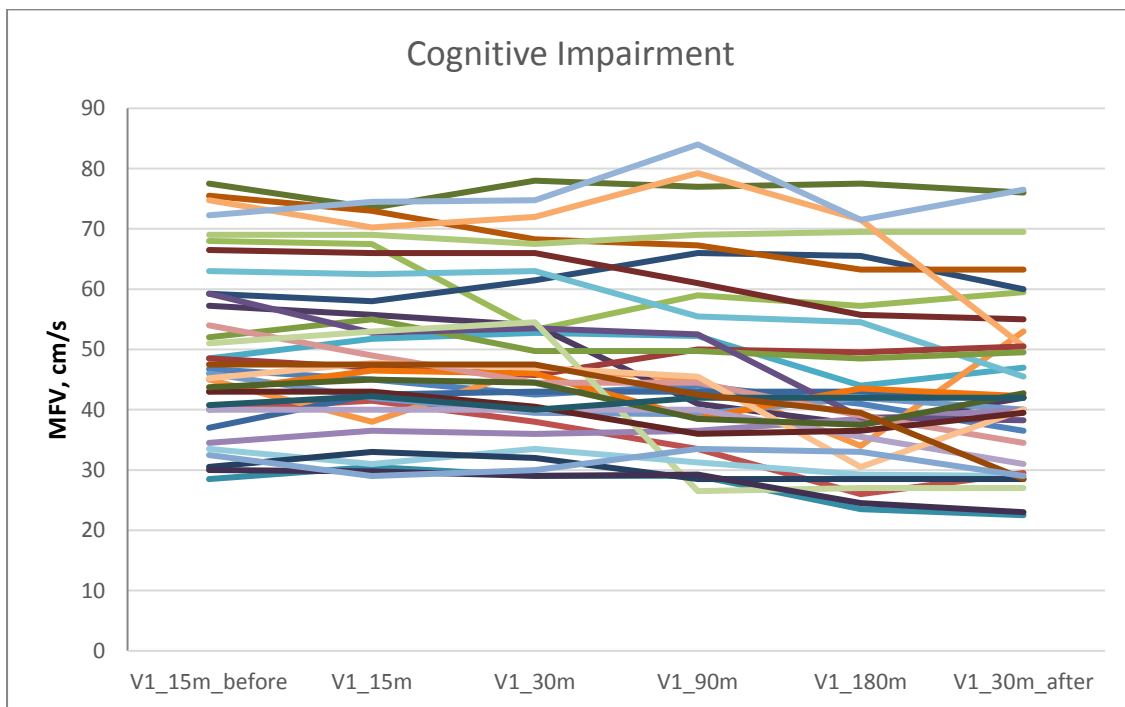
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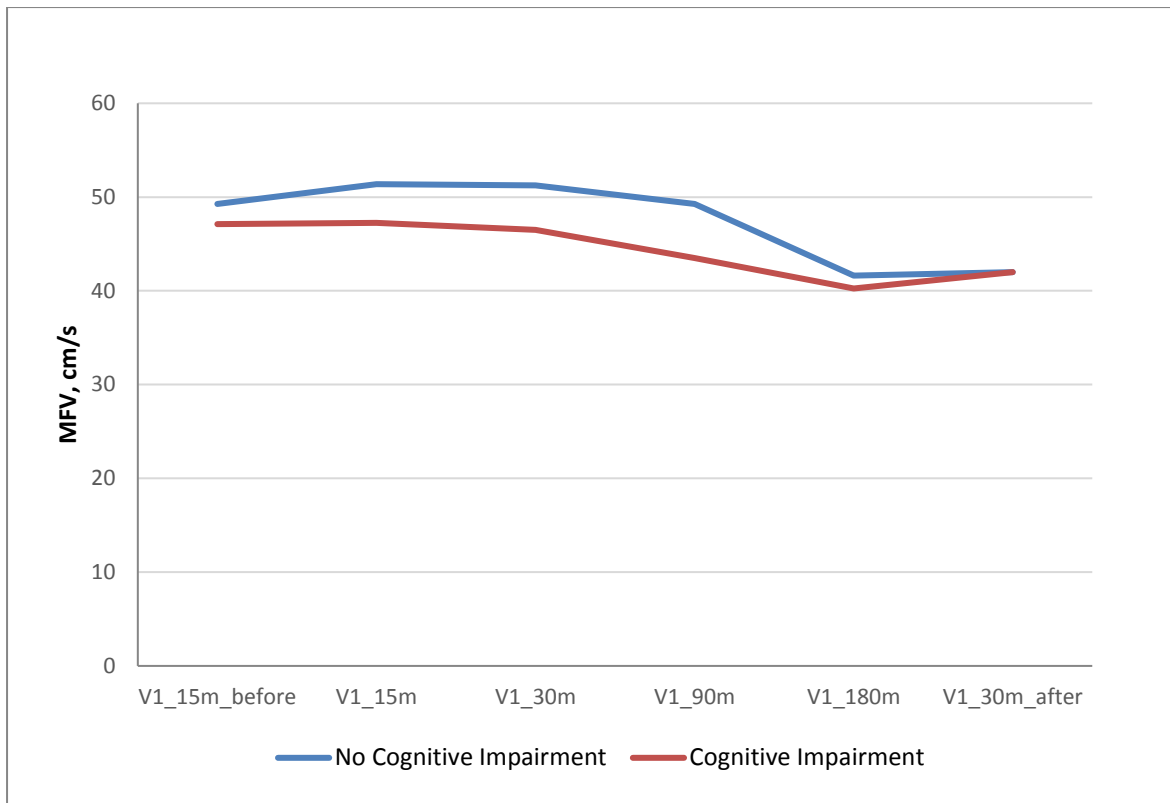
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Supplementary Figure 6 Trajectory of MFV during dialysis, in those without cognitive impairment



Supplementary Figure 7 Trajectory of MFV during dialysis, in those with cognitive impairment



Supplementary Figure 8 Trajectory of MFV during dialysis, in those with and without cognitive impairment grouped