Low mannose-binding lectin levels predict cardiovascular disease in hemodialysis patients

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Background

Hemodialysis (HD) is a lifesaving treatment. Nonetheless, patients receiving HD have higher cardiovascular morbidity and mortality compared to the general population. Mannose-binding lectin (MBL) plays an important role in the development of cardiovascular disease. However, this relationship is complex and studies suggest that MBL can be either detrimental or beneficial. In addition, it has been shown that MBL concentration and functionality are altered by HD. Therefore, this study aimed to determine the predictive value of MBL levels for cardiac and cardiovascular events and all-cause mortality in HD patients.

Methods

We conducted a prospective study of 107 HD patients on a three times per week dialysis schedule with a follow-up period of more than 3 years. Plasma MBL was measured before and after HD using a sandwich ELISA. The prognostic effect of MBL levels after HD was evaluated using Cox regression models. The primary endpoint was the incidence of cardiac (C-event) and cardiovascular events (CV-event). The secondary endpoint was all-cause mortality.

Results

During median follow-up of 27 months, 21 participants (20%) developed C-events, while 36 (34%) had CV-events. Furthermore, 37 patients (35%) died during the study and 21 (20%) received a kidney transplant. After the study period, 58% of patients with low MBL levels (<319 ng/mL) and 26% of patients with high MBL levels (≥319 ng/mL) had a CV-event. The incidence of both cardiac and cardiovascular events was significantly higher in patients with low MBL levels.

Figure 1

Figure 2

Table 1

	Patients			
	All (n=107)	**MBL low (n=26)**	**MBL high (n=81)**	**P-value**
MBL levels (ng/mL)	1000[319-1477]	98[33-146]	1290[671-1848]	<0.001
Demographics				
Age, years	62.5±15.6	65.3±12.1	61.56±16.6	0.29
Male gender, n (%)	71 (66)	17 (65)	54 (67)	1.00
Current diabetes, n (%)	25 (24)	9 (35)	16 (20)	0.18
Hypertension, n (%)	85 (84)	22 (88)	63 (83)	0.76
Cardiovascular history, n (%)	26 (25)	9 (35)	15 (19)	0.11
BMI, kg/m^2	25.8±4.4	27.0±4.5	25.4±4.4	0.14
Hemodialysis				
Dialysis vintage, months	25.5 [8.5-52.3]	18.2 [7.0-47.7]	32.8 [9.1-53.3]	0.22
Ultrafiltration volume, L	2.55±0.78	2.54±0.82	2.56±0.78	0.91
Ultrafiltration rate, ml/kg/h	8.56±2.63	7.81±2.39	8.80±2.67	0.10
Kidney transplant, n (%)	21 (20)	4 (15)	17 (21)	0.78
Laboratory measurements				
Hematocrit, %	34.9±3.8	34.5±4.1	35.0±3.7	0.55
HbA1c, mmol/mol	5.68±0.98	5.80±0.97	5.63±0.98	0.49
Albumin, g/L	39 [37-42]	39 [37-42]	39 [37-42]	0.94
Calcium, mmol/L	2.31±0.16	2.31±0.15	2.32±0.16	0.88
Phosphate, mmol/L	1.67±0.53	1.82±0.47	1.65±0.54	0.16
hsCRP, mg/L	6.7 [2.8-10.9]	6.1 [1.4-12.0]	6.7 [3.0-10.9]	0.72
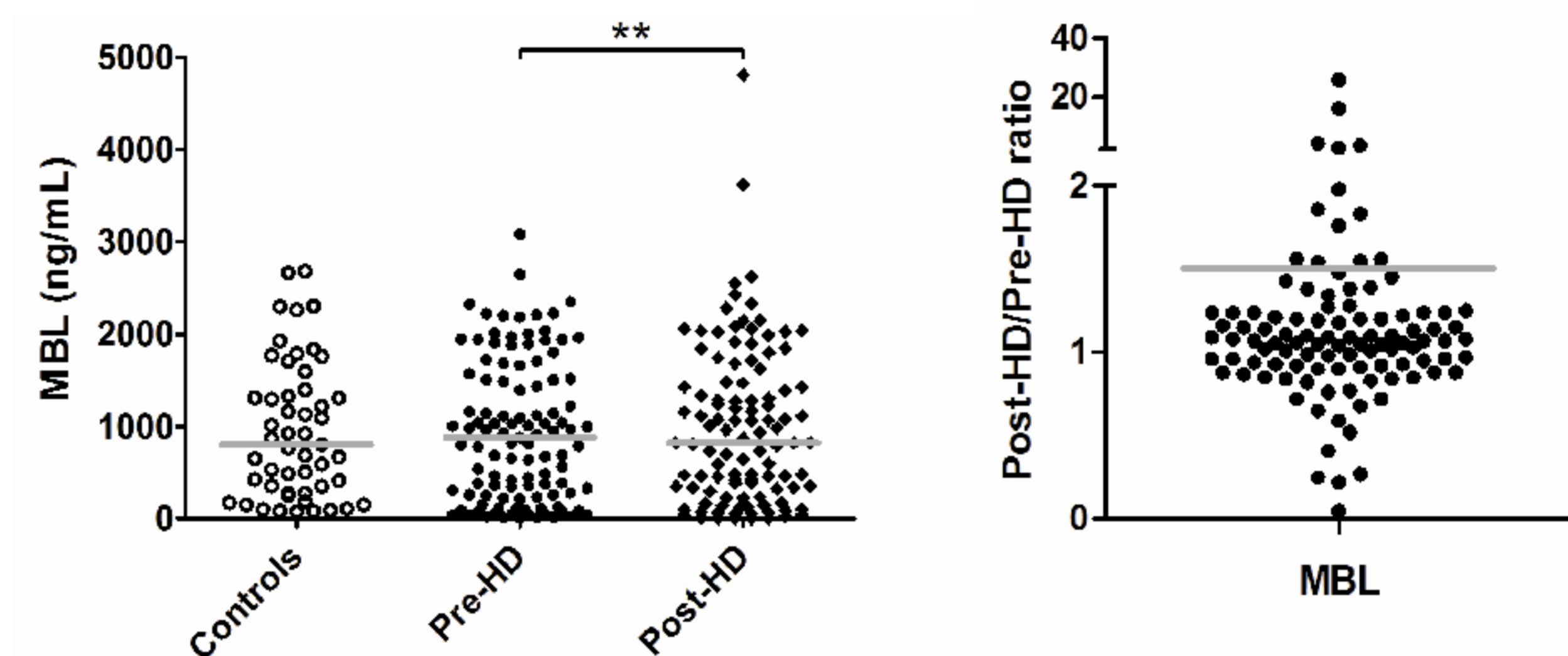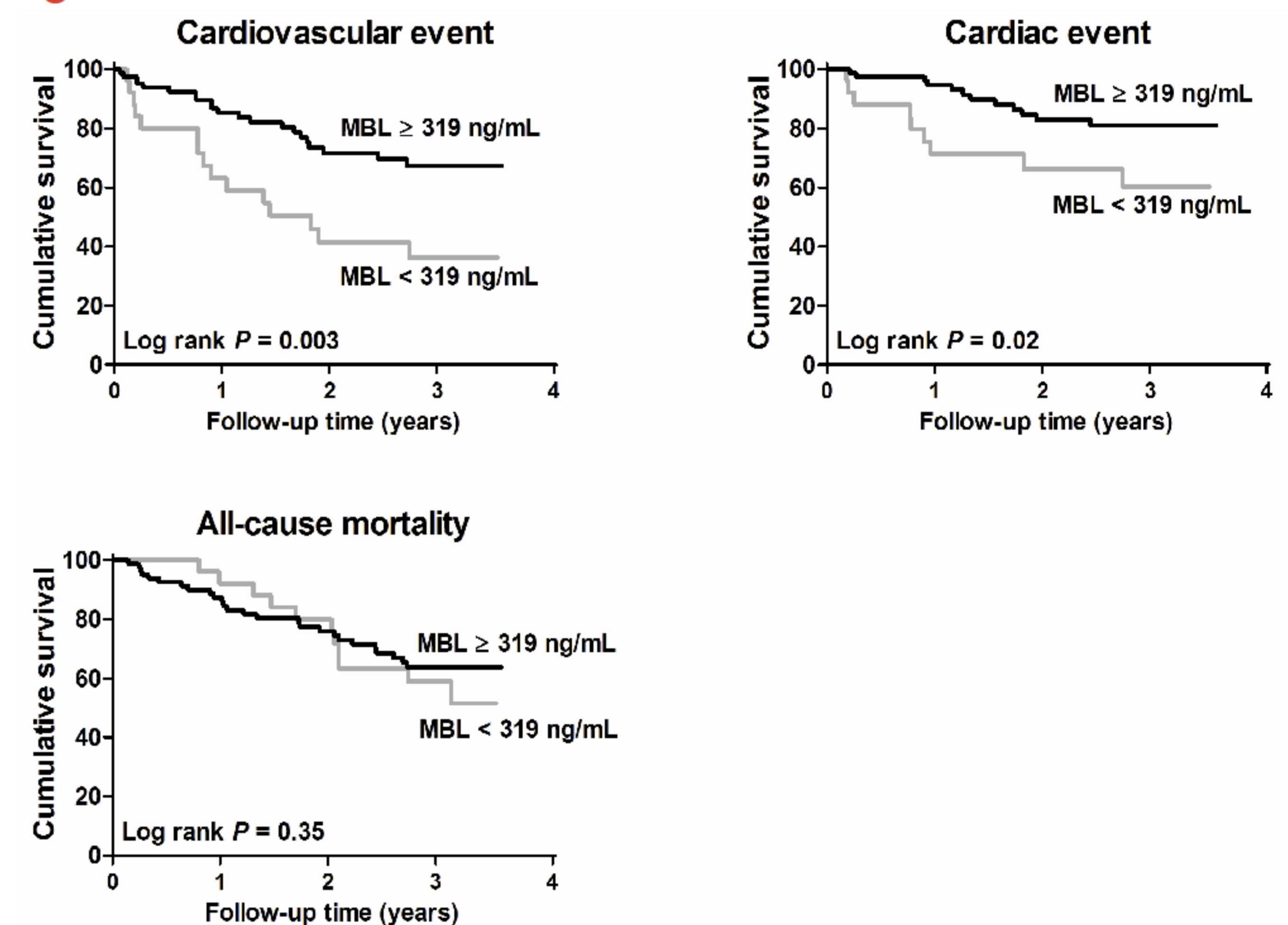
Table 2

Cardiovascular events						
	Low MBL			**MBL continuous**		
	HR	**95% CI**	**P**	**HR**	**95% CI**	**P**
Model 1	2.64	1.36 − 5.13	0.004	0.64	0.46 − 0.90	0.01
Model 2	2.75	1.39 − 5.44	0.004	0.61	0.43 − 0.88	0.008
Model 3	2.94	1.45 − 5.94	0.003	0.61	0.42 − 0.89	0.01
Model 4	3.55	1.70 − 7.40	0.001	0.58	0.40 − 0.84	0.004
Model 5	3.98	1.88 − 8.42	<0.001	0.56	0.38 − 0.81	0.002
Cardiac events						
Model 1	2.60	1.10 − 6.18	0.03	0.71	0.46 − 1.10	0.12
Model 2	2.49	1.04 − 5.96	0.04	0.73	0.46 − 1.16	0.19
Model 3	2.65	1.08 − 6.55	0.03	0.74	0.47 − 1.18	0.21
Model 4	3.82	1.48 − 9.87	0.006	0.62	0.38 − 1.01	0.06
Model 5	3.96	1.49 − 10.54	0.006	0.59	0.35 − 0.98	0.04

Model 1: crude. **Model 2:** adjusted for age and gender. **Model 3:** adjusted for model 2 plus ultrafiltration volume and dialysis vintage. **Model 4:** adjusted for model 3 plus cardiovascular history, diabetes and post-HD systolic blood pressure. **Model 5:** adjusted for model 4 plus hsCRP.

Conclusion

Low MBL is associated with a higher risk of cardiac and cardiovascular events, but not all-cause mortality. Of all the tested parameters in the multivariate analysis, low MBL displayed one of the strongest associations with cardiac and cardiovascular events in these HD patients. Therefore, MBL levels may help to identify HD patients who are susceptible to develop cardiovascular disease.