Print ISSN 1110-208X.

Online ISSN 2357-0016

The Relationships between Intra Dialytic Changes in Hemoglobin Level and Myocardial Injury in Patients with ESRD Undergoing Maintenance Hemodialysis

Ahmed E. Mansour , Moaz Bakr, El Metwally L. El Shahawy,

Shimaa Moustafa, Shimaa S. El-sayed

Abstract:

Background: Hemodialysis HD eliminate toxins from the blood through ultrafiltration and diffusion. This study aimed to Study the correlations between intra-dialytic changes in hemoglobin Hb level (post-HD-Hb/pre-HD-Hb) ratio and myocardial injury in patients with chronic kidney disease CKD (stage 5) who are undergoing maintenance HD and elucidate intradialytic changes of Hb levels in patients with CKD (stage 5) who are receiving maintenance HD. **Methods:** This prospective study included 100 patients who were divided into four groups according to baseline Hb level (post-Hb/pre-Hb) ratio: Group 1 (n=30) with post-Hb/pre-Hb ratio <1.0, group 2 (n=20) with post-Hb/pre-Hb ratio 1.0 to <1.1, group 3 (n=20) with post-Hb/pre-Hb ratio 1.1 to <1.2 and group 4 (n=30) with post-Hb/pre-Hb ratio ≥1.2. While 4 groups according to post HD Hb level: Group A (n=30) with post Hb level <10 g/dL, group B (n=20) with post Hb level 10 g/dL to < 11 g/dL, group C (n=20) with post Hb level 11 g/dL to < 12 g/dL and group D (n=30) with post Hb level >12 g/dL. **Results:** hs-cTnT at a cut-off of 12 demonstrated the highest diagnostic accuracy, with the greatest AUC (0.808), balanced sensitivity (75%) and specificity (81.6%), and a high NPV (91.2%), making it a reliable tool for ruling out myocardial injury. hs-cTnI at a cut-off of 8.9 showed a slightly lower AUC (0.796) and specificity (78.9%), with comparable sensitivity (75%) and NPV (90.9%), suggesting it is also effective, though slightly less so than hs-cTnT. **Conclusion:** The asymptomatic raising of hscTni, hscTnt and ckmb represent silent myocardial injury during HD.

Keywords: Cardiac Biomarkers, Cardiovascular Outcomes, ΔHB, Hemodialysis, Hemoglobin Changes

Internal Medicine and Nephrology Department, Faculty of Medicine Benha University, Egypt.

Corresponding to:
Dr. Moaz Bakr.
Internal Medicine and Nephrology Department, Faculty of Medicine Benha University, Egypt.
Email: moazbakr333@gmail.com

Received:
Accepted:

Introduction

The objective of hemodialysis (HD) is to eliminate debris, uremic toxins, and fluid from the blood through ultrafiltration and diffusion. Typically, ultrafiltration is employed to remove fluids in order to attain a clinical "dry weight." A global increase in the number of patients with HD has been observed. Patients with HD are at a greater risk of developing acute myocardial infarction than the general population. One of the primary obstacles faced by patients undergoing HD is the removal of fluid .Previous research on fluid removal in HD patients has noted an association between an interdialytic weight loss exceeding 5.7% of the post-dialytic body weight and an increased mortality rate [(1)]. Additionally, mortality is elevated when the ultrafiltration rate exceeds 10 mL/kg/h [(2)].

As indicated by a recent statement from the Chief Medical Officers of US dialysis facilities, adequate fluid management is one of the most critical unresolved issues for contemporary HD patients worldwide. Furthermore, this statement contributes to the concept of "volume first," which denotes the primary goal of dialysis care as volume control[(3)]. In addition, the removal of fluid results in hemoconcentration, which in turn increases the concentration of hemoglobin (Hb) following HD. Each 1 L of ultrafiltration led to an approximate 0.4 g/dL increase in Hb concentration [(1)]. Some patients experience a significant increase in Hb concentration after fluid removal, while others do not. In the event of an elevated Hb concentration, the ultrafiltration volume exceeds the replenishment volume from the interstitial spaces into the vascular space. However, when the ultrafiltration volume significantly exceeds the replenishment volume, it results in intravascular volume depletion and potentially intradialytic morbid events, such as intradialytic hypotension and muscle cramping. Risk factors for cardiovascular events are acknowledged in each of these incidents [(4)].

In past, the Hb level prior to HD was frequently used as an indicator for the treatment of renal anemia in patients who were undergoing HD. It is also incorporated into the majority of clinical research studies and guidelines [(5)]. The ratio of post-HD Hb (Post-HD-Hb) to pre-HD Hb (pre-HD-Hb) can be ascertained by measuring post-HD Hb levels and analyzing its correlation with cardiovascular events. This discovery was recently made [(6)].

The objective of this investigation was to investigate the correlations between myocardial injury and intra-dialytic changes in Hb level (post-HD-Hb/pre-HD-Hb) ratio in patients with chronic kidney disease (CKD) (stage 5) who are undergoing maintenance HD. Additionally, the study aimed to clarify the intradialytic changes of Hb levels in patients with CKD (stage 5) who are undergoing maintenance HD.

Patients and methods

This prospective study carried on 100 patients aged > 18 years old with CKD stage 5 undergoing maintenance HD at the Nephrology unit, Internal Medicine Department, at Benha University Hospitals. This study was performed between June 2022 and June 2024.

An informed written consent was obtained from the patients. Every patient received an explanation of the purpose of the study and had a secret code number. The study was done after being approved by the Research Ethics Committee, Faculty of Medicine, Benha University.

Exclusion criteria included Hb concentrations < 7.0 g/dL, blood transfusion myocardial Infarction, acute coronary syndrome, liver disease, severe chronic obstructive pulmonary disease, malignancy.

Grouping: According to baseline Hb level (post-Hb/pre-Hb) ratio categories all patients were divided into four groups (1):

Group 1 (n=20): with post-Hb/pre-Hb ratio <1.0, **group 2 (n=38):** with post-Hb/pre-Hb ratio 1.0 to <1.1, **group 3 (n=22):** with post-Hb/pre-Hb ratio 1.1 to <1.2 and **group 4 (n=20):** with post-Hb/pre-Hb ratio ≥1.2. While 4 groups according to post HD Hb level: **Group A (n=30):** with post Hb level <10 g/dL**, group B (n=20):** with post Hb level 10 g/dL to < 11 g/dL**, group C (n=20):** with post Hb level 11 g/dL to < 12 g/dL and **group D (n=30):** with post Hb level >12 g/dL.

All studied were subjected to the following: Complete history (history taking including age, gender and cause of CKD), underlying disease including hypertension (HTN), atrial fibrillation, diabetes mellitus (DM), coronary artery disease, hyperlipidemia, cerebrovascular disease and peripheral artery disease including vascular access, HD duration, postdialysis weight loss, ultrafiltration rate and length of HD session/hours**. Clinical examination included** pre-and post-dialysis systolic BP and body mass index (BMI). Predialysis **Laboratory investigations included** CBC, Hb, post-HD-Hb / pre-HD-Hb ratio, serum phosphorus, C-reactive protein (CRP) [(7)], random blood glucose, total cholesterol, HDL, LDL, triglycerides, albumin, phosphorous, PTH, creatinine, urea, uric acid, potassium, sodium, hsCRP, serum albumin, serum total calcium, Calculated as follows, the post-Hb/pre-Hb concentration ratio is as follows: The post-Hb concentration/pre-Hb concentration (post-Hb/pre-Hb) and Hb concentrations, as well as high-sensitivity cardiac troponin T (hs-cTnT) prior to and following HD, and creatine kinase (CK-MB) prior to and following HD, will be evaluated during the introductory session of the week.

Echocardiogram

Speckle Tracking Echocardiography (STE) is an advanced imaging technique that analyzes myocardial strain, providing insights into myocardial deformation and function. In HD patients, STE has been used to detect subclinical myocardial dysfunction, even in the presence of preserved ejection fraction. This modality can identify early myocardial changes that may not be apparent with conventional echocardiographic methods. A comprehensive evaluation of the left ventricular ejection fraction, end-diastolic diameter, and left ventricular end-diastolic diameter was performed for all patients [(8)].

ECG: pre- and post-hemodialysis: The ECG criteria for HD patients included ST-Segment elevation myocardial infarction. This was defined as an ST-segment elevation of ≥0.1 mV in at least two contiguous limb or precordial leads, excluding aVR. NCBI and non-ST-elevation myocardial infarction: T-wave inversion ≥0.1 mV or dynamic ST-segment depression ≥0.1 mV in at least two contiguous leads, accompanied by elevated cardiac biomarkers [(9)].

Approval code: MD 16-12-2021

Statistical analysis

The data was compiled, coded, and entered into a spreadsheet using Excel 2016 for Windows, a component of the Microsoft Office suite 2016 developed by Microsoft Corporation in the United States. IBM Corp. in Armonk, New York, published IBM SPSS Statistics for Windows, Version 26.0, for data analysis in this study. The Kolmogorov-Smirnov test was implemented to guarantee that the distribution was normal. Continuous data was rendered as the mean ± standard deviation, median, correlation coefficient, and interquartile range, while categorical data was represented as numbers and percentages. We considered a statistical value of less than 0.05 to be significant.

Results

There was a significant association between gender distribution and post -HB /Pre-HB ratio ($p < 0.001$), with males being predominant in groups 2, 3, and 4, while females were mainly in Group 1. Additionally, age showed a significant increasing trend across the groups ($p <$

0.001), with post-hoc comparisons revealing significant differences between most groups except between Groups 3 and 4. There was a significant association between the causes of CKD and the post -HB /Pre-HB ratio groups (p< 0.001), with polycystic kidney disease (PCK) becoming more prevalent as post -HB /Pre-HB ratio increases, while SLE and diabetic nephropathy are predominantly found in Group 1. HTN is a major cause across all groups, particularly in Groups 3 and 4. Similarly, underlying diseases show a significant correlation with post -HB /Pre-HB ratio groups (p< 0.001), with coronary artery disease more frequent in groups 2, while DM and hyperlipidemia are concentrated in group 1. There were a significant association between HD duration, post-dialysis weight loss, BMI, and ultrafiltration rate with changes in post-HB /Pre-HB ratio, (p<0.001). Patients with higher post-HB /Pre-HB ratio (≥1.2) had longer HD duration (median 12.0 hours), greater post-dialysis weight loss (median 5.0 kg), lower BMI (median 18.8 kg/m²), and higher ultrafiltration rates (median 5.0 L/h). Pairwise comparisons revealed significant differences among most groups, except for some non-significant comparisons (e.g., between group 3&4 in BMI and post-dialysis weight loss). **Table 1**

Group 1 and group 4 showed a statistically significant decrease in left ventricular ejection fraction (LVEF) over time (at the 6-month, 1-year, and 1.5-year time points compared to baseline). Group 1 had the lowest LVEF values across all time points and showed the most significant reduction in LVEF compared to other groups followed by group 4. Unlike, Group 2 and group 3 showed a statistically significant increase in LVEF, particularly between baseline and 1.5 years. At baseline, there was significant difference between the four groups regarding LVEF as group 4 had significantly higher LVEF than group 1 and group 3. At 6 months, group 1 showed the most significant drop in LVEF compared to group 2, group 3, and group 4. Group 1 and group 4 showed a statistically significant decrease in LVEF over time (at the 6-month, 1-year, and 1.5-year time points compared to baseline). Group 1 had the lowest LVEF values across all time points and showed the most significant reduction in LVEF compared to other groups followed by group 4. **Table 2**

There was no statistically significant difference in prevalence of myocardial affection among the four groups (p>0.05). Group D showed a slightly higher proportion of myocardial affection (33.3%) compared to the other groups (each at 20.0%). There was a statistically significant association between post Hb/preHb ratio and myocardial injury (p= 0.005). Groups with a smaller post Hb/preHb ratio (Groups 2 and 3) exhibited a notably lower incidence of myocardial affection (10.5% and 13.6%, respectively), whereas Groups 1 and 4, with the lowest (<1) and highest (≥1.2) post Hb/preHb ratio values, had significantly higher rates (40.0% and 45.0%, respectively). **Table 3**

There was statistically significant elevation in hs-cTnT, hs-cTnI, and CK-MB both before and after HD in patients with myocardial affection compared to those without (p< 0.001 for all comparisons). **Table 4**

Table 5, Figure 1 illustrate the diagnostic performance of hs-cTnT, hs-cTnI, and CK-MB in detecting myocardial injury. Among the markers, hs-cTnT at a cut-off of 12 demonstrated the highest diagnostic accuracy, with the greatest AUC (0.808), balanced sensitivity (75%) and specificity (81.6%), and a high NPV (91.2%), making it a reliable tool for ruling out myocardial injury. hs-cTnI at a cut-off of 8.9 showed a slightly lower AUC (0.796) and specificity (78.9%), with comparable sensitivity (75%) and NPV (90.9%), suggesting it is also effective, though slightly less so than hs-cTnT. CK-MB, while achieving perfect specificity and PPV (100%) at a cut-off of 23.5, had markedly low sensitivity (41.7%).

Table 1: Demographic data and clinical data according to post -HB /Pre-HB ratio categories, hemodialysis duration, post-dialysis weight loss, BMI and ultrafiltration rate according to post-HB /Pre-HB ratio categories

		Group (1) <1 (N= 20)		Group (2) 1- <1.1 (N= 38)		Group (3) 1.1- <1.2 (N= 22)		Group (4) ≥1.2 (N= 20)		P-value
		N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	
		Demographic data								
Gender	**Male**	4	20.0%	36	94.7%	22	100.0%	20	100.0%	**<0.001****
	Female	16	80.0%	2	5.3%	0	0.0%	0	0.0%	
Age (years)	**Median (IQR)**	45 (44- 55)		54 (50- 58)		60 (58- 64)		63 (61- 66)		**<0.001**** P_{1-2}=1.00 P_{1-3}**<0.001** P_{1-4}**<0.001** P_{2-3}**<0.001** P_{2-4}**<0.001** P_{3-4}=0.798
	Range	40- 60		40- 60		57- 66		58- 67		
		Clinical data								
Causes of CKD	**ADPCK**	0	0.0%	2	5.3%	6	27.3%	10	50.0%	**<0.001****
	Diabetic nephropathy	8	40.0%	4	10.5%	2	9.1%	0	0.0%	
	HTN	0	0.0%	16	42.1%	8	36.4%	10	50.0%	
	NSAID	0	0.0%	12	31.6%	4	18.2%	0	0.0%	
	SLE	12	60.0%	0	0.0%	0	0.0%	0	0.0%	
	Unknown	0	0.0%	4	10.5%	2	9.1%	0	0.0%	
Underling disease	**Coronary artery disease**	0	0.0%	10	26.3%	0	0.0%	0	0.0%	**<0.001****
	DM	8	40.0%	0	0.0%	0	0.0%	0	0.0%	
	DM and hyperlipidemia	4	20.0%	0	0.0%	0	0.0%	0	0.0%	
	HTN	8	40.0%	14	36.8%	12	54.5%	10	50.0%	
	Hyperlipidemia	0	0.0%	10	26.3%	6	27.3%	4	20.0%	
Items	**Groups**	**Mean**	**± SD**	**Median**		**IQR**		**Range**		**P-value**
Hemodialysis duration	**G1<1**	4.5	3.0	6.0		2.0		8.0		**<0.001****
	G2 1- <1.1	6.0	5.0	7.0		3.0		9.0		P_{1-2}=0.840
	G3 1.1- <1.2	9.0	8.0	11.0		5.0		13.0		P_{1-3}**<0.001**
	G4 ≥1.2	12.0	11.0	13.0		10.0		14.0		P_{1-4}**<0.001** P_{2-3}**<0.001** P_{2-4}**<0.001** P_{3-4}=0.126
Post-dialysis weight loss	**G1<1**	1.5	1.0	1.5		1.0		1.5		**<0.001****
	G2 1- <1.1	2.5	2.0	3.5		1.0		4.0		P_{1-2}=0.073
	G3 1.1- <1.2	3.5	3.5	5.0		3.0		5.5		P_{1-3}**<0.001**
	G4 ≥1.2	5.0	5.0	5.0		4.5		5.0		P_{1-4}**<0.001** P_{2-3}**=0.001** P_{2-4}**<0.001** P_{3-4}=0.189
BMI (Kg/m^2)	**G1<1**	27.5	27.0	29.0		26.6		29.0		**<0.001****
	G2 1- <1.1	23.5	23.0	25.0		21.0		27.3		P_{1-2}=**0.024**
	G3 1.1- <1.2	22.5	19.5	24.0		19.0		25.0		P_{1-3}**<0.001**
	G4 ≥1.2	18.8	18.0	19.0		17.5		20.0		P_{1-4}**<0.001** P_{2-3}**<0.001** P_{2-4}**<0.001** P_{3-4}=0.494
Ultrafiltration rate	**G1<1**	1.3	1.0	1.5		1.0		1.5		**<0.001****
	G2 1- <1.1	2.5	2.0	3.5		1.0		4.0		P_{1-2}**<0.001**
	G3 1.1- <1.2	4.5	3.5	5.5		3.0		6.0		P_{1-3}**<0.001**
	G4 ≥1.2	5.0	5.0	5.0		4.5		5.5		P_{1-4}**<0.001** P_{2-3}=0.527 P_{2-4}**<0.001** P_{3-4}=**0.006**

Data presents as mean ± SD, Median, IQR,Range or frequency (%). HTN: Hypertension, ADPCK: autosomal dominant polycystic kidney disease, SLE: systemic lupus erythematosus, DM: diabetes mellitus, BMI: body mass index

Table 2: Left ventricular ejection fraction (LVEF)according to post Hb/preHb ratio categories

		EF (%)							
		Mean	**SD**	**Median**	**IQR**		**Range**		**P-value**
Baseline	**Group (1)**	56.13	1.27	55.6	55.3	56.1	55.1	59.0	**0.003****
	Group (2)	56.92	1.99	55.9	55.7	58.0	55.0	62.0	P_{1-2}=0.117,
	Group (3)	55.82	0.32	55.7	55.6	55.9	55.5	56.5	P_{1-3}=1.00
	Group (4)	57.58	2.39	56.7	55.8	58.5	55.5	63.0	P_{1-4}=**0.008**, P_{2-3}=0.321 P_{2-4}=1.00, P_{3-4}=**0.025**
At 6th month	**Group (1)**	55.48	1.41	55.1	54.5	55.8	53.6	58.0	**0.001****
	Group (2)	57.00	2.01	56.1	55.8	57.5	55.5	62.7	P_{1-2}=**0.001**,
	Group (3)	56.15	0.49	55.9	55.8	56.2	55.8	57.3	P_{1-3}=**0.021**
	Group (4)	57.11	2.45	56.3	55.4	58.1	54.4	62.5	P_{1-4}=**0.021**, P_{2-3}=1.00 P_{2-4}=1.00, P_{3-4}=1.00
At 1 year	**Group (1)**	55.15	1.62	55.0	54.2	55.8	53.0	57.9	<**0.001****
	Group (2)	57.42	2.12	56.6	55.9	57.8	55.7	62.8	P_{1-2}<**0.001**,
	Group (3)	55.89	1.32	56.2	55.9	56.5	52.9	57.5	P_{1-3}=0.106
	Group (4)	56.71	2.36	55.7	55.2	56.4	55.0	62.3	P_{1-4}=0.358, P_{2-3}=0.331 P_{2-4}=0.116, P_{3-4}=1.00
At 1.5 year	**Group (1)**	54.94	1.58	54.8	54.0	55.5	52.8	57.6	<**0.001****
	Group (2)	57.99	2.35	57.0	56.7	58.2	55.8	63.8	P_{1-2}<**0.001**,
	Group (3)	56.28	1.27	56.8	55.4	57.1	54.1	57.7	P_{1-3}=0.134
	Group (4)	56.09	2.54	55.1	55.0	56.1	53.5	62.0	P_{1-4}=1.00, P_{2-3}=0.306 P_{2-4}=**0.003**, P_{3-4}=1.00
P-value over time (Friedman Test)		**Group (A); p<0.001**, Group (B); p<0.001** Group (C); p<0.001**, Group (D); p<0.001****							

Data presents as mean ± SD, Median, IQR or Range. *p≤0.05 is significant, **p≤0.01 is highly significant, EF: ejection fraction

Table 3: Asymptomatic myocardial injury according to post HD-Hb level categories and according to post Hb/preHb ratio categories

		Group (A) (N= 30)		Group (B) (N= 20)		Group (C) (N= 20)		Group (D) (N= 30)		P-value
		N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	
Myocardial injury	**No**	24	80.0%	16	80.0%	16	80.0%	20	66.7%	0.593MC
	Yes	6	20.0%	4	20.0%	4	20.0%	10	33.3%	
		Group (1) (N= 20)		**Group (2) (N= 38)**		**Group (3) (N= 22)**		**Group (4) (N= 20)**		**P-value**
		N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	
Myocardial injury	**No**	12	60.0%	34	89.5%	19	86.4%	11	55.0%	**0.005****
	Yes	8	40.0%	4	10.5%	3	13.6%	9	45.0%	

Data presents as mean ± SD or frequency (%). *p≤0.05 is significant, **p≤0.01 is highly significant,

Table 4: Relation between hs-cTnT, hs-cTnI and CK-MB in detection of myocardial injury

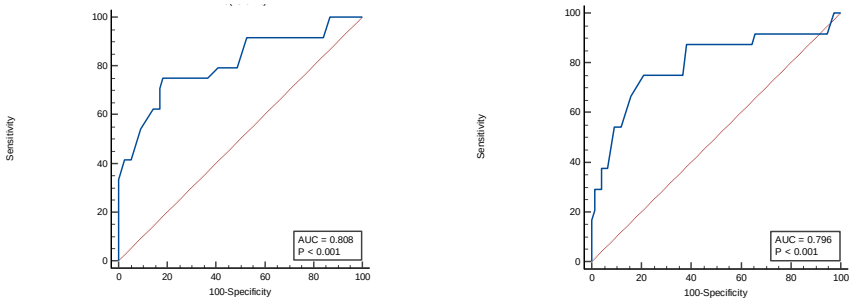
	No myocardial affection							Myocardial affection							P-value
	Mean	**SD**	**Median**	**IQR**		**Range**		**Mean**	**SD**	**Median**	**IQR**		**Range**		
Pre (hs-cTnt)	10.13	2.16	10.5	8.5	12.0	5.5	13.0	12.07	1.68	12.8	11.6	13.1	7.5	13.5	**<0.001***
Post (hs-cTnt)	10.69	2.23	11.2	8.9	12.5	5.9	13.5	12.54	1.76	13.3	12.2	13.5	7.8	14.5	**<0.001***
Pre (hs-cTnI)	7.12	1.81	6.5	5.5	8.9	4.0	11.5	9.45	2.17	10.0	8.4	11.0	4.5	12.1	**<0.001***
Post (hs-cTnI)	7.00	1.81	6.5	5.5	8.9	4.1	11.1	9.36	2.24	10.0	8.4	11.0	4.2	12.0	**<0.001***
Pre (CK-MB)	18.65	3.56	20.0	15.4	22.0	12.0	23.5	21.33	4.06	22.2	20.7	24.5	13.5	25.0	**<0.001***
Post (CK-MB)	19.00	3.60	20.3	15.8	22.3	12.6	23.9	21.77	4.10	22.5	21.1	25.0	14.1	25.9	**<0.001***

Data presents as mean ± SD, Median, IQR or Range. CK-MB: creatine kinase, *P value <0.05 is significant, **p<0.01 is highly significant.

Table 5: Diagnostic performance of hs-cTnT, hs-cTnI and CK-MB in detection of myocardial injury

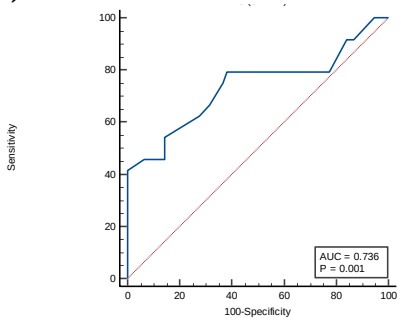
	Cut off	AUC	Sensitivity	Specificity	PPV	NPV	p-value
hs-cTnT	12	0.808	75%	81.6%	56.2 %	91.2%	**<0.001***
hs-cTnI	8.9	0.796	75%	78.9%	52.9%	90.9%	**<0.001***
CK-MB	23.5	0.736	41.7%	100%	100%	84.4%	**0.001***

Data presents as numbers. CK-MB: creatine kinase , AUC: Area under curve, PPV: positive predictive value, NPV: negative predictive value. hs-cTnT: high-sensitivity cardiac troponin T. hs-cTnI: high-sensitivity cardiac troponin I.



(A)

(B)



(C)

Table 6: (A): ROC curve of hs-cTnT in detection of myocardial injury, (B): ROC curve of hs-cTnI in detection of myocardial injury, (C): ROC curve of CK-MB in detection of myocardial injury

Discussion

CKD represents a global health challenge, particularly in its end-stage form (ESRD), requiring renal replacement therapy. Cardiovascular morbidity and mortality are significant among patients who are undergoing maintenance hemodialysis, with approximately 50% of fatalities attributable to cardiovascular causes. The optimal approach to monitoring and preventing cardiovascular complications remains elusive, despite advancements in anemia management and dialysis technology [(10)]. In this vulnerable population, the dynamic fluctuations in hemoglobin levels during hemodialysis sessions have been identified as a potential indicator of cardiovascular risk [(1)].

When examining the relationship between gender and post/pre-dialysis hemoglobin ratio, we found a striking association with males dominating in groups with higher Post HB/PreHB ratio values (≥1.1), while females were predominantly in the group with Post HB/PreHB ratio <1.

This finding aligns with existing research highlighting gender-based differences in hemoglobin dynamics among hemodialysis patients. Studies have consistently reported that women on hemodialysis often require higher doses of erythropoiesis-stimulating agents to achieve and maintain target hemoglobin levels compared to men. For instance, research conducted in Northern Colombia found that women undergoing chronic hemodialysis required significantly higher doses of recombinant erythropoietin (EPO) than men to maintain hemoglobin targets [(11)]. These findings suggest that the observed gender disparities in Post HB/PreHB ratio values may be attributed to inherent biological differences in erythropoiesis and hemoglobin regulation between males and females and potential variations in responsiveness to anemia treatments.

A striking finding in this study was the strong association between hemodialysis duration and Post HB/PreHB ratio. Patients with higher Post HB/PreHB ratio values had significantly longer dialysis vintage, with the Post HB/PreHB ratio ≥1.2 group having a median dialysis duration of 12 years compared to 4.5 years in the Post HB/PreHB ratio <1 group. This relationship may reflect the adaptation of erythropoiesis and fluid homeostasis with prolonged dialysis therapy.

Hoppe et al. [(12)] have reported that longer dialysis vintage is associated with changes in body composition and fluid distribution, which might explain the observed differences in hemoglobin dynamics. In contrast, another study has shown that lower Post HB/PreHB ratio was related to HD [(13)].

Post-dialysis weight loss and ultrafiltration rate also showed significant positive associations with Post HB/PreHB ratio ($p<0.001$) in this study. Patients with higher Post HB/PreHB ratio had greater fluid removal during dialysis, with the Post HB/PreHB ratio ≥1.2 group having a median post-dialysis weight loss of 5.0 kg compared to 1.5 kg in the Post HB/PreHB ratio <1 group.

This finding is consistent with basic physiological principles, as greater fluid removal would result in more pronounced hemoconcentration and higher post-dialysis hemoglobin levels [(14)]. In line with us, Pstras et al. [(15)] found that Hb levels increased during hemodialysis, making it reliable for estimating relative blood volume changes.

In contrast, an earlier study did not identify any correlation between variations in intradialytic hematocrit levels and ultrafiltration volume, regardless of whether the treatment was administered during the midweek or at the beginning of the subsequent week. This indicates that greater fluid removal does not necessarily cause more pronounced hemoconcentration or higher post-dialysis hemoglobin levels, suggesting that other factors, such as patient-specific

characteristics, influence hematocrit changes during hemodialysis [16].

Arteriovenous fistula (AVF) was the predominant vascular access across all our groups (86.7-90.0%), consistent with current clinical practice guidelines that recommend AVF as the preferred access for hemodialysis [17].

A particularly interesting finding was the U-shaped relationship between the Post HB/PreHB ratio and cardiac outcomes. Patients with extreme Post HB/PreHB ratio values, either very low (<1 g/dL) or very high (≥1.2 g/dL), demonstrated higher rates of myocardial affection (40.0% and 45.0%, respectively) compared to those with moderate changes (10.5% and 13.6% for Post HB/PreHB ratio 0-1 g/dL and 1.1-1.2 g/dL, respectively).

This U-shaped relationship is consistent with findings from Hara et al. [1], In Japanese hemodialysis patients, they observed a comparable pattern in which an elevated risk of significant adverse cardiovascular events was associated with both a very low and very high Post HB/PreHB ratio. In comparison to the reference group (Post HB/PreHB ratio ≥1.1 to <1.2), they reported hazard ratios of 1.69, 1.29, and 1.31 for Post HB/PreHB ratios <1.0, ≥1.0 to <1.1, and ≥1.2, respectively. Nishiwaki et al. [13] found that lower Post HB/PreHB ratio is associated with a higher risk of 1-year mortality, consistent with our findings that patients with Post HB/PreHB ratio <1.0 had higher rates of adverse outcomes. This suggests that patients who fail to show the expected increase in hemoglobin concentration after fluid removal during dialysis may have volume overload or other pathophysiological processes contributing to poor outcomes.

The mechanisms underlying this U-shaped relationship likely involve the balance between ultrafiltration and plasma refilling during hemodialysis. A low Post HB/PreHB ratio indicates that plasma refilling exceeds ultrafiltration, suggesting inadequate fluid removal during hemodialysis [1]. This can result in chronic volume imbalance, a well-established risk factor for adverse cardiovascular outcomes in hemodialysis patients. Even in the absence of acute coronary events, chronic volume excess can lead to elevated cardiac troponin levels, diastolic dysfunction, and ultimately heart failure, which are all contributed to by left ventricular hypertrophy [18].

The diagnostic efficacy of these biomarkers for detecting myocardial injury was evaluated in this study. The results indicated that hs-cTnT had the highest diagnostic accuracy (AUC 0.808) at a cutoff of 12 ng/dL, with adequate sensitivity (75%) and specificity (81.6%). hs-cTnI exhibited a slightly reduced but still reasonable performance (AUC 0.796, sensitivity 75%, specificity 78.9%).

The current cut-off value for hs-cTnT in the diagnosis of acute myocardial infarction would be of no utility to patients undergoing chronic hemodialysis, as nearly all patients in this study exhibited elevated levels of hs-cTnT. As a result, the diagnosis of acute myocardial infarction should be made on the basis of a significant increase and subsequent decline in sequential hs-cTnT levels, rather than a single elevated level of hs-cTnT.

The prognostic value of hs-cTnT in pre-dialysis advanced CKD patients has been the subject of previous research. In comparison to the standard cutoff level employed in individuals with normal renal function, they found that individuals with a GFR of less than 20 ml/min/1.73 m2 exhibited a 2.5-fold increase in the hs-cTnT cutoff level to predict long-term cardiovascular outcomes. The threshold level of hs-cTnT in this patient group has been suggested to be 35 ng/dL [19]. Nevertheless, the prognostic value of hs-cTn in patients with ESRD is inconsistently reported. In certain studies, the hs-cTn T is a more precise predictor of long-term cardiovascular outcomes than the hs-cTnI in patients with chronic hemodialysis [20-23]. Larger studies that

employ hs-cTn to predict the long-term prognosis in patients with ESRD are necessary to elucidate this matter. In order to clarify this issue, it is imperative to conduct larger studies that utilize hs-cTn to predict the long-term prognosis in patients with ESRD.

When stratified by Post HB/PreHB ratio categories, our echocardiographic findings further support and explain the U-shaped relationship between Post HB/PreHB ratio and adverse cardiac outcomes. Patients with extreme Post HB/PreHB ratio values (Group 1: Post HB/PreHB ratio <1 and Group 4: Post HB/PreHB ratio ≥1.2) showed greater deterioration in cardiac structure and function over time. Group 1 had the lowest EF values at all time points and showed the most significant reduction in EF over the follow-up period. Group 4, despite starting with relatively preserved EF, also showed significant deterioration over time. This suggests that both insufficient increase in hemoglobin concentration (potentially indicating volume overload) and excessive increase (potentially indicating excessive ultrafiltration) during dialysis are associated with adverse cardiac remodeling.

A study assessed the variability of hs-cTnI levels before and after hemodialysis sessions.

The results showed that hs-cTnI levels did not significantly change post-hemodialysis, suggesting a stable release pattern of this biomarker in the studied population. This discovery may have implications for the timing and interpretation of hs-cTnI measurements in clinical practice [(24)].

The limitations of the study were relatively small sample size and it was a single center study.

Conclusion

The asymptomatic raising of hscTni, hscTnt and ckmb represent silient myocardial injury during hemodialysis. The intradialytic changes in Hb level post HB /preHB ratio were associated with higher cardiac troponin level (hs Tni and hscTnt) and ckmb. There is an association between the intradialytic changes in hemoglibin level with asymptomatic myocardial injury.

Therefore, the study recommended that it is post-to-pre-dialysis Hb ratios as part of routine clinical care to identify patients at increased cardiovascular risk and using hs-cTnI rather than hs-cTnT when evaluating suspected acute cardiac events in hemodialysis patients due to its greater specificity.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

No conflicts of interest

References

1. Hara T, Kimachi M, Ikenoue T, Akizawa T, Fukuhara S, Yamamoto Y. Intra-Dialytic Hemoglobin Changes and Cardiovascular Events: A Cohort Study on Dialysis Outcomes and Practice Patterns in Japan. Am J Nephrol. 2019;50:272-80.

2. Assimon MM, Wang L, Flythe JE. Intradialytic hypertension frequency and short-term clinical outcomes among individuals receiving maintenance hemodialysis. Am J Hypertens. 2018;31:329-39.

3. Weiner DE, Brunelli SM, Hunt A, Schiller B, Glassock R, Maddux FW, et al. Improving clinical outcomes among hemodialysis patients: a proposal for a "volume first" approach from the chief medical officers of US dialysis providers. Am J Kidney Dis. 2014;64:685-95.

4. MacEwen C, Sutherland S, Daly J, Pugh C, Tarassenko L. Relationship between hypotension and cerebral ischemia during hemodialysis. J Am Soc Nephrol 2017;28:2511-20.

5. Yamamoto H, Nishi S, Tomo T, Masakane I, Saito K, Nangaku M, et al. 2015 Japanese Society for Dialysis Therapy: Guidelines for Renal Anemia in Chronic Kidney Disease. Ren Replace Ther. 2017;3:36-44.

6. Nishiwaki H, Fukuma S, Hasegawa T, Kimachi M, Akizawa T, Fukuhara S. Dialysis-related practice patterns among hemodialysis patients with cancer. Health Sci Rep. 2018;1:46-52.

7. Pan F, Yang L, Li Y, Liang B, Li L, Ye T, et al. Factors associated with death outcome in patients with severe coronavirus disease-19 (COVID-19): a

case-control study. Int J Med Sci. 2020;17:1281-92.
8. Leitman M, Lysyansky P, Sidenko S, Shir V, Peleg E, Binenbaum M, et al. Two-dimensional strain–a novel software for real-time quantitative echocardiographic assessment of myocardial function. J Am Soc Echocardiogr 2004;17:1021-9.
9. Krane V, Heinrich F, Meesmann M, Olschewski M, Angermann C, Sto S, et al. Electrocardiography and outcome in patients with diabetes mellitus on maintenance hemodialysis. J Am Soc Nephrol 2009;4:394-9.
10. Bello AK, Okpechi IG, Osman MA, Cho Y, Htay H, Jha V, et al. Epidemiology of haemodialysis outcomes. Nat Rev Nephrol. 2022;18:378-95.
11. Coronado Daza JA, Cuchi GU. Gender Differences in Dose of Erythropoietin to Maintain Hemoglobin Target in Hemodialysis Patients. Indian J Nephrol. 2019;29:160-5.
12. Hoppe K, Schwermer K, Kawka A, Klysz P, Baum E, Kaluzna M, et al. Dialysis vintage stratified comparison of body composition, hydration and nutritional state in peritoneal dialysis and hemodialysis patients. Arch Med Sci. 2018;14:807-17.
13. Nishiwaki H, Hasegawa T, Koiwa F, Hamano T, Masakane I. The association of the difference in hemoglobin levels before and after hemodialysis with the risk of 1-year mortality in patients undergoing hemodialysis. Results from a nationwide cohort study of the Japanese Renal Data Registry. PLoS One. 2019;14:21-53.
14. Stuard S, Ridel C, Cioffi M, Trost-Rupnik A, Gurevich K, Bojic M, et al. Hemodialysis Procedures for Stable Incident and Prevalent Patients Optimize Hemodynamic Stability, Dialysis Dose, Electrolytes, and Fluid Balance. J Clin Med. 2024;13:32-41.
15. Pstras L, Debowska M, Wojcik-Zaluska A, Zaluska W, Waniewski J. Hemodialysis-induced changes in hematocrit, hemoglobin and total protein: Implications for relative blood volume monitoring. PLoS One. 2019;14:22-76.
16. Ku C-C, Chiu W-Y, Wu S-W, Chang H-R, Lian J-D. The Association between Post-Dialysis Hematocrit Levels and Ultrafiltration Volume in Maintenance Hemodialysis Patients. Acta Nephrologica. 2011;25:182-5.
17. Lok CE, Huber TS, Lee T, Shenoy S, Yevzlin AS, Abreo K, et al. KDOQI clinical practice guideline for vascular access: 2019 update. Am J Kidney Dis. 2020;75:S1-S164.
18. Neeland IJ, Drazner MH, Berry JD, Ayers CR, deFilippi C, Seliger SL, et al. Biomarkers of Chronic Cardiac Injury and Hemodynamic Stress Identify a Malignant Phenotype of Left Ventricular Hypertrophy in the General Population. JACC. 2013;61:187-95.
19. Canney M, Tang M, Er L, Barbour SJ, Djurdjev O, Levin A, et al. Glomerular filtration rate-specific cutoffs can refine the prognostic value of circulating cardiac biomarkers in advanced chronic kidney disease. Can J Cardiol. 2019;35:1106-13.
20. Kalaji FR, Albitar S. Predictive value of cardiac troponin T and I in hemodialysis patients. Saudi J Kidney Dis Transpl. 2012;23:939-45.
21. Porter G, Norton T, Bennett W. Long term follow up of the utility of troponin T to assess cardiac risk in stable chronic hemodialysis patients. Clin Lab. 2000;46:469-76.
22. Hickman PE, McGill D, Potter JM, Koerbin G, Apple FS, Talaulikar G. Multiple biomarkers including cardiac troponins T and I measured by high-sensitivity assays, as predictors of long-term mortality in patients with chronic renal failure who underwent dialysis. Am J Cardiol. 2015;115:1601-6.
23. Khan IA, Wattanasuwan N, Mehta NJ, Tun A, Singh N, Singh HK, et al. Prognostic value of serum cardiac troponin I in ambulatory patients with chronic renal failure undergoing long-term hemodialysis: a two-year outcome analysis. J Am Coll Cardiol. 2001;38:991-8.
24. Wongcharoen W, Chombandit T, Phrommintikul A, Noppakun K. Variability of high-sensitivity cardiac troponin T and I in asymptomatic patients receiving hemodialysis. Sci Rep. 2021;11:17-34.

To cite this article: Ahmed E. Mansour , Moaz Bakr, El Metwally L. El Shahawy, Shimaa Moustafa, Shimaa S. El-sayed. The Relationships between Intra Dialytic Changes in Hemoglobin Level and Myocardial Injury in Patients with ESRD Undergoing Maintenance Hemodialysis. BMFJ XXX, DOI: 10.21608/bmfj.2025.394660.2532.