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Evaluating Growth Differentiation Factor-15 Serum Levels and Left Ventricular Dysfunction Using Different Techniques in Pediatric Hemodialysis Patients

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Abstract

Background: The standard echocardiography is limited in detecting subclinical left ventricular (LV) dysfunction in pediatric hemodialysis patients. However, speckle-tracking echo (STE) analysis has emerged as a viable alternative. Furthermore, Growth Differentiation Factor-15 (GDF-15) is a stress-responsive biomarker generated by cardiac tissues. **Aim**: Evaluate left ventricular function using a range of echocardiography modalities and determine the most effective modality. Additionally, it seeks to quantify the diagnostic accuracy of GDF-15 as an early indicator of cardiac dysfunction in pediatric patients undergoing regular hemodialysis and explore the association between GDF-15 levels and left ventricular dysfunction. **Subjects and Methods**: An assessment of the LV functions and dimensions in a cohort of 40 pediatric patients undergoing regular hemodialysis compared to a control group of 40 healthy children. Our evaluation encompassed the utilization of GDF-15, hsCRP serum levels, conventional Echocardiography, tissue Doppler imaging (TDI), and Speckle Tracking Echocardiography (STE), in conjunction with routine laboratory investigations, to analyze the subjects post-hemodialysis (HD). **Results**: Children on hemodialysis showed significantly higher levels of GDF-15 and hsCRP. Furthermore, 67.5% of the patients displayed impaired left ventricular function as identified through conventional and TDI, while 82.5% exhibited global left ventricular strain as determined by STE. A strong correlation was found between EF% and serum cholesterol and triglyceride levels. Additionally, a notable association was discovered between GDF-15 and systolic blood pressure, left ventricular interventricular septal diameter (LVIVSD), and serum calcium levels. **Conclusion:** STE has shown its superiority over conventional and (TDI) in the early identification of LV changes in pediatric hemodialysis patients. GDF-15 is a sensitive indicator for early left ventricular dysfunction and shows a significant correlation with hypertension, left ventricular interventricular septal end-diastolic dimension (LVIVSD), and serum calcium levels.

Keywords

Hemodialysis, Children, GDF-15, Speckled Tracking Echo

1. Introduction

Cardiovascular disease is the leading cause of death in patients with ESRD. Half of the patients with ESRD who undergo dialysis or kidney transplantation will die from cardiovascular causes [1].

Growth differentiation factor 15 (GDF-15) is a member of the TGF-β cytokine superfamily widely expressed and may be induced in response to tissue injury. Elevations in GDF-15 may identify a novel pathway in kidney function loss among patients with CKD [2].

Elevated levels of GDF-15 have been linked to higher rates of both cardiovascular and non-cardiovascular mortality. This protein plays a crucial role in the development and progression of various cardiovascular diseases, such as heart failure, coronary artery disease, and atrial fibrillation, as well as non-cardiovascular diseases, such as chronic kidney disease, diabetes, cancer, and cognitive impairment. However, its comparative prognostic performance across different atherosclerotic cardiovascular disease (ASCVD) presentations remains unknown [3] [4].

Pediatric ESRD patients may experience systolic left ventricular hypertrophy (LVH) and function. However, children with ESRD show preserved systolic LV function, as per the 2-dimensional echocardiography and tissue Doppler measurements [5].

Speckle tracking echocardiography (STE) is a noninvasive ultrasound imaging technique that evaluates myocardial mechanics, global and regional myocardial function, and deformation at the early stages of chronic kidney disease (CKD). This method accurately assesses myocardial function independently of the angle of insonation and cardiac translational movements [6].

Our research aims to explore different echocardiography techniques for early detection of left ventricular (LV) dysfunction, assess GDF-15 as an early indicator of cardiovascular risk, and identify potential links between LV dysfunction and GDF-15 in pediatric patients with chronic kidney disease undergoing regular hemodialysis.

2. Subjects and Methods

This case-control study included 80 children recruited from Al-Zahraa Hospital at Al Azhar University, Cairo, Egypt. The children were divided into two groups: 40 children with CKD who were on regular hemodialysis (HD) for more than three months at the time of the study and 40 children without CKD who served as the control group. The children with CKD attended the pediatric hemodialysis unit during the study period. They underwent hemodialysis for 4 hours, three times a week, using a polysulfone low flux membrane dialyzer by 4008 Fresenius and 5008 S-classic machines.

The predominant aetiology of end-stage renal disease (ESRD) was acquired in 16 patients, representing 40% of the study population, while hereditary causes accounted for ESRD in 9 patients (22.5%). The patient cohort's age range spanned from 4 to 18 years. Exclusion criteria encompassed pediatric subjects with congenital or acquired cardiac conditions, as well as those with acute heart failure or other acute or chronic comorbidities such as diabetes or hepatic disease.

Comprehensive history taking was conducted, which included aetiology, the onset of chronic kidney disease, duration of hemodialysis, and laboratory investigations. Informed consent was obtained from the parents of the participating children by the guidelines of the ethical committee of Alzhraa Hospital, Al-Azhar University, Cairo, Egypt. The study was conducted in collaboration with the pediatric hemodialysis unit, the cardiology department of Alzhraa Hospital, Al-Azhar University, and the clinical pathology department of the National Heart Institute.

2.1. Sampling

Blood samples were collected in the morning before starting a dialysis session, following a fast of at least 12 hours. Three tubes were used to withdraw the blood using a vacuum system: one containing EDTA and two containing gel. The EDTA sample was used to analyze CBC on the automated cell counter Swelab alpha. One of the gel tubes was used to measure urea, creatinine, calcium, phosphorous, sodium, potassium, cholesterol, and triglycerides. The second tube was centrifuged, and serum was separated into two tubes, carefully labelled, and stored at −20˚C until the assay of hsCRP and GDF-15 by ELISA. The kit was supplied by ELAab and tested using Hydroflex ELISA washer from Tecan Austria and Infinit 50 ELISA reader fromTecan Austria.

2.1.1. hsCRP and GDF-15 Assay

Each kit includes a microtiter plate pre-coated with specific antibodies for either hsCRP or GDF-15. Standard concentrations or samples are added to the appropriate wells on the plate, followed by a conjugated monoclonal antibody preparation. The plates are then incubated, and a TMB standard solution is added to each well. The wells containing hsCRP or GDF-15 will appear blue due to the enzyme-substrate reaction. The reaction is stopped by adding a sulphuric acid solution, and the colour change is measured spectrophotometrically at a wavelength of 450 nm. The sample's concentration of hsCRP or GDF-15 is determined by comparing the samples' optical density (O.D.) to the standard curve. The assay range was 0.3 - 10 ng/ml for human hsCRP and 15.6 - 1000 pg/ml for GDF-15.

2.1.2. ECHO Assessment

An ECHO assessment was performed after the hemodialysis session to avoid the volume overload effect.

Echo Doppler was conducted in the cardiology department using the GE Vivid-7 system (GE Ultrasound; Horten, Norway) with tissue Doppler imaging capability. Cases were examined using a multi-frequency (2.5 MHz) matrix probe M3S for TTE, M-Mode, 2D, Doppler (pulsed and continuous wave), and colour flow mapping. All detected echo-Doppler studies were displayed in the standard signal. The same investigator took all measurements over at least three cardiac cycles and calculated the average value for each parameter. Echocardiography was performed within 1 - 2 hours after dialysis when patients' weight was close to their target weight.

LV assessment was conducted using 2D-guided M-mode echocardiography to evaluate several parameters, including LVEDD, LVESD, IVSD, LVPWD, and fractional shortening (FS) [7]. Additionally, 2D echocardiography was employed to determine ejection fraction (EF%) using the Simpson method and segmental wall motion abnormalities [8]. To assess transmitral maximal velocities, pulsed wave Doppler (PWD) was utilized, measuring peak (E) and peak (A) velocities, the E/A ratio, and the deceleration time of early mitral flow. Furthermore, peak S, E, and A velocities were evaluated using TDI [9].

Speckle tracking analysis performed on the LV was obtained in apical 4, 2, and 3 chambers. The LV longitudinal was assessed using 2D speckle-tracking analysis with QRS onset as the reference point, applying a commercially available LV strain software package to the left ventricle.

During analysis, the endocardial border was manually traced at end-systole, and the region of interest width was adjusted to include the entire myocardium. The LV deformation parameters in each of the 18 segments were assessed. The global strain was evaluated by averaging the strain of all segments. Typical GLS values are $\geq -20\%$, as reported by the American Society of Echocardiography and the European Association of Cardiovascular Imaging [10].

2.2. Statistical Analysis

The data was collected, revised, coded, and entered into the Statistical Package for the Social Science version 20 (IBM Corp., Armonk, NY, USA).

Qualitative data were presented as numbers and percentages, while quantitative data were presented as mean, standard deviations, and ranges in cases where their distribution was parametric. In instances of nonparametric distribution, quantitative data were presented as medians with interquartile ranges (IQR). Analysis of two groups with qualitative data entailed using the Chi-square test, with the Fisher exact test employed instead of the Chi-square test when the expected count in any cell was less than [5].

Spearman correlation coefficients were used to assess the correlation between two studied parameters in the same group. To determine the best cutoff point with sensitivity and specificity, the Receiver Operating Characteristic (ROC) curve was used. The interpretation of probability values is as follows: P > 0.05 is considered non-significant, and P < 0.05 is considered significant.

3. Results

Table 1 demonstrates a noticeable decrease in weight and height z-scores among patients compared to controls and a significant increase in systolic blood pressure in hemodialysis children compared to their controls. Additionally, there was a substantial increase in serum levels of urea, creatinine, phosphate, potassium, cholesterol, and triglycerides in hemodialysis patients compared to controls. Furthermore, the serum levels of GDF-15 and hsCRP were also significantly elevated.

Table 1. Comparison between the patients and the control group regarding blood pressure, Z score for anthropometric measurements, and laboratory data.

Groups / Variables	Control Group	Patients Group	Mann Whitney Test	
	No. = 40	No. = 40	t	P-value
Z-score Wt	0.17 (−0.52 - 0.74)	0.49 (−0.74 – 0.14)	−2.368	0.018
Z-score Ht	0.52 (−0.39 - 1.05)	−0.13 (−0.91 – 0.39)	−2.893	0.004
Z-score BMI	0.01 (−0.54 - 0.35)	−0.25 (−0.63 – 0.23)	−1.179	0.238
	Mean ± SD	Mean ± SD	t	P-value
SBP BP (mm/Hg)	116 ± 4.96	124.5 ± 23.75	−2.216•	0.030
DBP BP (mm/Hg)	76.75 ± 4.74	80.5 ± 14.67	−1.539•	0.128
Urea (mg/dl)	12 (10 - 15)	36.5 (26 - 53.5)	−7.188•	0.001
Creat (mg/dl)	0.64 ± 0.17	2.96 ± 1.87	−7.806•	0.001
Ca (mg/dl)	10.14 ± 0.76	10.03 ± 1.91	0.361•	0.719
Phos (mg/dl)	3.96 ± 0.34	5.85 ± 1.19	−9.626•	0.001
Na (mEq/l)	138.2 ± 2.42	137.08 ± 4.75	1.334•	0.186
K (mEq/l)	3.96 ± 1.04	4.42 ± 0.46	2.552•	0.013
Cholesterol (mg/dl)	116.68 ± 10.88	135.9 ± 25.5	−4.386•	0.001
TG (mg/dl)	120.15 ± 10.75	136.75 ± 13.82	−5.998•	0.001
Median (IQR) GDF 15 (pg/ml)	130 (91.5 - 169)	650 (415.5 - 794.5)	130	0.001
Median (IQR) HS CRP (ng/ml)	4.05 (3.60 - 4.75)	13.05 (9.90 - 16.95)	−7.695	0.001

*: Chi-square test; •: Independent t-test.

Table 2 presents the frequency of left ventricular dysfunction detected by conventional ECHO, TDI strain, and speckle-tracking imaging in 40 hemodialysis children. The results showed that 27 out of 40 children (67.5%) had left ventricular dysfunction as indicated by reduced EF%, while the same number (27 out of 40, 67.5%) showed left ventricular dysfunction detected by reduced TDI. Additionally, 33 out of 40 children (82.5%) had left ventricular dysfunction observed using speckle tracking ECHO.

Table 2. Comparison between patients and the control group regarding M-mode conventional ECHO finding of left ventricular.

Variables \ Groups	Control Group No. (40)	Patients Group No. (40)	t-Test	
	Mean ± SD	Mean ± SD	t	P-value
LVEDD (ml)	35.28 ± 4.99	43.58 ± 8.53	−5.314	0.001
LVSD (ml)	21.4 ± 3.22	28.28 ± 8.02	−5.031	0.001
LVPWD (ml)	5.8 ± 1.29	9.43 ± 2.52	−8.105	0.001
LVIVSD (ml)	6.7 ± 1.29	9.65 ± 2.49	−6.669	0.001
LVEF (%)	60.53 ± 7.22	49.6 ± 9.81	5.672	0.001
LVFS (%)	37.15 ± 8.18	37 ± 8.07	0.083	0.934
E wave (ml)	9.35 ± 1.34	1.02 ± 0.26	38.539	0.001
A wave (ml)	5.55 (5 - 6)	7 (5.2 - 9.5)	−3.106	0.002
E/A ratio	1.6 (1.5 - 1.85)	1.33 (1 - 1.85)	−2.406	0.016
E/E' ratio	0.8 (0.7 - 0.8)	2.1 (1.6 - 2.65)	−7.764	0.001

LVEDD: left ventricular end diastolic. **LVSD**: left ventricular systolic. **LVPWD:** left ventricular posterior wall. **LVIVSD**: left ventricular interventricular septum. **E wave (ml):** Peak early diastolic trans-mitral flow velocity. **A wave (ml):** Peak late diastolic trans-mitral flow velocity. **EF (%):** ejection Fraction. **FS:** Fractional shortening. **E/A ratio:** ratio of peak velocity blood flow in early diastole to peak velocity flow in late diastole caused by atrial contraction. **E/E ratio: ratio of the** maximum velocity of E-wave of mitral valve inflow by the maximal velocity of E.

In Table 3, a comparative analysis was conducted between the patients and the control group based on the M-mode conventional ECHO findings related to the dimensions and functions of the left ventricle. The findings indicate a statistically significant increase in the left ventricle dimensions, including LVEDD, LVESD, LVPWD, and LVIVSD (measured in mm), in the hemodialysis group compared to the control group. Moreover, the hemodialysis group demonstrated a notable reduction in EF% compared to the control group, while no significant variance in FS% was observed between the two cohorts. Additionally, the diastolic function of the left ventricle was notably impaired in the hemodialysis group, characterized by an elevation in MV A velocity (measured in meters per second), a decline in MV E/A ratio, and an increase in E/E ratio in comparison to the control group.

Table 3. Frequency of left ventricular dysfunction by conventional ECHO, TDI strain, and speckled tracking ECHO.

Variables \ Groups		No	%
LVEF (%)	Preserved	13	(32.5%)
	Impaired	27	(67.5%)
Avg LV TDI strain (%)	Preserved	13	(32.5%)
	Impaired	27	(67.5%)
LV 2D GLS-STE (%)	Preserved	7	(17.5%)
	Impaired	33	(82.5.0%)

EF (%): Ejection fraction. **Avg LV TDI strain:** Average Left Ventricular tissue Doppler.

Table 4 shows a significant decrease in left ventricular function assessed by (TD velocity, TDI strain, and 2D GLS-STE) in the patient's group compared to their controls.

Table 4. Comparison of left ventricle function by (TD velocity, TD strain, and global strain by speckle echo) between patients and the control group.

Variables \ Groups		Control Group No = 40	Patients Group No = 40	Independent t-Test	
		Mean ± SD	Mean ± SD	t	P-value
Tissue doppler velocity	Avg S	6.11 ± 1.56	4.73 ± 1.32	4.289	0.001
	Avg E	11.69 ± 1.49	4.78 ± 1.71	19.261	0.001
Avg LV TDI strain		24.74 ± 5.09	13.02 ± 6.32	9.133	0.001
GLS-STE		21.18 ± 2.12	15.22 ± 4.73	7.270	0.001

Avg S: Average systolic velocity. **Avg E:** Average Diastolic velocity. **Avg LV TDI strain:** Average Left Ventricular tissue Doppler Imaging strain. **GLS-STE:** Global longitudinal strain—speckle tracing echo.

Table 5 presents the optimal cut-off point and positive and negative predictive values of several biomarkers, namely GDF-15, hsCRP, EF%, TDI strain, and GLS-Speckled tracking, for predicting left ventricular dysfunction in pediatric hemodialysis patients. The specificity and sensitivity of GDF15, Hs CRP, EF%, TDI strain, and GLS-Speckled for the early detection of left ventricular dysfunction were determined to be 97.5% and 100%, 67.5% and 85.0%, and 80.0% and 100%, respectively.

Figure 1 shows a significant negative correlation between serum cholesterol and LVEF%.

Figure 2 demonstrates a significant negative correlation between LVEF% and serum triglyceride level.

Table 5. Sensitivity and specificity (%) of (GDF 15, hsCRP, EF%, LV TDI strain%, and LV 2D GLS-STE%).

Variables	Cut off Point	AUC	Sensitivity	Specificity	+PV	−PV
GDF-15	>261	0.988	97.50	100.00	100.0	97.6
Hs CRP (ng/ml)	>5.80	0.997	97.50	97.50	97.6	97.5
EF (%)	≤51	0.824	67.50	90.00	87.1	73.5
Avg LV TDI strain	≤19.5	0.796	80.00	82.50	82.1	80.5
LV 2D GLS-STE (%)	≤18.1	0.931	90.00	92.50	92.3	90.2

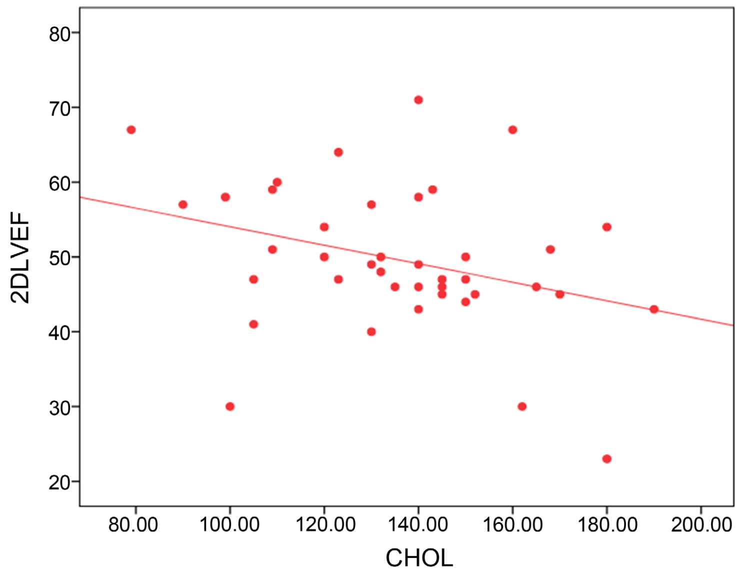

Figure 1. Negative correlation between LVEF% and serum cholesterol.

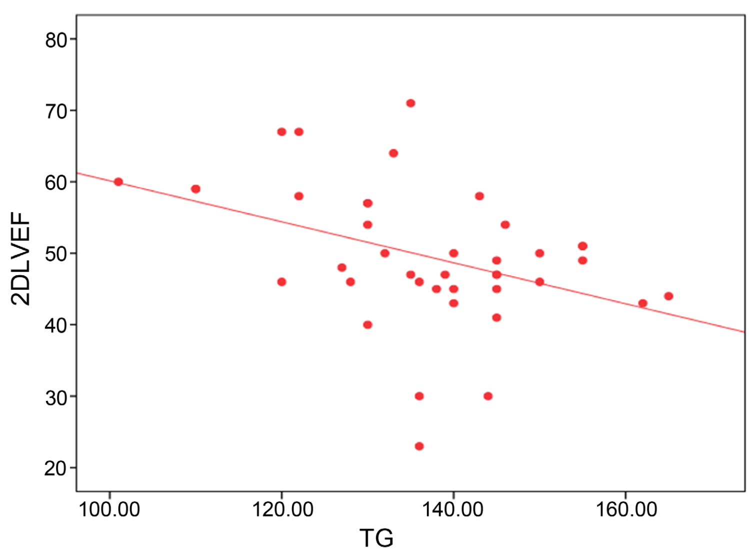

Figure 2. Negative correlation between LVEF% and serum triglyceride.

Figure 3 demonstrates a positive correlation between GDF-15 and LVIVSD.

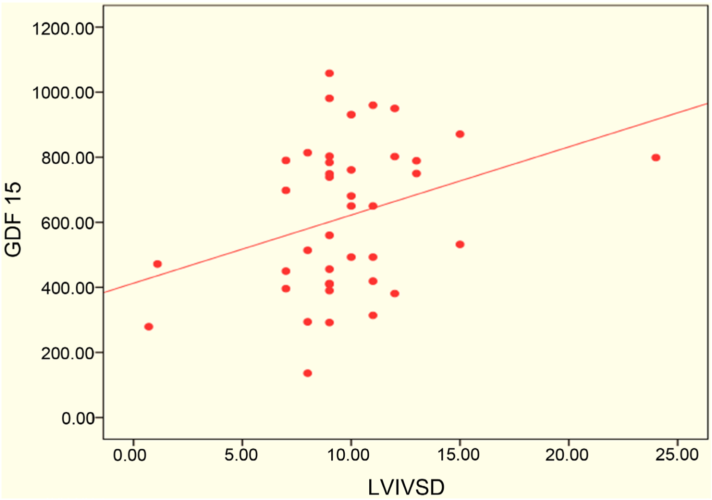

Figure 3. Correlation between GDF-15 and LVIVSD.

Figure 4 demonstrates a positive correlation between GDF-15 and serum Ca level.

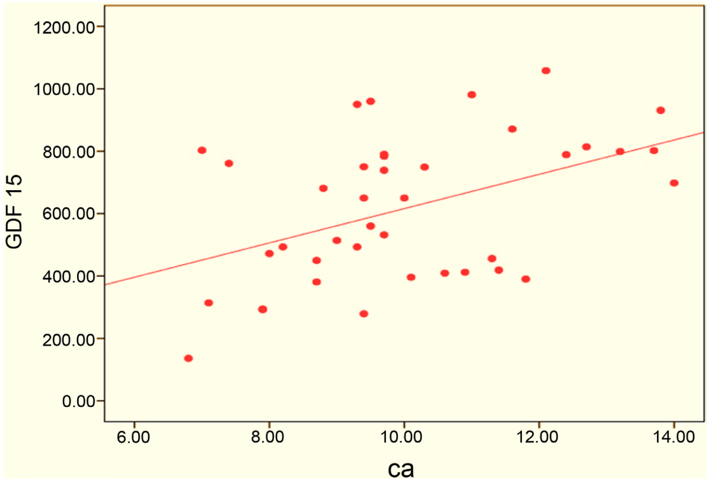

Figure 4. Correlation between plasma GDF-15 and serum ca.

Figure 5 shows a positive correlation between GDF-15 and blood pressure.

In **Figure 6**, one of the study patient groups, the conventional echocardiogram (M-mode) indicates preserved left ventricular dimensions and function.

**Figure 7: **The application of biplane disc summation has demonstrated conserved measurements of left ventricle volume and function in the control cohort of the study.

In **Figure 8**, the implementation of biplane disc summation has demonstrated diminished measurements of left ventricle volume and function within a specific patient cohort of the study. The biplane EF% stands at 42%.

In **Figure 9**, The speckled tracking assessment of the global and regional left ventricular (LV) strain revealed a significant global peak systolic strain in one patient within the study cohort.

Figure 10: ROC curve for sensitivity and specificity of GDF-15, hsCRP, 2D LVEF% LV TDI strain%, and GLS-STE%.

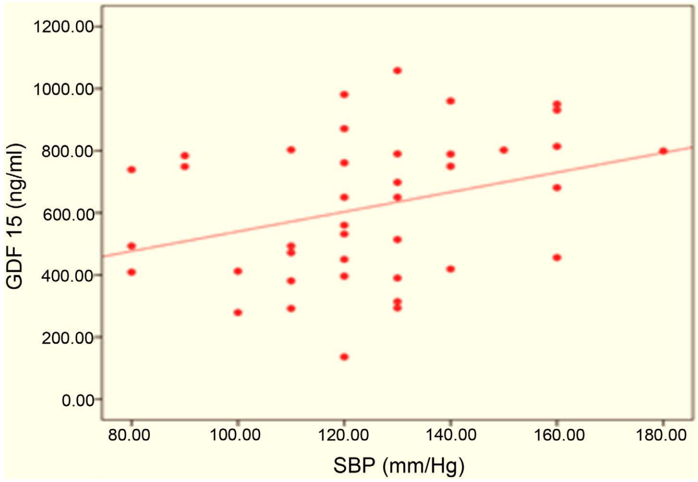

Figure 5. Correlation between plasma GDF-15 and SBP.

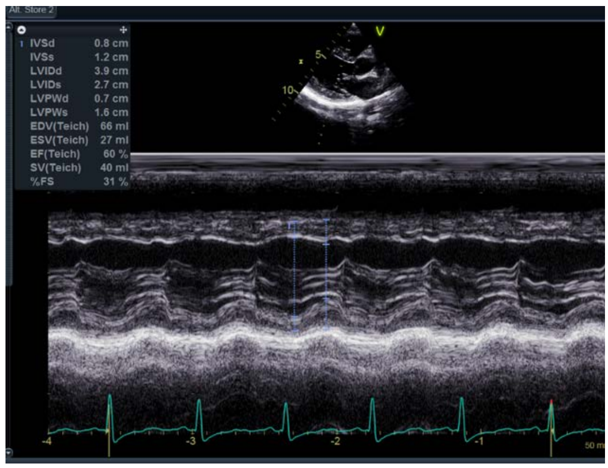

Figure 6. Conventional Echo (M-mode) presents the left ventricular dimensions and function of one of the patient group.

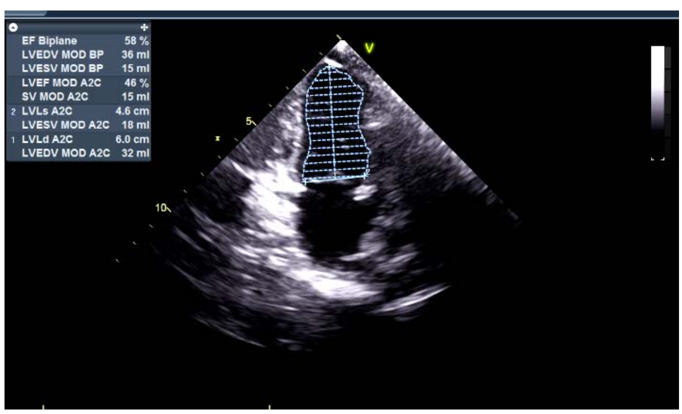

Figure 7. Biplane disc summation illustrates precise volume and function measurements of the LV in one of the control group.

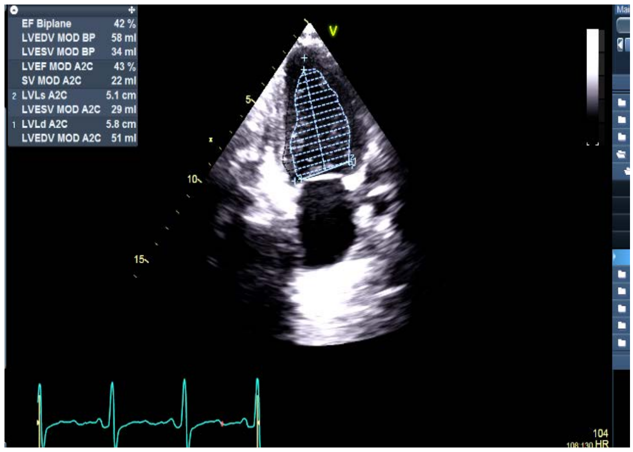

Figure 8. Biplane disc summation illustrates precise volume and function measurements of the LV in one of the patient's group.

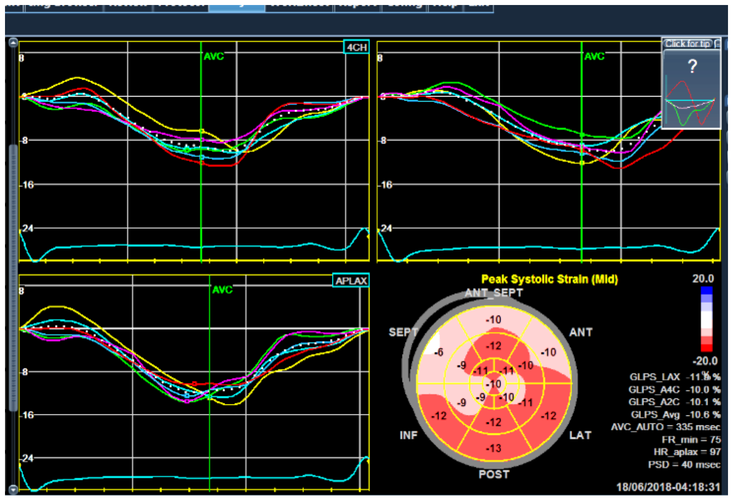

Figure 9. Illustrates the LV systolic global and regional strain obtained through speckle-tracking echocardiography within one of the patient groups.

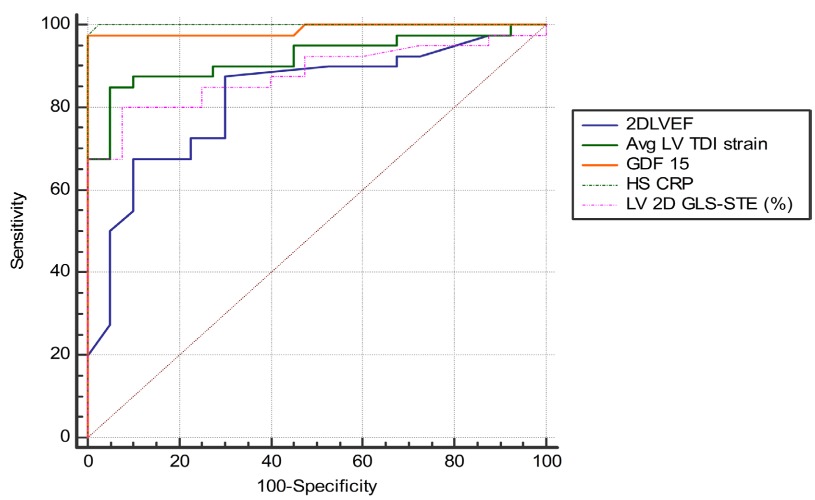

Figure 10. ROC curve for sensitivity and specificity of GDF-15, hsCRP, 2D LVEF% LV TDI strain%, and GLS-STE%.

4. Discussion

The assessment of left ventricular (LV) function can utilise various echocardiographic variables. Our analysis found that 67.5% of patients exhibited LV dysfunction when assessed using conventional and TDI strain (ECHO), whereas 82.5% showed dysfunction when 2D GLS-speckle Echo was used. It is common for children undergoing conventional hemodialysis to experience a reduction in their systolic myocardial function.

This decrease in left ventricular function may be associated with intradialytic hypotension, leading to reduced coronary perfusion and changes in volume loading [11]. Recurrent myocardial stunning may result in chronic damage and, in some instances, lead to chronic left ventricular systolic dysfunction [12].

Tissue Doppler echocardiography cannot assess regional deformation or abnormalities [13]. Strain echocardiography, which utilizes the speckle-tracking technique, can identify subclinical left ventricular dysfunction before the left ventricular ejection fraction decreases. Amoozgar *et al.* observed no changes in GLS after dialysis in a pediatric cohort and concluded that speckle-tracking echocardiography in children is independent of preload [14].

Myocardial deformation analysis using two-dimensional (2D) strain in speckle-tracking echocardiography presents a quantitative approach for detecting subtle left ventricular (LV) dysfunction, which cannot be adequately assessed through semi-quantitative conventional echocardiography. According to [15]), left ventricular global longitudinal strain (GLS) has been proposed as a novel indicator of systolic function.

Our study identified a significant inverse association between the patient cohort's left ventricular ejection fraction (LVEF%) and serum cholesterol and triglycerides (TG) levels. However, we did not observe any statistically significant correlation between left ventricular 2D global longitudinal strain (LV 2D GLS-STE) and clinical or laboratory data. Consistent with our findings, Moustafa et al. reported a significant correlation between an increased A wave value (peak late diastolic annular velocity) and elevated serum cholesterol and anaemia [16].

In our study, we examined children's left ventricular (LV) dimensions. The children undergoing dialysis showed a significant increase in left ventricular dimensions (LV EDD, LV PWD, LVSD, and LVIVSD) compared to the control group. Left ventricular hypertrophy is a common and often severe condition in children with chronic kidney failure and those undergoing kidney replacement therapy. It is important to consider factors beyond high blood pressure and anemia as significant contributors to this condition. There is evidence of a connection between serum creatinine and increased left ventricular mass before reaching end-stage kidney failure [17].

An increased left ventricular end-diastolic diameter (LVEDD) indicates abnormal relaxation of the left ventricle's muscles and incomplete ventricle filling. This condition also reverses the E: A ratio, commonly used as a clinical marker of diastolic dysfunction. Over time, untreated high blood pressure can result in diastolic heart failure, a condition like longstanding untreated hypertension [18].

The present study indicates that pediatric patients undergoing hemodialysis exhibit notably higher serum levels of GDF15 than their counterparts in the control group. GDF15, not typically present in tissue, displays notable activation in response to physiological injury. Moreover, elevated GDF15 levels have been observed in the context of cardiovascular injuries, including but not limited to pressure overload, myocardial infarction, chronic heart failure, and atherosclerosis. Furthermore, augmented circulating concentrations of GDF15 have been associated with the development and progression of cardiovascular pathologies [19] [20].

The observed correlation between GDF-15 levels, systolic blood pressure, and LVWT is statistically significant. These findings suggest that elevated GDF-15 levels in the bloodstream, commonly identified in cardiac conditions, indicate cardiac injury and its broader ramifications [21]. Furthermore, the upregulation of GDF-15 in response to pressure overload and its pivotal role in regulating cardiac remodelling indicate a link between GDF-15 levels in the bloodstream and LVH in individuals with hypertension [22]. Comparable outcomes have been documented in other studies [23] [24].

Our recent study has revealed a significant correlation between GDF-15 and serum calcium levels. Imbalances in calcium levels are common in various heart conditions, such as heart attack, irregular heartbeat, heart enlargement, heart failure, and heart muscle diseases [25]. Alterations in calcium levels within the heart cells ([Ca2+]) are the principal factors influencing heart function. However, our understanding of changes in [Ca2+] in heart muscle disease caused by chronic kidney disease (CKD) is limited. Elucidating this could elucidate the strong association observed in GDF-15 levels among the cohort of patients. This association will yield novel insights and facilitate enhanced comprehension in the future.

Moreover, we identified a substantial positive correlation between hsCRP and body mass index and traditional cardiovascular risk factors such as hypertension, dyslipidemia, anaemia, ferritin, and PTH. This correlation could be attributed to the more pronounced inflammatory conditions in the study or the exacerbated cardiovascular and kidney diseases in the patients [26].

During our investigation, ROC curve analysis revealed the sensitivity and specificity for GDF-15, Hs CRP, 2DLVEF%, LV TDI strain%, and LV 2D GLS-STE%. The results indicated that GDF 15 exhibited a sensitivity of 97.5% and a specificity of 100%, Hs CRP showed a sensitivity of 67.5% and specificity of 97.5%, 2DLVEF% demonstrated a sensitivity of 85.0% and a specificity of 90.0%. In comparison, the LV TDI strain displayed a sensitivity of 85.0% and a specificity of 85.0%. Furthermore, LV 2D GLS-STE% manifested a sensitivity of 80.0% and a specificity of 92.5%. These findings underscore the potential of these biomarkers and different ECHO modalities in predicting left ventricular dysfunction in pediatric hemodialysis patients. Notably, GDF 15 was determined to have a specificity of 100%.

A prior investigation concerning coronary heart disease determined that the optimal threshold value of GDF-15 stood at 1233 ng/L, demonstrating 71% specificity and 71% sensitivity in diagnosing cardiovascular disease. The disparity in these metrics is ascribed to the divergent etiologies of heart disease among the cohorts under examination [27].

Our research observed that the specificity of LV 2D GLS-STE% surpassed that of conventional and tissue Doppler echocardiography. Previous studies have indicated that despite appearing normal in conventional echocardiography, patients can exhibit impaired LV systolic and diastolic functions, which can be accurately identified and assessed using two-dimensional speckle tracking echocardiography [28].

5. Conclusion

Children undergoing hemodialysis commonly present with left ventricular dysfunction. GDF-15 can be an early and specific biomarker for predicting LV dysfunction in this population. Furthermore, speckle-tracking echocardiography exhibits superior efficacy over conventional and Doppler echocardiography in the early detection of LV dysfunction in these patients.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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