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Original Article

Diastolic Function Parameters in Different Stages of Children with Chronic Kidney Disease: A Subclinical Speckle Tracking Echocardiography Study

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Abstract

Background: Chronic Kidney Disease (CKD) in children was associated with an increased risk of long-term cardiovascular morbidity and mortality. Diastolic dysfunction, represented by an early cardiac manifestation of CKD, was often subclinical and might not be detected by conventional echocardiography. Speckle Tracking Echocardiography (STE), which assesses left atrial function, provided a potentially sensitive evaluation of early diastolic functional changes. This study aimed to compare stages of CKD in children with diastolic function parameters assessed by STE.

Methods: An analytic cross-sectional study conducted at RSUP M. Djamil Padang from September to December 2025, involving 44 children with CKD who were divided equally into two groups: Group I, early-stage CKD (stages 1–3) children, and Group II, advanced-stage CKD (stages 4–5) children. STE was performed to assess Left Atrial Reservoir Strain (LASr), Conduit Strain (LAScd), and Contractility Strain (LASct). Combination with echocardiography, conventional and STE by evaluating Left Atrial Stiffness Index (LASI) from E/e' / LASr, and Left Atrial Filling Index (LAFI) from E transmitral velocity / LASr was performed in both groups. Statistical analyses included the Shapiro–Wilk normality test, followed by an independent t-test or Mann–Whitney test.

Results: In this study, no significant differences were found in age, sex, comorbidities, therapy, Left Ventricular Ejection Fraction (LVEF), and Left Atrium dimension between the two groups. The left atrial speckle tracking parameters in Groups I and II were as follows: LASr 44.89±2.22% vs 30.54±6.25% (p=0.000); LAScd −33.50±3.66% vs. −21.65±7.57% (p=0.000); LASct −11.35% (−5.4 to −17.8%) vs −7.70% (−2.1 to −21.0%) (p=0.018); LASI 0.15 (0.12–0.26) vs 0.32 (0.18–0.82) (p=0.000); and LAFI 1.99 (1.38–3.04) vs. 2.93 (2.19–6.65) (p=0.000).

Conclusions: Children with advanced-stage CKD demonstrated significantly reduced LASr, LAScd, and LASct and increased LASI and LAFI compared with those with early-stage CKD, indicating impaired diastolic function detected by left atrial STE.

Keywords: Children chronic kidney disease, Diastolic function, Speckle tracking echocardiography, Left atrial strain.

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Introduction

Chronic Kidney Disease (CKD) in children represents a growing global health challenge with substantial long-term cardiovascular consequences. Although the prevalence of pediatric CKD is lower than that in adults, affected children are exposed to prolonged uremic burden, metabolic disturbances, and hemodynamic stress over decades, placing them at high risk for premature cardiovascular disease. Cardiovascular complications are consistently reported as the leading cause of morbidity and mortality in children and young adults with CKD, even after renal replacement therapy or kidney transplantation.[1]

Importantly, cardiovascular involvement in pediatric CKD often begins silently. Structural and functional cardiac alterations may develop early in the disease course and progress in parallel with declining renal function, long before overt clinical symptoms appear. Among these alterations, Left Ventricular (LV) diastolic dysfunction has been identified as one of the earliest manifestations of uremic cardiomyopathy and is closely associated with subsequent heart failure and adverse cardiovascular outcomes.[2]

Assessment of diastolic function in children remains challenging. Conventional echocardiographic parameters, including transmitral flow velocities, tissue Doppler indices, and derived ratios, are influenced by age, heart rate, and loading conditions, and validated pediatric-specific diagnostic algorithms are limited. As a result, subtle or early diastolic abnormalities may be underestimated when conventional echocardiography is used as the sole assessment modality in children with CKD.[3]

The Left Atrium (LA) plays a central role in LV filling and acts as a sensitive marker of chronic elevation in LV filling pressure. Left atrial function reflects the cumulative hemodynamic burden imposed on the ventricle and undergoes adaptive and maladaptive changes during the progression of diastolic dysfunction. Speckle Tracking Echocardiography (STE) enables angle-independent quantification of LA myocardial deformation and provides a detailed assessment of LA reservoir, conduit, and contractile function throughout the cardiac cycle.[4]

In addition to individual strain components, combination-derived indices such as the Left Atrial Stiffness Index (LASI) and Left Atrial Filling Index (LAFI) integrate LA deformation with conventional Doppler parameters, offering a more comprehensive representation of atrial compliance and functional contribution to ventricular filling. Previous studies in pediatric CKD populations have demonstrated impaired LA strain compared with healthy controls; however, data examining differences across CKD stages remain limited.[5-6]

Therefore, this study aimed to evaluate the association between CKD stage and diastolic function parameters assessed by conventional echocardiography and LA-focused STE in children. By focusing on stage-related differences, this study seeks to clarify the role of LA functional assessment in identifying early and progressive cardiac involvement in pediatric CKD.

Methods

Study Design and Population

This analytic cross-sectional study was conducted at Dr. M. Djamil General Hospital, Padang, Indonesia, between September and December 2025. Inclusion criteria were children aged >2 years with a diagnosis of CKD who were consecutively recruited from the pediatric nephrology outpatient clinic and inpatient wards. CKD was defined according to Kidney Disease Improving Global Outcomes (KDIGO) criteria and staged based on estimated GFR calculated using the modified Schwartz formula. We excluded patients with unstable hemodynamics, acute infection, non-sinus rhythm Electrocardiogram (ECG), poor echocardiographic windows, significant valve disease, and congenital heart disease.

The calculation of the minimum sample size for this study population was calculated using the analytical formula for two unpaired groups, yielding a minimum of 22 patients per group. The total population was 50 patients during the study period. There were 44 patients who met the inclusion criteria without any exclusion criteria. Patients were divided equally into two groups: early-stage CKD (stages 1–3) and advanced-stage CKD (stages 4–5). There were 17 patients (77%) from advanced-stage CKD who routinely underwent hemodialysis 2 times per week.

Echocardiographic Assessment

All participants underwent comprehensive transthoracic echocardiography using Philips Affiniti CVx echocardiography. Conventional echocardiographic measurements included LV dimensions, Left Ventricular Ejection Fraction (LVEF), Tricuspid Annular Plane Systolic Excursion (TAPSE), Left Ventricular Mass Index (LVMI), Relative Wall Thickness (RWT), transmitral E and

A velocities, E/A ratio, tissue Doppler e' velocities (septal and lateral), E/e' ratio, Isovolumic Relaxation Time (IVRT), tricuspid regurgitation maximal velocity, and Systolic Pulmonary Artery Pressure (SPAP).

LA STE analysis was performed using Tomtec Software in Philips Echocardiography, with 50 – 70 frames per rate, ECG-triggered sinus rhythm from R to R lead, 3 averaged cardiac cycles, and manually adjusted tracking of LA from apical four-chamber views, measuring LA Reservoir Strain (LASr), Conduit Strain (LAScd), and Contractile Strain (LASct). LASI was calculated as the ratio of E/e' to LASr, and LAFI was calculated as the ratio of transmitral E velocity to LASr.

Statistical Analysis

Data distribution was assessed using the Shapiro–Wilk test. Continuous variables were expressed as mean ± standard deviation or median (minimum–maximum), as appropriate. Group comparisons were performed using independent t-tests or Mann–Whitney tests in numerical data. The chi-square test was used to compare categorical data. A p-value <0.05 was considered statistically significant. Variability analysis using the Intraclass Correlation Coefficient (ICC) test to measure the reliability of three observers in echocardiography speckle tracking, based on 6 echocardiography patients (>10% of the sample).

Results

Table 1. Baseline characteristics of study population.

Variable	Early stage CKD (n=22)	Advanced stage CKD (n=22)	P-value
Age, median (min-max) (years)	11 (6 – 17)	14 (6 – 17)	0.085
Sex, n(%)			0.531
Male	15 (68)	13 (59)	
Female	7 (32)	9 (41)	
BMI, median (min-max) (kg/m^2)	16.2 (13.7 – 28)	15.3 (12 – 21.3)	0.011*
Systolic Blood Pressure, mean±SD (mmHg)	110 ± 15.6	117 ± 19.1	0.180
Diastolic Blood Pressure, mean ±SD (mmHg)	67 ± 12.9	71 ± 17.4	0.322
Hypertension History, n(%)			1.000
Hypertension	21 (96)	20 (91)	
No Hypertension	1 (4)	2 (9)	
Hypertension Therapy, n(%)			0.223
RAS-blocker	15 (68)	11 (50)	
Non RAS-blocker	0 (0)	0 (0)	
Combination RAS-non RAS-blocker	6 (27)	9 (41)	
Without Therapy	1 (5)	2 (9)	
Heart Rate, median (min-max)	83 (61 – 99)	91 (66-99)	0.078
Etiology, n(%)			0.052
Glomerular	18 (82)	12 (55)	
Non-glomerular	4 (18)	10 (45)	
CKD Stage, n(%)			
Stage I	11 (50)	0 (0)	
Stage II	9 (41)	0 (0)	
Stage III	2 (9)	0 (0)	
Stage IV	0 (0)	5 (23)	
Stage V	0 (0)	17 (77)	
Proteinuria, n(%)			0.021***
Positive	16 (73)	22 (100)	
Negative	6 (27)	0 (0)	

Hemoglobin, mean ±SD (g/dl)	13.1 ± 1.9	9.3 ± 1.1	0.000**
Urea, median (min-max) (mg/dl)	26.5 (13 – 71)	89 (40 – 197)	0.000*
Creatinine, median (min-max) (mg/dl)	0.6 (0,4 – 1,5)	5 (2,4 – 12)	0.000*
Serum Albumin, median (min-max) (mg/dl)	4.3 (1.9 – 4.9)	3.8 (1.8 – 4.6)	0.041*
Urine Output, median (min-max) (ml/kgBB/jam)	1.6 (0.9 – 2.9)	0.5 (0.1 – 1.1)	0.000*
Serum Calcium, mean ±SD (mg/dl)	9.64 ± 0.43	8.92 ± 1.05	0.006*
Estimated GFR, median (min-max) (ml/min/1,73m^2)	89.5 (35 – 121)	11.5 (5 – 22)	0.000*
CKD Duration, median (min-max) (years)	2 (1 – 7)	2 (1 – 6)	0.932

*: significant p-value Mann-Whitney test p< 0.05; **: significant p-value T-independent test p< 0.05; ***: significant chi-square test n p< 0.05.

Table 2. Conventional echocardiographic parameters according to CKD stage.

Variable	Early stage CKD (n=22)	Advanced stage CKD (n=22)	P-value
LVDD, mean±SD (mm)	36.8 ± 5.6	40.7 ± 8.4	0.082
LVSD, mean ±SD (mm)	23.7 ± 4.1	26.1 ± 6.5	0.144
IVSD, median (min-max) (mm)	7 (4 – 8)	8 (5 – 13)	0.014*
IVSS, median (min-max) (mm)	9 (6 – 13)	10 (6 – 22)	0.086
LVEF, mean ±SD (%)	63.4 ± 4.5	64.7 ± 4.7	0.360
TAPSE, median (min-max) (cm)	2.05 (1.7 – 2.6)	2.05 (1.7 – 2.6)	0.626
LVMI, median (min-max) (g/m^2)	68 (49 – 116)	92.5 (51 – 230)	0.000*
RWT, median (min-max)	0.4 (0.3 – 0.6)	0.5 (0.2 – 0.8)	0.030*
IVC maximum diameter, median (min-max)	11 (8 – 14)	11 (8 – 15)	0.648
IVC maximum diameter, median (min-max)	7 (5 – 11)	7 (5 – 12)	0.777
LA diameter, median (min-max) (mm)	24 (15 - 32)	23.5 (19 – 43)	0.953
LA volume index, median (min-max) (ml/m^2)	20.5 (9 - 31)	22 (11 – 56)	0.953
Mitral E, mean±SD (cm/s)	94.5 ± 19.6	96.4 ± 23.2	0.767
Mitral A, median (min-max) (cm/s)	51.5 (34 – 126)	82.5 (47 – 111)	0.001*
Mitral E/A, mean ±SD	1.75 ± 0.38	1.28 ± 0.42	0.000**
TDI septal e', mean ±SD (cm/s)	11.05 ± 2.34	9.56 ± 2.56	0.051
TDI lateral e', mean ±SD (cm/s)	16.61 ± 4.28	12.3 ± 3.95	0.001**
E/e' septal, median (min-max)	7.9 (6.1 – 14.5)	10.35 (6.3 – 18.5)	0.010*
E/e' lateral, mean±SD	6.06 ± 1.84	8.69 ± 3.08	0.002**
E/e' mean, median (min-max) (cm/s)	6.9 (5.2 – 11.7)	10.2 (5.9 – 19.6)	0.001*
IVRT, mean ±SD (ms)	71.59 ± 8.31	58.09 ± 9.50	0.000**
TR V Max, median (min-max) (m/s)	1.7 (0 – 2.5)	2.1 (0 – 3.1)	0.007*
SPAP, median (min-max) (mmHg)	20 (8 – 34)	27 (8 – 48)	0.009*
Ratio S/D PV, median (min-max)	0.9 (0.6 – 1.3)	0.8 (0.5 – 1.3)	0.126

*: significant p-value Mann-Whitney test p< 0.05; **: significant p-value T-independent test p< 0.05.

Table 3. Left atrial speckle tracking parameters according to CKD stage.

Parameter (Mean±SD)	Children CKD Group		P-value	95% Confidence Interval (CI)
	Early-stage CKD (n=22)	Advanced stage CKD (n=22)		
Left atrial strain reservoir (LASr) (%)	44.89 ± 2.22	30.54 ± 6.25	0.000**	11.49 to 17.20
Left atrial strain conduit (LAScd) (%)	-33.50 ± 3.66	-21.65 ± 7.57	0.000**	-15.47 to -8.24
Left atrial strain contractility (LASct) (%)	-11.35 (-5.4 - -17.8)	-7.70 (-2.1 - -21.0)	0.018*	0.015 to 0.020
Left atrial stiffness index (LASI)	0.15 (0.12 – 0.26)	0.32 (0.18 – 0.82)	0.000*	0.00 to 0.00
Left atrial filling index (LAFI)	1.99 (1.38 – 3.04)	2.93 (2.19 – 6.65)	0.000*	0.00 to 0.00

*: significant p-value Mann-Whitney test $p < 0.05$; **: significant p-value T-independent test $p < 0.05$.

Table 4. Intraclass Correlation Coefficient (ICC) test on left atrial speckle tracking parameters.

Parameter (Mean±SD)	R - ICC	P-value	95% Confidence Interval (CI)
Left atrial strain reservoir (LASr)	0.850	0.668	0.364 to 0.977
Left atrial strain conduit (LAScd)	0.789	0.990	0.108 to 0.968
Left atrial strain contractility (LASct)	0.760	0.768	0.016 to 0.964
Left atrial stiffness index (LASI)	0.966	0.912	0.856 to 0.995
Left atrial filling index (LAFI)	0.836	0.797	0.305 to 0.975

Discussion

The baseline characteristics of the two groups compared in this study. The median ages of the two groups did not differ significantly, suggesting that age is not a major contributor to the observed differences in cardiovascular function between the groups. Most of the participants in both early and advanced CKD groups were male, which is consistent with the higher prevalence of CKD in children, especially in male patients. Blood pressure and hypertension status were not significantly different between groups due to the majority of the samples having been on hypertension therapy with stable conditions. Hypertension can alter diastolic function by increasing cardiac workload, thereby contributing to myocardial fibrosis and diastolic stiffness. independent of CKD stage, underscoring the importance of managing these conditions alongside the progression of CKD.[7]

However, the significant differences in laboratory parameters such as hemoglobin, urea, creatinine, albumin, and calcium levels between the early and advanced CKD groups showed us that these baseline characteristics progressively worsen in the advanced CKD stage, reflecting the differences between early and advanced stages of kidney disease. The lower hemoglobin levels in the advanced CKD group indicate more severe anemia, which is commonly associated with impaired kidney function. Increased levels of urea and creatinine in the advanced CKD group indicate a greater degree of renal dysfunction, which is expected to affect cardiovascular burden through disturbances in fluid balance and electrolyte homeostasis, as well as increased systemic vascular pressure. Serum calcium disturbances, especially hypocalcemia, are common in CKD and are known to negatively impact myocardial compliance and function. The lower albumin levels in the advanced group are indicative of chronic inflammation and malnutrition, as is a significant difference in Body Mass Index (BMI) between the two groups, which may be influenced by nutritional status and metabolic conditions that differ at the stage of CKD, which can affect cardiac structure and function. The interplay of these factors highlights the complex progressive stage of CKD-related cardiac changes and underscores the importance of addressing both metabolic disturbances and renal dysfunction in managing pediatric CKD.[8]

This study demonstrates that progression of CKD in children is associated with significant deterioration of diastolic function, while systolic ventricular performance remains preserved. Children with advanced-stage CKD exhibited marked abnormalities in conventional diastolic parameters and LA deformation indices compared with those in early-stage CKD, highlighting the presence of subclinical cardiovascular remodeling that evolves in parallel with renal dysfunction.[9]

The absence of significant differences in LVEF and right ventricular systolic function between CKD stages suggests that systolic function is relatively preserved during the earlier phases of uremic cardiomyopathy. This finding is consistent with prior pediatric studies reporting that diastolic abnormalities and structural remodeling precede systolic impairment in CKD. Such a pattern underscores the importance of focusing on diastolic indices for early detection of cardiovascular risk in this population.[10]

Significant increases in LVMI and RWT observed in advanced CKD reflect concentric LV remodeling, which is commonly driven by chronic pressure overload, volume expansion, anemia, and neurohormonal activation. These structural changes are known contributors to impaired myocardial relaxation and increased ventricular stiffness, thereby promoting diastolic dysfunction despite preserved systolic performance.[11]

Alterations in transmitral flow patterns and tissue Doppler indices further support the presence of impaired LV relaxation and elevated filling pressures in advanced CKD. Increased transmitral A velocity, altered E/A ratio, reduced lateral e' velocity, prolonged IVRT, and elevated E/e' ratio collectively indicate progressive deterioration of diastolic function. These findings reinforce the concept that conventional echocardiography can identify diastolic abnormalities in pediatric CKD, although its sensitivity may be limited in the early stages of disease.12,13 Although there is no validated algorithm for diagnosing diastolic dysfunction in children as in adults, some studies have reported average E/e' ratios>13.4 and E/A ratios <1, indicating clinically significant diastolic dysfunction in children.[14-15]

Left Atrial Strain (LAS) analysis provided additional insights beyond conventional parameters. Children with advanced CKD showed significant reductions in LASr, LAScd, and LASct strain, indicating impairment across all phases of LA function. Among these components, LA reservoir strain demonstrated the strongest association with CKD stage, consistent with its role as an integrative marker of chronic LV filling pressure and atrial compliance.10,16 Meta-analysis showed that in normal children, LASr, LAScd, and LASct were 54.8±9.5%, 42.7±8.9%, and 12±5.3%, respectively. In this study, several children in the early CKD group had relatively preserved conventional indices (such as the E/A and E/e' ratios) but exhibited abnormal LA strain.[10,17]

The observed increase in LASI and LAFI further emphasizes the functional consequences of progressive atrial remodeling. LASI integrates LA deformation with impaired relaxation (stiffness), while LAFI reflects the effective contribution of the atrium to ventricular filling pressure. LASI value > 0.26 and LAFI value > 3.27 showed increased mortality, rehospitalization, and worse cardiovascular outcomes. Changes in these indices suggest reduced atrial compliance and diminished hemodynamic efficiency in advanced CKD, even in the absence of overt systolic dysfunction.[6,18]

The majority of patients with advanced CKD in this study were CKD stage 5, who required regular hemodialysis twice per week. Hemodialysis affects LAS and function. Dialysis-related factors, such as fluctuations in blood volume, shifts in fluid status, and hemodynamic changes during dialysis, can influence left atrial dynamics. However, the LA strain provided more benefit than conventional echocardiography, with minimal influence from loading conditions, which is beneficial in children with CKD. Additionally, repeated cycles of fluid overload and removal may contribute to chronic atrial remodeling, which manifests as altered LA stiffness and filling indices. The potential influence of dialysis on LA strain highlights the need for further research to explore the long-term impact of dialysis on left atrial function in children with end-stage renal disease, and to understand how these factors interact with the underlying progression of CKD.[10-11,16]

These findings are clinically relevant, as impaired LA function has been linked to adverse cardiovascular outcomes in adult CKD and dialysis populations. The demonstration of similar alterations in children with advanced CKD suggests that atrial dysfunction may represent an early stage in the trajectory toward future cardiovascular events. Early identification of such changes may enable timely intervention to modify cardiovascular risk.[14,19]

The findings of this study have significant implications for clinical practice in pediatric CKD.

STE provides a sensitive, non-invasive method for assessing left atrial function and can be used for early cardiovascular risk stratification in children with CKD. Given the progressive nature of CKD and its silent cardiovascular impacts, regular monitoring of LA strain, along with conventional echocardiographic parameters, may help detect early signs of diastolic dysfunction before overt heart failure symptoms appear. The inclusion of the LA strain and other LA-focused indices (LASI, LAFI) in routine evaluations may help clinicians identify children at risk of adverse cardiovascular outcomes, enabling earlier and more targeted interventions. Overall, this study supports the integration of LA-focused STE into the routine cardiac evaluation of children with CKD.

Limitations

This study has several limitations. The cross-sectional design precludes causal inference and longitudinal assessment of disease progression. The single-center setting may limit generalizability. Additionally, pediatric reference values for diastolic function is not yet well established.

Conclusion

In children with CKD, advancing CKD stage is associated with significant impairment of diastolic function, as detected by both conventional echocardiography and left atrial speckle-tracking echocardiography, while systolic ventricular function remains preserved. Reduced LAS (LASr, LAScd, LASct), together with increased LASI and LAFI, provides sensitive markers of early and progressive diastolic dysfunction and may improve cardiovascular risk stratification in pediatric CKD.

List of Abbreviations

BMI	Body Mass Index
CKD	Chronic Kidney Disease
ECG	Electrocardiogram
ICC	Intraclass Correlation Coefficient
IVRT	Isovolumic Relaxation Time
KDIGO	Kidney Disease Improving Global Outcomes
LA	Left Atrium
LAS	Left Atrial Strain
LAFI	Left Atrial Filling Index
LAScd	Left Atrial Strain Conduit
LASct	Left Atrial Strain Contractility
LASI	Left Atrial Stiffness Index
LASr	Left Atrial Reservoir Strain
LV	Left Ventricular
LVEF	Left Ventricular Ejection Fraction
LVMI	Left Ventricular Mass Index
RWT	Relative Wall Thickness
SPAP	Systolic Pulmonary Artery Pressure
STE	Speckle Tracking Echocardiography
TAPSE	Tricuspid Annular Plane Systolic Excursion

Ethical Clearance

All methods were carried out in accordance with relevant guidelines and regulations, after obtaining approval and recommendations from the Ethics Committee Review Board of Dr. M. Djamil General Hospital, with reference number DP.04.03/D. VXI.10.1/343/2025.

Publication Approval

All authors consent to the publication of this manuscript.

Authors' Contributions

AF contributed to the conception and design of the study, data collection, statistical analysis, interpretation of data, and drafting of the manuscript. DH contributed to the study supervision, development of the research methodology, interpretation of results, critical revision of the manuscript, and final approval of the submitted version. N contributed to patient recruitment, clinical data acquisition, echocardiographic assessment, interpretation of clinical findings, and critical revision of the manuscript. FA contributed to pediatric nephrology-related aspects, data analysis, interpretation of findings, and critical revision of the manuscript. All authors have read and approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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Conflict of Interest

None.

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