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ORIGINAL ARTICLE

Dilatation of the aorta in children with advanced chronic kidney disease

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Abstract

Background The peculiarity of the cardiovascular risk profile with increased arterial vulnerability is well known in adults with chronic kidney disease (CKD). It is explained by an increased incidence of traditional cardiovascular risk factors together with other comorbidities related to the uremic condition and cardiorenal syndrome (CRS). The present study aimed to determine the cardiovascular impact of the uremic condition in a pediatric population with advanced CKD.

Methods From 2016 to 2018, 39 consecutive patients with advanced CKD who underwent echocardiographic evaluation were included. All echocardiographic examinations were performed by the same operator (FE). Demographic, clinical, biological, and echocardiographic data were collected.

Results The mean age at echocardiographic exam was 9.7 ± 4.6 years. Twenty-four (61.5%) patients were on hemodialysis; 17 (43.6%) patients were in a peritoneal dialysis program of whom 11 switched at a later stage to hemodialysis. Eight (20.5%) patients had an arteriovenous fistula (AVF). Hypertension was present in 30 (76.9%) patients while left ventricular hypertrophy (LVH) was described in 13 (33.3%) patients. Dilatation of the ascending aorta (Z-score > 2) was found in 15 (38.4%) patients and was statistically (in univariate analysis) related to gender, hypertension, the presence of an AVF, and the use of hemodialysis after peritoneal dialysis ($p = 0.024$, $p = 0.016$, $p = 0.006$, $p = 0.009$, respectively).

Conclusion In addition to classical and predictable abnormalities related to CKD, we found a high prevalence of dilatation of the ascending aorta in children with advanced CKD. Hypertension, AVF, and hemodialysis were associated factors.

Keywords Children · Chronic kidney disease · Dilatation of the ascending aorta · Echocardiography · Left ventricular hypertrophy · Cardiorenal syndrome · Cardiovascular

Abbreviations

AD	Aortic dilatation
A4C	Apical 4 chamber
AVF	Arteriovenous fistula
CRS	Cardiorenal syndrome
CD	Cardiovascular disease
CKD	Chronic kidney disease
CKD-5	Chronic kidney disease stage 5
KRT	Kidney replacement therapy
KT	Kidney transplant
LV	Left ventricle
LVH	Left ventricular hypertrophy
LVMI	Left ventricular mass index
PWD	Power wave Doppler

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TDI	Tissue Doppler imaging
TTE	Transthoracic echocardiography
2D	Two dimensional

Background

Cardiovascular complications are the main cause of death in adults with stage 5 chronic kidney disease (CKD-5), but those complications undoubtedly start during childhood. Clinical and epidemiological studies have shown that CKD induces structural and functional changes in large arteries, thereby increasing mortality in adult uremic patients [1, 2]. This excessive arterial vulnerability is attributed to increased traditional cardiovascular risk factors, uremic condition, and cardiorenal syndrome (CRS). CRS has been defined as disorders of the heart and kidneys whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction of the other [3].

The first pediatric kidney transplant (KT) was performed over 50 years ago. Morbidity and mortality after KT for CKD-5 remain high, with estimated mortality rates 30 times higher when compared to children without kidney failure. Cardiovascular disease (CD) is, as in adults, the most common cause of death (up to 45%) [4]. The combination of kidney and heart disease, which share common risk factors, is associated with worse prognosis [5]. Those risk factors are considered rare in children but data are scarce [6].

Our institutional practice includes at least one annual transthoracic echocardiography (TTE) in all patients with CKD or KT. In addition to the usual indices, we additionally looked for aortic root dilation. In adults, indeed, aortic root enlargement has shown to be a marker of cardiac and extra-cardiac target organ damage [7]. Subsequent aortic regurgitation [8] and aneurysm formation with rupture are reported [9]. Isolated dilatation of the aorta is on the contrary rare in children. The present study aimed to determine the cardiovascular impact of the uremic condition in a pediatric population with advanced CKD.

Methods

Study design

We retrospectively analyzed all TTE performed between 2016 and 2018 in 39 children with CKD-5, either on kidney replacement therapy (KRT—hemodialysis or peritoneal dialysis) or after KT. Patients with connective tissue disease and congenital heart disease were excluded from the analysis.

Clinical data

Demographic, clinical, biological, and TTE data were collected from medical records. The clinical parameters collected were those recorded on the day of the echocardiography. The biological parameters collected were those performed on the day or within the month of the echocardiography. The Dubois formula was used to estimate the BSA (BSA $(m^2) = 0.007184 \times \text{height (cm)}^{0.725} \times \text{weight (kg)}^{0.425}$) [10]. In order to determine the hypertensive status of each patient, we conducted 24-h ambulatory blood pressure monitoring. Hypertension was defined as BP ≥ 95th percentile adjusted for age, gender, and height, for more than 25% of the ambulatory measurements. Ongoing cardiovascular treatments were collected. The study was approved by the La Timone Children's Hospital Clinical Investigation Committee.

Echocardiographic data

All measurements were performed with the children resting in the lateral supine position, using an Epic cardiology ultrasound machine (Philips, EPIQ CVx). The most recent study was selected and, if possible, the one performed 1 year earlier. Two TTE could be analyzed for all except 3 patients, for whom only one TTE was available. The measurements performed straightaway at the time of the TTE were used for the analysis and included two-dimensional (2D) and M-mode data acquired according to the recommendations of the European Society of Echocardiography [11].

The left ventricle (LV) mass calculations were made using the following formula: $0.8 \times [1.04 \times (\text{LVIDd} + \text{PWTd} + \text{SWTd})^3 - (\text{LVIDd})^3] + 0.6$ and the left ventricular mass index (LVMI) was assessed as $\text{LVMI} = \text{LVM}/m^{2.7}$. The aortic annular diameter was measured between the hinge points of the aortic valve leaflets in the left parasternal long-axis view during systole. For sinuses of Valsalva, sinotubular junction, and tubular ascending aorta dimensions, we measured the end-diastolic dimensions from inner edge to inner edge. Z-scores were remotely calculated for every measurement. The Detroit Z-score (Children's Hospital of Michigan) was used for aortic and ventricular dimensions [12].

Statistical analysis

Continuous variables are expressed as mean or as median values (with ranges), where appropriate. Discrete or binary variables are presented as number (percentage). We divided the population into two groups:

Group 1: Dilated ascending aorta, $n = 15$
Group 2: Not dilated ascending aorta, $n = 24$

We used the χ^2 test or Fisher's exact test (if appropriate) for categorical variables and the Mann-Whitney test for continuous variables to assess influencing factors. The Wilcoxon test was used to determine whether there was statistical evidence that the size of the ascending aorta during follow-up varied significantly.

p values < 0.05 were considered as statistically significant. Kaplan-Meier methods were used to produce the survival curve. All statistics were performed using IBM SPSS Statistics 17.0.

Results

Mean age of our cohort was 9.7 ± 4.6 years. Seventeen (43.6%) patients received peritoneal dialysis and 24 (61.5%) had a history of hemodialysis. Twenty-two of them were transplanted at the end of the study period. Most patients were treated by two or three KRT modalities, as shown in Table 1. The most common causes of CKD were urinary tract malformation, hypoplasia of the kidney, and nephronophthisis (Fig. 1). Eight (20.5%) patients had an AVF and hypertension was present in 27 patients (69.2%). Biological data are detailed in Table 2. Left ventricular hypertrophy (LVH) was found in 13 (33.3%) patients. Dilatation of the ascending aorta (Z-score > 2) was found in 15 (38.4%) patients. Table 3 details the echocardiographic characteristics.

Patients with dilated ascending aorta (group 1) were compared with those without (group 2). Univariate statistical analysis showed significant associations between dilated ascending aorta and gender, hypertension, the presence of AVF, and the use of hemodialysis (p = 0.024, p = 0.016, p = 0.006, p = 0.009 respectively). The results of the univariate analysis are shown in Table 4.

Annual monitoring showed that dilatation of the ascending aorta tends to persist and even increase significantly (p = 0.029) (Table 5, Fig. 2). All hypertensive patients, except one, benefited from successful medical hypertension control during the year of follow-up. In one patient, hypertension remained uncontrolled despite triple therapy.

Discussion

This study was conducted to evaluate, retrospectively, the cardiovascular impact of advanced CKD in a pediatric cohort. A high prevalence of dilatation of the ascending aorta was observed in our population. Knowledge regarding CD in CKD-5 patients mainly comes from adult studies describing atherosclerotic heart disease as the main cause of morbidity and mortality. Atherosclerosis is however very rare in younger patients. Recent papers focus on LVH [13], LV diastolic dysfunction [14], and increased carotid intima-media

Table 1 Demographic characteristics

Characteristics	Mean ± standard deviation *n* (percentage)
Gender, *n* (%)	
Male	27 (69.2)
Female	12 (30.8)
Age (years)	9.7 ± 4.6
Weight (kg)	34.8 ± 18.7
Past or current kidney replacement therapy	
CKD-5 without KRT	3 (7.7)
Peritoneal dialysis only	3 (7.7)
Peritoneal dialysis and transplantation	3 (7.7)
Peritoneal dialysis, hemodialysis, and transplantation	11 (28.2)
Hemodialysis only	2 (5)
Hemodialysis and transplantation	11 (28.2)
Transplantation	6 (15.5)
Arterial hypertension, *n* (%)	27 (69.2)
Obesity, *n* (%)	3 (7.7)
Arteriovenous fistula, *n* (%)	8 (20.5)

CKD-5, stage 5 chronic kidney disease; *KRT*, kidney replacement therapy

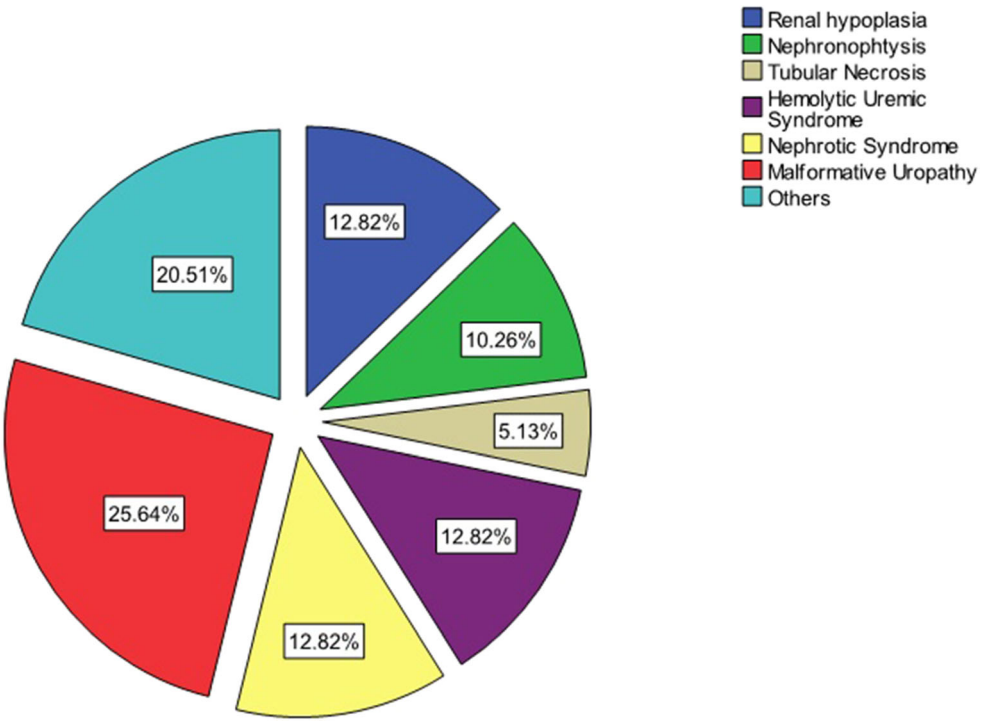

Fig. 1 The most common causes of CKD were urinary tract malformation, hypoplasia of the kidney, and nephronophthisis

thickening [15] but dilatation of the ascending aorta in young CKD-5 patients has rarely been described.

Cardiac remodeling

The prevalence of LVH is high, as expected, in our cohort. Ventricular remodeling refers to changes in the size, shape, structure, and function of the heart. It can be physiological (as a result of exercise) and reversible or pathological and irreversible. In adults, ventricular remodeling typically occurs after acute myocardial infarction, at distance from the acute event. A series of histopathological and structural changes occur in the left ventricular myocardium, with cardiomyocytes being the major cells involved in the remodeling process. In children, where myocardial infarction is rare, other forms of strain including pressure and volume overload may lead to cardiac remodeling. In CKD children, chronic hypertension and reduced vessel compliance increase afterload while salt and fluid load, anemia, and intravascular volume expansion increase preload [16, 17]. Finally, CKD patients accumulate

Table 2 Biological data

Biological characteristics	Median [IQR] number (percentage)
Hemoglobin (g/L)	11.6 [10.80–12.70]
Calcium (mmol/L)	2.4 [2.37–2.50]
Phosphorus (mmol/L)	1.49 [1.30–1.67]
Protein (g/L)	71.5 [67.75–75.25]
Albumin (g/L)	42.5 [41–46]
Intact PTH (pmol/L)	18.5 [6.25–42]
Cholesterol (mmol/L)	3.8 [3.1–4.7]
Triglycerides (mmol/L)	1.1 [0.78–1.78]
Low vitamin D, *n* (%)	33 (84.6)
CRP > 5 mg/L, *n* (%)	6 (15.4)

Intact PTH, intact parathyroid hormone; *CRP*, C-reactive protein

Table 3 Echocardiographic characteristics

Echocardiographic characteristics	Median [IQR] number (percentage)
LV end diastolic diameter (mm)	3.9 [3.4–4.8]
LV end diastolic Z-score	− 0.03 [− 0.1–0.9]
Interventricular septum (mm)	7.6 [6–8.9]
Interventricular septum Z-score	1.22 [0.76–1.9]
Posterior wall (mm)	7.5 [6–9]
Posterior wall Z-score	1.7 [0.7–2.2]
LV mass index (g/m^2)	84 [57–122]
LV mass Z-score	1.36 ± 0.31
LV hypertrophy	13 (33.3)
Z-score of aortic annulus > 2	3 (7.7)
Sinuses of Valsalva (cm)	2.19 ± 0.46
Z-score of sinuses of Valsalva > 2	4 (10.2)
Sinotubular junction (cm)	1.94 ± 0.44
Z-score of STJ > 2	6 (15.4)
Tubular ascending aorta (cm)	2.08 ± 0.42
Z-score of TAA > 2	17 (43.6)

LV, left ventricle; *STJ*, sinotubular junction; *TAA*, tubular ascending aorta

Table 4 Factors associated with dilated ascending aorta in univariate analysis

	Dilated AA $N = 15$	Non-dilated AA $N = 24$	p
Male gender	13 (86.7)	13 (58.3)	0.024
Arterial hypertension	12 (80)	15 (62.5)	0.016
Arteriovenous fistula	5 (33.3)	3 (12.5)	0.006
Kidney replacement therapy			0.009
- HD	11 (73.3)	13 (54.2)	
- Others	4 (28.7)	11 (45.8)	
Biological characteristics			
- Hemoglobin (g/dL)	11.6 ± 1.3	11.7 ± 1.13	0.75
- Calcium (mmol/L)	2.3 ± 0.13	2.4 ± 0.11	0.35
- Phosphorus (mmol/L)	1.6 ± 0.33	1.44 ± 0.29	0.11
- Cholesterol (mmol/L)	4.5 ± 0.8	3.8 ± 1.3	0.14
- Triglycerides (mmol/L)	1.3 [0.96–2.26]	1.14 [0.78–1.66]	0.31
- Intact PTH (pg/mL)	21.5 [13.2–73.5]	12 [4–42]	0.26
- Albumin (g/L)	44 .7 ± 6.3	42.6 ± 3.8	0.42
- CRP > 5 mg/L	1 (6.7)	5 (20.8)	0.16
- Low vitamin D	13 (86.7)	19 (79.2)	042

AA, ascending aorta; *HD*, hemodialysis; *Intact PTH*, intact parathyroid hormone; *CRP*, C-reactive protein

related factors with synergistic effects. The cardiorenal syndrome could then encompass concomitant cardiovascular and kidney disorders that result from systemic diseases with their related neurohormonal, inflammatory, immunologic, and fibrotic consequences [18]. This fibrogenic response may lead to parenchymal scarring, cellular dysfunction, and cardiac remodeling.

Aortic dilatation

The association between the dilated ascending aorta and kidney failure is rarely described in young patients. One of the reasons for this might be the fact that aortic root measurements are not routinely performed in those settings. Paris et al. found that aortic root dimensions were higher in hypertensive CKD children when compared to primary hypertensive ones, but they excluded patients with CKD-5 [19]. Kaddourah et al. found that out of 78 patients on KRT and 19 KT recipients, 30 patients (30.9%) had aortic dilatation [20]. Our cohort is characterized by a high prevalence of ascending aorta dilatation. Hypertension, the presence of AVF, and hemodialysis were associated with dilated ascending aorta. Except for hypertension [21], those associations have not been described in the adult population. Our hypothesis is that this is a pediatric peculiarity, which may be linked to the high flexibility of younger vessels compared to the adult population. Nayir et al. reported histopathological findings of internal iliac artery samples obtained at the time of kidney transplantation in 12 children [22]. The authors showed that 5 of the 12 arteries had evidence of atherosclerosis or arteriosclerotic lesions, including fibrous or fibroelastic intimal thickening, disruption of the internal elastic lamella, and atheromatous plaques. This evidence of early arterial damage and especially disruption of the internal elastic lamella could explain the distention of the ascending aorta. Increased preload and hypervolemia might be responsible for the dilatation of the aorta as observed in some pediatric congenital diseases. Other factors such as the uremic condition might be involved. Abnormal mineral metabolism (high phosphorus, calcium-phosphorus product, and PTH) has been identified as the major predictor of vascular changes in children on KRT and a recent study suggests that both low and high levels of 1.25-dihydroxyvitamin D are associated with high carotid intima-media thickness (cIMT) [23]. This hypothesis is supported by the fact that KT, while improving uremia-related risk factors, increases life expectancy when compared with long-

Table 5 Evolution of Z-scores of ascending aorta during 1-year follow-up (36 patients)

	First TTE	Second TTE	p
Aortic annulus (Z-score)	0.3 [− 0.32–0.82]	0.66 [− 0.1–1.3]	0.06
Sinuses of Valsalva (Z-score)	0.31 [− 0.8–1.1]	0.01 [− 0.3–1.3]	0.12
Sinotubular junction (Z-score)	1.1 [0.11–1.5]	0.01 [− 0.3–1.3]	0.48
Tubular ascending aorta (Z-score)	1.7 [0.9–2.3]	2.1 [1.4–2.6]	0.029

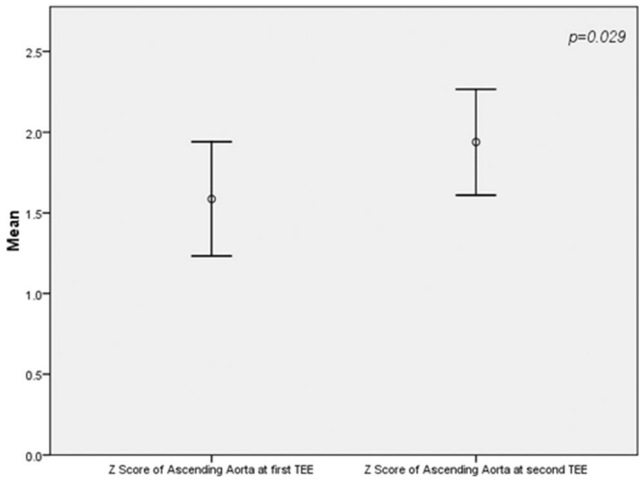

Fig. 2 Annual monitoring showed that dilatation of the ascending aorta tends to persist and even increase significantly

term KRT [24]. While hypertension has already been described as a risk factor for ascending aorta dilation in adults [14, 23] and children [8], it remains however unanswered whether aggressive antihypertensive treatment (including beta-blockers) slows down the progression of ascending aorta dilation in children.

In this study, we measured the sinuses of Valsalva, the sinotubular junction, and the tubular ascending aorta. Sinuses of Valsalva and sinotubular junction were not significantly dilated. Similar findings have been described in hypertensive adults [25].

Study limitations

This study has several limitations. Only 39 patients were analyzed. This small sample size was insufficient to yield statistically significant results for some parameters (CKD etiologies and some biological parameters). Secondly, the impact of medication and blood pressure control was not fully analyzed because of the retrospective character of the study and the short follow-up (1 year). A long-term observational cohort is needed to study cardiac and vascular changes and analyze the impact of treatments, especially beta-blockers. It is of note that the inter-operator variability of the TTE analysis was not considered, as the same practitioner did all the measurements.

Conclusion

Our analysis shows that dilatation of the ascending aorta is a common phenomenon in children with advanced CKD, in the presence of hypertension, AVF, and in those who are on hemodialysis. The exact mechanisms of this aortic root dilatation have yet not been determined. We hypothesize the interaction between CKD-specific hemodynamics and hormonal conditions. Children with advanced CKD could potentially benefit from aggressive therapy to prevent and treat CD.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00467-020-04887-8.

References

1. Chirakarnjanakorn S, Navaneethan SD, Francis GS, Tang WHW (2017) Cardiovascular impact in patients undergoing maintenance hemodialysis: clinical management considerations. Int J Cardiol 232:12–23. https://doi.org/10.1016/j.ijcard.2017.01.015
2. Johnstone LM, Jones CL, Grigg LE, Wilkinson JL, Walker RG, Powell HR (1996) Left ventricular abnormalities in children, adolescents and young adults with renal disease. Kidney Int 50:998–1006. https://doi.org/10.1038/ki.1996.401
3. Ronco C, McCullough P, Anker SD, Anand I, Aspromonte N, Bagshaw SM, Bellomo R, Berl T, Bobek I, Cruz DN, Daliento L, Davenport A, Haapio M, Hillege H, House AA, Katz N, Maisel A, Mankad S, Zanco P, Mebazaa A, Palazzuoli A, Ronco F, Shaw A, Sheinfeld G, Soni S, Vescovo G, Zamperetti N, Ponikowski P, Acute Dialysis Quality Initiative (ADQI) consensus group (2010) Cardio-renal syndromes: report from the consensus conference of the Acute Dialysis Quality Initiative. Eur Heart J 31:703–711. https://doi.org/10.1093/eurheartj/ehp507
4. McDonald SP, Craig JC, Australian and New Zealand Paediatric Nephrology Association (2004) Long-term survival of children with end-stage renal disease. N Engl J Med 350:2654–2662. https://doi.org/10.1056/NEJMoa031643
5. Schrier RW (2007) Cardiorenal versus renocardiac syndrome: is there a difference? Nat Clin Pract Nephrol 3:637–637. https://doi.org/10.1038/ncpneph0673
6. Hadjiphilippou S, Kon SP (2016) Cardiorenal syndrome: review of our current understanding. J R Soc Med 109:12–17. https://doi.org/10.1177/0141076815616091
7. Cuspidi C, Meani S, Fusi V, Valerio C, Sala C, Zanchetti A (2006) Prevalence and correlates of aortic root dilatation in patients with essential hypertension: relationship with cardiac and extracardiac target organ damage. J Hypertens 24:573–580. https://doi.org/10.1097/01.hjh.0000209992.48928.1f
8. Roman MJ, Devereux RB, Niles NW, Hochreiter C, Kligfield P, Sato N, Spitzer MC, Borer JS (1987) Aortic root dilatation as a cause of isolated, severe aortic regurgitation. Ann Intern Med 106:800–807. https://doi.org/10.7326/0003-4819-106-6-800
9. Gawinecka J, Schönrath F, von Eckardstein A (2017) Acute aortic dissection: pathogenesis, risk factors and diagnosis. Swiss Med Wkly 147:w14489. https://doi.org/10.4414/smw.2017.14489
10. Du Bois D, Du Bois EF (1989) A formula to estimate the approximate surface area if height and weight be known. 1916. Nutr Burbank Los Angel Cty Calif 5:303–311 discussion 312-313
11. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF 3rd, Dokainish H, Edvardsen T, Flachskampf FA, Gillebert TC, Klein AL, Lancellotti P, Marino P, Oh JK, Popescu BA, Waggoner AD (2016) Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 29:277–314. https://doi.org/10.1016/j.echo.2016.01.011
12. Pettersen MD, Du W, Skeens ME, Humes RA (2008) Regression equations for calculation of z scores of cardiac structures in a large cohort of healthy infants, children, and adolescents: an echocardiographic study. J Am Soc Echocardiogr 21:922–934. https://doi.org/10.1016/j.echo.2008.02.006

13. Chavers BM, Li S, Collins AJ, Herzog CA (2002) Cardiovascular disease in pediatric chronic dialysis patients. Kidney Int 62:648–653. https://doi.org/10.1046/j.1523-1755.2002.00472.x
14. Mitsnefes MM, Kimball TR, Border WL, Witt SA, Glascock BJ, Khoury PR, Daniels SR (2004) Impaired left ventricular diastolic function in children with chronic renal failure. Kidney Int 65:1461–1466. https://doi.org/10.1111/j.1523-1755.2004.00525.x
15. Briet M, Bozec E, Laurent S, Fassot C, London GM, Jacquot C, Froissart M, Houillier P, Boutouyrie P (2006) Arterial stiffness and enlargement in mild-to-moderate chronic kidney disease. Kidney Int 69:350–357. https://doi.org/10.1038/sj.ki.5000047
16. Hayashi T, Joki N, Tanaka Y, Hase H (2015) Anaemia and early phase cardiovascular events on haemodialysis. Nephrology 20(Suppl 4):1–6. https://doi.org/10.1111/nep.12642
17. Martin LC, Franco RJS, Gavras I, Matsubara BB, Garcia S, Caramori JT, Barretti BB, Balbi AL, Barsanti R, Padovani C, Gavras H (2004) Association between hypervolemia and ventricular hypertrophy in hemodialysis patients. Am J Hypertens 17:1163–1169. https://doi.org/10.1016/j.amjhyper.2004.07.017
18. Zannad F, Rossignol P (2018) Cardiorenal Syndrome Revisited. Circulation 138:929–944. https://doi.org/10.1161/CIRCULATIONAHA.117.028814
19. Paris G, Gorla SR, Arenas-Morales AJ, Seeherunvong W, Swaminathan S (2019) Comparison of echocardiographic changes in children with primary hypertension and hypertension due to mild to moderate chronic kidney disease. Pediatr Nephrol 34:487–494. https://doi.org/10.1007/s00467-018-4096-y
20. Kaddourah A, Uthup S, Madueme P, O'Rourke M, Hooper DK, Taylor MD, Colan SD, Jefferies JL, Rao MB, Goebel J (2015) Prevalence and predictors of aortic dilation as a novel cardiovascular complication in children with end-stage renal disease. Clin Nephrol 83:262–271. https://doi.org/10.5414/CN108489
21. Covella M, Milan A, Totaro S, Cuspidi C, Re A, Rabbia F, Veglio F (2014) Echocardiographic aortic root dilatation in hypertensive patients: a systematic review and meta-analysis. J Hypertens 32:1928–1935; discussion 1935. https://doi.org/10.1097/HJH.0000000000000286
22. Nayır A, Bilge I, Kiliçaslan I, Ander H, Emre S, Sirin A (2001) Arterial changes in paediatric haemodialysis patients undergoing renal transplantation. Nephrol Dial Transplant 16:2041–2047. https://doi.org/10.1093/ndt/16.10.2041
23. Shroff RC, Donald AE, Hiorns MP, Watson A, Feather S, Milford D, Ellins EA, Storry C, Ridout D, Deanfield J, Rees L (2007) Mineral metabolism and vascular damage in children on dialysis. J Am Soc Nephrol 18:2996–3003. https://doi.org/10.1681/ASN.2006121397
24. Mitsnefes MM (2012) Cardiovascular disease in children with chronic kidney disease. J Am Soc Nephrol 23:578–585. https://doi.org/10.1681/ASN.2011111115
25. Kim M, Roman MJ, Cavallini MC, Schwartz JE, Pickering TG, Devereux RB (1996) Effect of hypertension on aortic root size and prevalence of aortic regurgitation. Hypertension 28:47–52. https://doi.org/10.1161/01.HYP.28.1.47