Is N-terminal pro-brain natriuretic peptide a reliable marker for body fluid status in children with chronic kidney disease?

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Abstract

Introduction: Brain natriuretic peptides, released in response to left ventricular stress, have a strong prognostic value in dialysis patients. However, their role in detecting abnormalities of fluid status is under debate; the relationship between volume status and brain natriuretic peptide (BNP) differs among various studies. The aim of our study was to evaluate the clinical utility of N-terminal proBNP in the assessment of fluid status and cardiovascular risk in this setting.

Material and methods: The study included 65 children: 10 pre-dialysis, 13 hemodialysis, 12 peritoneal dialysis patients and 30 healthy controls. Volume status was determined by multifrequency bioimpedance and N-terminal proBNP, as well as echocardiography to estimate the left ventricle structure and function.

Results: The median log NT-proBNP values of hemodialysis and peritoneal dialysis patients were 3.66 (2.05–4.90) and 3.57 (2.51–4.13) pg/ml, respectively, and significantly higher compared with the control group (p < 0.001, p < 0.001). On simple correlation, NT-proBNP was correlated with markers of volume overload and cardiac dysfunction. On multivariate regression analysis, only left ventricle mass index (β = 0.402, p = 0.003) and left atrium diameter (β = 0.263, p = 0.018) were independently associated with NT-proBNP (adjusted R² of the model: 0.707, p < 0.001).

Conclusions: Our research suggested that NT-proBNP, which was correlated with LV systolic and diastolic dysfunction and fluid overload as assessed by bioimpedance, can be used to evaluate cardiovascular states in a chronic kidney disease (CKD) population. From the early stages of CKD, periodic monitoring of NT-proBNP levels may be essential for early detection of patients with high risk of cardiovascular events, and for taking preventive intervention as soon as possible.

Key words: chronic kidney disease, pediatrics, bioimpedance analysis, volume status, N-terminal pro-brain natriuretic peptide.

Introduction

Cardiovascular disease (CVD) is prevalent in patients with chronic kidney disease (CKD) and remains the major cause of mortality [1, 2].
Although there are many potential cardiovascular risk factors that play an important role in the development of CVD, including both traditional and uraemia-related risk factors, many recent studies have focused on novel risk factors such as malnutrition, inflammation, and overhydration in the CKD population [1, 3–5]. Overhydration as well as accumulation of uremic toxins may influence the development of hypertension, left ventricular hypertrophy (LVH), and LV dysfunction and eventually leads to the development of congestive heart failure in patients with CKD [6]. This suggests that accurately measuring the volume state will profoundly impact on dialysis patients’ blood pressure, cardiac health, and clinical outcome [1, 7, 8].

Several objective methods have been proposed to support the correct estimation of volume status in dialysis patients, because interpretation of clinical indicators is subjective and lacks precision in diagnosing excess intravascular volume [9]. The most commonly used methods include ultrasound of the inferior vena cava, radionuclide dilution techniques, assessment of extracellular water (ECW) by bioimpedance analysis (BIA) and brain natriuretic peptide (BNP) and N-terminal pro-brain natriuretic peptide (NT-proBNP) as biochemical markers [10–21]. Among them, the brain natriuretic peptides (BNPs), BNP and NT-proBNP, released in response to left ventricular stress, have been repeatedly reported to be predictive of increased cardiovascular mortality. However, their role in detecting abnormalities of fluid status is under debate; the relationship between volume status and BNPs differs among various studies [22–25]. The prevalence of volume overload during the earlier stages of CKD is unclear and its significance has not been explained. Only a limited number of studies have been conducted in CKD patients not yet on dialysis [26–28].

In this study, we aimed to assess the relationship of NT-proBNP with fluid status measured by BIA and with cardiovascular changes in children undergoing hemodialysis (HD), peritoneal dialysis (PD), and in children with CKD with no need of renal replacement.

**Material and methods**

This single-center cross-sectional study involved 35 CKD pediatric patients (13 patients on HD, 12 patients on PD and 10 patients with stage 3B-4 CKD) and 30 age- and sex-matched healthy individuals as controls. Patients with CKD who underwent HD or PD for at least 6 months and patients with stage 3B-4 CKD who were followed up in the nephrology outpatient clinic with a glomerular filtration rate (GFR) of 15-44 ml/min/1.73 m² were included in the study. The HD patients underwent 3.5–4 h lasting dialysis 3 times per week. Ten patients in the PD group underwent automated peritoneal dialysis (APD) using a standard calcium dialysate and 2 patients received continuous ambulatory peritoneal dialysis (CAPD). Exclusion criteria were infections (as judged by the attending pediatric nephrologist), the presence of congenital or acquired heart disease, contraindications for BCM (an implanted electronic medical device) or connection to an external electronic medical device (pacemaker), any kind of metal implants or amputations; overnight enteral nutrition. Also those who did not sign the informed consent form were excluded from the study.

Baseline demographic data were collected. Age (years), weight (kg), height (cm), body mass index (BMI) (kg/m²), body surface area (BSA), CKD etiologies and types and duration (month) of renal replacement therapies of children were recorded. Paleness, tachypnea, tachycardia, and presence of edema in the physical examination was recorded. The systolic and diastolic blood pressure of HD patients were measured before dialysis and during routine outpatient examinations in PD patients in a sitting position with a cuff appropriate for their arm using an electronic oscillometric device. Blood sampling, and echocardiographic and BIA calculations were performed before dialysis in the HD patients, when the abdomen was empty in PD patients, during routine follow-up in the predialysis group and early in the morning in the control group. Plasma levels of NT-proBNP were measured before and after each HD session.

**Ethics**

The study is compliant with ethical standards. Ethics board approval of Ondokuz Mayis University Faculty of Medicine was granted (24.11.2011, Decree no: 2011/443) and the study was supported by Ondokuz Mayis University Scientific Research Projects Commission (Project code PYO. TIP.1901.12.019). The study was initiated after the study content was clearly explained to the parents of all children (patients and controls), and informed consent was provided.

**BIA evaluation**

We applied the Body Composition Monitor (BCM, Fresenius Medical Care) using multi-frequency bioimpedance spectroscopy (BIS) in order to assess the hydration status. The children were laid on a non-conductive surface, and metal jewelry was removed. Skin cleansing was performed before the procedure and two electrodes were then fixed on the dorsal surfaces of one foot and hand on the same side, vertical to the extremity axis, as described in the operator’s manual. Contact of the upper extremities and body and lower
extremities with one another was avoided during the procedure. The device connection was enabled with these electrodes. Calculations were completed in 1 to 4 min after the data of sex, height (cm), body weight (kg), and blood pressure (systolic and diastolic as mm Hg) of each child were recorded. Body composition analysis was performed using the Fluid Management Tool version 3.2.11. The calculations were repeated by re-replacement of electrodes when the required data quality could not be provided. Accordingly, the parameters (overhydration (OH), relative fluid load (OH/ECW %), total body water (TBW) (l), ECW (l), intracellular water (ICW) (l), the ratio of ECW to ICW (E/I)) were recorded.

**NT-proBNP evaluation**

The blood samples were transferred to red-topped vacuum blood collection tubes and clotting was allowed to occur. Complete blood samples were centrifuged at +4°C for 5 min for 4000 cycles/min on Jouan C4i (France) centrifugation apparatus for degradation of serum after blood clotting. The obtained sera were transferred to Eppendorf tubes and preserved in a −20°C freezer. Kits and serum samples were heated to +25°C room temperature before initiation of the study. Serum NT-proBNP levels were determined using VIDAS PC apparatus (bioMérieux, France) and NT-proBNP commercial kits with enzyme-linked fluorescent assay (ELFA) in the research laboratories of Ondokuz Mayıs University Faculty of Medicine. The results were specified as pg/ml. The analytic calculation reference range of NT-proBNP kit was 20–25 000 pg/ml. The study was performed in accordance with the manufacturer’s instructions.

**Echocardiographic evaluation**

M mode and 2 dimensional calculations were performed using 3.5 and 5.5 MHz probes appropriate to the children’s age in a lying position after rest (10–30 min) using a Toshiba Apio SSA-770 Cardiac Imaging system echocardiography device. Left atrium diameter (LAD), left ventricular end diastolic diameter (LVEDD), left ventricular end systolic diameter (LVESD), left ventricular ejection fraction (EF) (%), left ventricular shortening fraction (SF) (%), left ventricular mass index (LVMi), and left ventricular mass (LVM)/height2.7 were calculated using the Devereux formula (LVM = 1.04 × ((PWT + IVST + LVDd3) − (LVDd3)) − 13.6)). Calculations higher than 39.36 g/m² in boys, and 36.88 g/m² in girls were considered as left ventricular hypertrophy. Mitral valve early diastolic flow rate to late atrial filling velocity ratio (E/A) was recorded on Doppler examination for evaluation of diastolic dysfunction.

Statistical analysis

Analyses were done using IBM SPSS Statistics 22.0 (SPSS IBM Corp, Armonk, New York, USA). Compatibility of variables was investigated using visual (histogram and probability diagrams) and analytic (Shapiro-Wilk) tests. The characteristics of patient and control groups were determined using descriptive statistics. Parameters compatible with a normal distribution were defined as mean ± standard deviations (SD), and parameters that did not fit a normal distribution were defined as median and distribution (lower-upper limit). The nonparametric variable of NT-proBNP was log transformed for analysis. We used the parametric variant analysis ANOVA for comparison of more than two groups, and the nonparametric variant analysis Kruskal-Wallis test for parameters that did not show a normal distribution. In HD patients, the paired t-test was used to assess measurements of log NT-proBNP obtained before and after HD. The correlation coefficients and statistical significance between intergroup variables were calculated using Pearson’s correlation test or Spearman’s test. The effect of independent variables on dependent variables was evaluated using regression analysis. The p-values smaller than 0.05 were considered as statistically significant.

**Results**

**Baseline characteristics of the study population**

Table I summarizes the baseline characteristics of the total study population as well as patient subgroups. The main frequent cause of CKD was congenital kidney abnormalities (54.3%), followed by nephronophthisis (20%). There was no statistically significant difference considering age, sex, body weight, and BSA between the HD, PD, predialysis patients and controls; a significant difference was detected between the systolic and diastolic blood pressure levels (p < 0.001, p < 0.001 respectively). Accordingly, systolic blood pressure of the HD and PD groups was significantly higher compared with the control group (p = 0.002, p = 0.002, respectively), and the diastolic blood pressures of PD, HD and predialysis groups were significantly higher compared with the control group (PD control p = 0.002; HD control p = 0.04; predialysis control p = 0.015).

The highest NT-proBNP levels were detected in the HD group, and a significant increase was detected in HD and PD groups compared with the controls (HD control p < 0.001; PD control p < 0.001) (Figure 1). Although the log NT-proBNP level of the predialysis group was found to be increased compared with the control group, the difference was not statistically significant (p = 0.08).
### Table I. Baseline clinical characteristics and results of NT-proBNP, BIA and echocardiographic data of the study cohort

| Variables | HD group (n = 13) | PD group (n = 12) | Predialysis group (n = 10) | Control group (n = 30) | P-value |
|-----------|------------------|------------------|---------------------------|-----------------------|---------|
| Age [years] | 11.92 ±3.13 | 11.42 ±3.18 | 10.50 ±2.27 | 10.11 ±3.74 | 0.366 |
| Boys/girls | 7/6 | 4/8 | 7/3 | 14/16 | 0.372 |
| Dialysis vintage [months] | 11 (7–60) | 33.50 (6–79) | – | – | 0.068 |
| Weight [kg] | 35.44 ±12.71 | 31.95 ±12.48 | 40.65 ±13.84 | 35.83 ±16.48 | 0.595 |
| BSA [m²] | 1.17 ±0.32 | 1.09 ±0.29 | 1.23 ±0.31 | 1.13 ±0.35 | 0.772 |
| Urine output [ml/day] | 300 (10–1000) | 150 (50–2500) | 1530 (1200–4400) | – | < 0.001<sup>ab</sup> |
| Systolic blood pressure [mm Hg] | 123.6 ±16.9 | 124.1 ±19.2 | 117.2 ±12.2 | 106 ±10.5 | < 0.001<sup>bc</sup> |
| Diastolic blood pressure [mm Hg] | 80 (60–100) | 77.5 (60–100) | 80 (60–87) | 60 (46–82) | < 0.001<sup>ab</sup> |
| NT-proBNP [pg/ml]: | | | | | |
| NT-proBNP | 4576 (112–80324) | 3783 (323–13540) | 230 (20–47604) | 26 (20–151) | < 0.001<sup>ab</sup> |
| Log NT-proBNP | 3.66 (2.05–4.90) | Pre-HD: 3.63 ±0.84 | Post-HD: 3.57 (2.51–4.13) | 2.35 (1.3–4.68) | 1.41 (1.2–2.18) | < 0.001<sup>a</sup> |
| BIA parameters: | | | | | |
| OH [l] | 1.77 ±1.72 | 1.04 ±1.30 | 0.34 ±0.95 | –0.02 ±0.48 | < 0.001<sup>abcd</sup> |
| Rel OH (%) | 15.1 ±14.59 | 7.69 ±13.04 | 0.19 ±12.06 | –0.52 ±5.17 | < 0.001<sup>ad</sup> |
| TBW [l] | 21.47 ±8.36 | 17.38 ±8.31 | 21.59 ±8.87 | 19.52 ±7.93 | 0.532 |
| ECW [l] | 10.04 ±3.88 | 8.04 ±3.98 | 9.46 ±3.89 | 8.50 ±3.51 | 0.447 |
| ECW/ICW | 0.89 ±0.18 | 0.85 ±0.12 | 0.78 ±0.58 | 0.76 ±0.04 | 0.002<sup>c</sup> |
| ECW/TBW | 0.46 ±0.05 | 0.45 ±0.03 | 0.43 ±0.02 | 0.43 ±0.01 | 0.003<sup>b</sup> |
| Echocardiographic examination (systolic-diastolic functions): | | | | | |
| LAD [mm] | 32.98 ±5.53 | 30.95 ±5.28 | 30.53 ±2.87 | 25.78 ±3.51 | < 0.001<sup>ab</sup> |
| LVEDD [mm] | 46.57 ±8.74 | 42.73 ±7.21 | 43.48 ±7.99 | 40.6 ±5.09 | 0.084 |
| LVESD [mm] | 31.01 ±9.81 | 27.27 ±6.51 | 27.67 ±7.09 | 25.96 ±3.13 | 0.131 |
| LVMI [g/m²]: | | | | | |
| LVMI [g/m²]: | 95.29 ±24.59 | 85.21 ±22.32 | 63.03 ±15.53 | 31.62 ±9.64 | < 0.001<sup>abcd</sup> |
| LVEF (%) | 65.90 (31.1–77.9) | 70.10 (45.2–77.5) | 67.65 (46.6–76.9) | 66.70 (56.5–73.9) | 0.739 |
| LVSF (%) | 36.80 (14.9–45.8) | 39.60 (22.6–44.7) | 37.5 (23.7–45.2) | 36.60 (28.7–42.3) | 0.720 |
| E/A | 1.64 ±0.35 | 1.54 ±0.65 | 1.81 ±0.70 | 2.01 ±0.41 | 0.005<sup>ab</sup> |

Data are presented as means ± standard deviations (x ± SD) or as median with range. P < 0.05 was considered significant. NT-proBNP – N-terminal pro-B-type natriuretic peptide, OH – absolute fluid overload (AFO), Rel OH – relative fluid overload (RFO) is defined as the AFO to ECW ratio, ECW – extracellular water, ICW – intracellular water, TBW – total body water, LAD – left atrial dimension, LVEDD – left ventricular end-diastolic diameter, LVESD – left ventricular end-systolic diameter, LVMI – left ventricular mass index, LVEF – left ventricular ejection fraction, LVSF – left ventricular shortening fraction, E/A – mitral E wave to A wave ratio. *Significant difference between HD and control group. **Significant difference between PD and control group. *Significant difference between predialysis and control group. **Significant difference between HD and predialysis group. ***Significant difference between PD and predialysis group.
The measurements of log NT-proBNP levels before and after HD are shown in Figure 2. Our results show that there were no significant changes in log NT-proBNPs after HD ($p = 0.76$).

Table I shows the parameters obtained using BIS. HD patients had a significantly higher hydration status by BIS. The OH value was significantly higher in the HD group compared with the PD and control groups; the Rel OH value was significantly higher in the HD group compared with the predialysis and control group, and the E/I and ECW/TBW ratios were significantly higher in the HD group compared with the control group. A statistically significant difference was detected between the groups considering the LAD, LVMI and E/A ratio ($p < 0.001$, $p < 0.001$, $p = 0.005$, respectively). LAD and LVMI were higher in the HD, PD, and predialysis groups compared with the control group. A significant decrease was detected in the E/A ratio in the HD and PD group compared with the control group (HD control $p = 0.039$; PD control $p = 0.01$) (Table I).

**Correlations between NT-proBNP and other baseline variables**

NT-proBNP was found to be positively correlated with diastolic blood pressure ($r = 0.460$, $p < 0.001$), OH ($r = 0.483$, $p < 0.001$), Rel OH ($r = 0.448$, $p < 0.001$), E/I ($r = 0.410$, $p = 0.001$), and ECW/TBW ($r = 0.391$, $p = 0.001$).

Whereas a positive correlation was detected between NT-proBNP and LAD and LVMI ($r = 0.571$, $p < 0.001$, $r = 0.793$, $p < 0.001$, respectively), a negative correlation was detected between NT-proBNP and E/A ($p < 0.001$, $r = –0.474$) (Figure 3).

Multivariate regression analysis included NT-proBNP as the dependent variable and diastolic blood pressure, BIA parameters and systolic–diastolic cardiac functions that were previously identified in univariate analyses as independent variables. As shown in Table II, LVMI and LAD were independently associated with NT-proBNP (adjusted $R^2$ of the model: 0.707, $p < 0.001$).

**Discussion**

In the current study, we found higher baseline plasma concentrations of NT-proBNP in a cohort of pediatric chronic dialyzed patients. We show concentrations of NT-proBNP to be correlated with LV systolic and diastolic dysfunction and fluid overload as assessed by bioimpedance. After adjustment for known clinical variables, NT-proBNP concentration was found to have an independent effect on both LAD and LVMI. We investigated, in addition, the acute effect of a HD session on plasma NT-proBNP and observed no significant change.

Natriuretic peptides are involved in the regulation of blood pressure and body fluid homeostasis. They are mainly synthesized by cardiac myocytes against increased wall stress and separated as BNP and NT-proBNP after secretion as prohormones. Many studies have demonstrated that the normal reference range of BNP and NT-proBNP levels may vary regarding age, sex, the kit used for the calculation and measurement method because there is no standardized calculation method for determining serum levels of natriuretic peptides [29–31]. We decided to measure NT-proBNP, as it is a larger peptide with a longer half-life, and so less likely to be affected by dialysis. In addition, BNP is less stable than NT-proBNP in vitro, especially if analysis is delayed. Recent studies have revealed the strong association between natriuretic peptides and left ventricular hypertrophy and systolic dysfunction [32–36]. As such there has been debate in the published literature as to whether measurement of NT-proBNP can add value in aiding clinical judg-
Figure 3. Correlation of log NT-pro-BNP level with diastolic blood pressure (A), Rel OH (B), OH (C), ECW/TBW (D), E/I (E), LVMI (F), LAD (G), mitral E/A (H)
In a recent study, Milani et al. [18] studied 16 young patients undergoing dialysis and assessed TBW and ECW volumes using multifrequency bioimpedance and deuterium-bromide dilution as reference tests. They concluded that multifrequency bioimpedance measurements could not precisely estimate TBW and ECW in children receiving dialysis.

The results of the present study revealed that LAD and LVMI were significantly higher in HD, PD and predialysis patients compared with the control group whereas E/A ratio was significantly lower in the HD-PD group compared with the controls. There was no significant difference between the groups considering EF and SF levels, which are indicators of left ventricular systolic functions [43, 44]. In our study we found that diastolic functions are affected much earlier than suggested by several previous studies [43, 45]. We found a positive correlation between levels of NT-proBNP and OH, Rel OH, ECW/ICW, LAD, and LVMI and an inverse correlation with E/A ratio. These results are in accordance with the experience in recent reports [38–41]. However, other studies failed to detect a positive association between fluid removed and change of NT-proBNP in patients receiving dialysis [19, 25, 29] suggesting that this mechanism needs to be further elucidated. We identified that high levels of NT-proBNP (p < 0.001) were a significant independent risk factor for the increase of LVMI.

It is important to interpret our findings within the context of the study limitations. This study is limited by a relatively small cohort size and a lack of long-term, longitudinal follow-up. For the purpose of our study, no additional follow-up or gold standard measure of fluid overload, namely deuterium dioxide dilution, was used due to ethical concerns about repeated blood sampling in children. It is also important to note that our data represent a single center report. Finally, our findings represent associations, and further studies are needed to evaluate whether implementing NT-proBNP would improve outcomes. Despite these limitations, this pediatric study shows the correlation between NT-proBNP and volume status, as well as LAD and LVMI.

In conclusion, assessment of NT-proBNP appears as a promising diagnostic and prognostic tool in dialysis and predialysis patients. We believe that the use of NT-proBNP from the early stages of CKD is a simple and applicable method for close follow-up and prognosis. When NT-proB-

| Variable     | β     | Standard error | P-value |
|--------------|-------|---------------|---------|
| LVMI [g/m²]  | 0.402 | 0.005         | 0.003   |
| LAD [mm]     | 0.263 | 0.024         | 0.018   |

Selected variables: diastolic blood pressure, OH, Rel OH, ECW/ICW, ECW/TBW, mitral E/A, LAD, LVMI.
NP values are significantly elevated, a suggested approach might be to assess the volume status exactly using both clinical and additional evaluation methods. In case of persistent and significant elevations despite adequate management of overhydration, patient referral for further cardiac evaluation should be considered. However, studies are needed to establish whether this approach results in improved outcome of dialysis patients. Moreover, reference values for dialysis patients should be validated in future studies.

Conflict of interest

The authors declare no conflict of interest.

References

1. Mitsnefes M. Cardiovascular complications of pediatric chronic kidney disease. Pediatr Nephrol 2008; 23: 27-39.
2. Foley RN, Parfrey PS. Cardiovascular disease and mortality in ESRD. J Nephrol 1998; 11: 239-45.
3. Sterwinke E, Chung SH, Heimburger O, Lindholm B. Malnutrition, inflammation, and atherosclerosis in peritoneal dialysis patients. Perit Dial Int 2001; 21: 157-62.
4. Agarwal R. Hypervolemia is associated with increased mortality among haemodialysis patients. Hypertension 2010; 56: 512-7.
5. Căpușa C, Stefan G, Stancu S, Ilies A, Dorobanțu N, Mircescu G. Subclinical cardiovascular disease markers and vitamin D deficiency in non-dialysis chronic kidney disease patients. Arch Med Sci 2016; 12: 1015-22.
6. Parfrey PS, Harnett JD, Griffiths SM, Gault MH, Barré PE. Congestive heart failure in dialysis patients. Arch Intern Med 1988; 148: 1519-25.
7. Wizemann V, Wabel R, Chamney P, et al. The mortality risk of overhydration in haemodialysis patients. Nephrol Dial Transplant 2009; 24: 1574-9.
8. Savilangam M, Suresh M, Farrington K. Comparison of B-type natriuretic peptide and NT proBNP as predictors of survival in patients on high-flux haemodialysis and hemodialfiltration. Hemodial Int 2011; 15: 359-65.
9. Agarwal R, Andersen M, Pratt JH. On the importance of pedal edema in hemodialysis patients. Clin J Am Soc Nephrol 2009; 13: 153-8.
10. Jaeger JQ, Mehta RL. Assessment of dry weight in hemodialysis: an overview. J Am Soc Nephrol 1999; 10: 392-403.
11. Haciomeroglu P, Ozkaya O, Gunal N, Baysal K. Venous collapsibility index changes in children on dialysis. Nephrology (Carlton) 2007; 12: 135-9.
12. Wang AV, Lai KN. Use of cardiac biomarkers in end-stage renal disease. J Am Soc Nephrol 2009; 19: 1643-52.
13. Jaffrin MY, Morel H. Body fluid volumes measurements by impedance: a review of bioimpedance spectroscopy (BIS) and bioimpedance analysis (BIA) methods. Med Eng Phys 2008; 30: 1257-69.
14. Moissl U, Arias-Guillén M, Wabel P, et al. Bioimpedance guided fluid management in hemodialysis patients. Clin J Am Soc Nephrol 2013; 8: 1575-82.
15. O’Lone EL, Visser A, Finney H, Fan SL. Clinical significance of multi-frequency bioimpedance spectroscopy in peritoneal dialysis patients: independent predictor of patient survival. Nephrol Dial Transplant 2014; 29: 1430-7.
16. Žalošević A, Schaefer B, Schaefer F, et al. Hydration measurement by bioimpedance spectroscopy and blood pressure management in children on hemodialysis. Pediatr Nephrol 2013; 28: 2169-77.
17. Kyle UG, Earthman CP, Pichard C, Coss-Bu JA. Body composition during growth in children: limitations and perspectives of bioelectrical impedance analysis. Eur J Clin Nutr 2015; 69: 1298-305.
18. Milani GP, Groothoff JW, Vianello FA, et al. Bioimpedance and fluid status in children and adolescents treated with dialysis. Am J Kidney Dis 2017; 12: pii: S0272-6386(16)30633-3.
19. Cooper BA, Aslani A, Ryan M, et al. Comparing different methods of assessing body composition in end-stage renal failure. Kidney Int 2000; 58: 408-16.
20. Sheen V, Bhalla V, Tulua-Tata A, et al. The use of B-type natriuretic peptide to assess volume status in patients with end-stage renal disease. Am Heart J 2007; 153: 244.e1-e5.
21. Sun L, Sun Y, Zhao X, et al. Predictive role of BNP and N-proBNP in haemodialysis patients. Nephron Clin Pract 2008; 110: 178-84.
22. Lee JA, Kim DH, Yoo SJ, Oh DJ, Yu SH, Kang ET. Association between serum n-terminal brain natriuretic peptide concentration and left ventricular dysfunction and extracellular water in continuous ambulatory peritoneal dialysis patients. Perit Dial Int 2006; 26: 360-5.
23. Sommerer C, Beimler J, Schwenger V, et al. Cardiac biomarkers and survival in haemodialysis patients. Eur J Clin Invest 2007; 37: 350-6.
24. Jacobs LH, van der Kerkhof J, Mingels AM, et al. Inflammation overhydration and cardiac biomarkers in haemodialysis patients: a longitudinal study. Nephrol Dial Transplant 2010; 25: 243-8.
25. Goldfarrb-Rumyantzev AS, Chelamcharla M, Bray BE, et al. Volume indicators and left ventricular mass during aggressive volume management in patients on thrice weekly haemodialysis. Nephron Clin Pract 2009; 113: 270-80.
26. Bellizzi V, Scafili I, Terracciano V, et al. Early changes in bioelectrical estimates of body composition in chronic kidney disease. J Am Soc Nephrol 2006; 17: 1481-7.
27. Hung SC, Kuo KL, Peng CH, et al. Volume overload correlates with cardiovascular risk factors in patients with chronic kidney disease. Kidney Int 2014; 85: 703-9.
28. Yilmaz A, Yilmaz B, Küçükseymen S, Özpeli E, Pekel N. Association of overhydration and cardiac dysfunction in patients with chronic kidney disease but not yet dialysis. Nephrol Ther 2016; 12: 94-7.
29. Davis GK, Bampton F, Sarpa A, Dicke F, Rabi Y, Lyon ME. B-type natriuretic peptide in pediatrics. Clin Biochem 2006; 39: 600-5.
30. Levin ER, Gardner DG, Samson WK. Natriuretic peptides. N Engl J Med 1998; 339: 321-8.
31. Koch A, Singer H. Normal values of B type natriuretic peptide in infants, children, and adolescents. Heart 2003; 89: 875-8.
32. Mair J, Friedl W, Thomas S, Puschendorf B. Natriuretic peptides in assessment of left-ventricular dysfunction. Scand J Clin Lab Invest Suppl 1999; 230: 132-42.
33. Zoccali C, Mallamaci F, Benedetto FA, et al. Cardiac natriuretic peptides are related to left ventricular mass and function and predict mortality in dialysis patients. J Am Soc Nephrol 2001; 12: 1508-15.
34. Naganuma T, Sugimura K, Wada S, et al. The prognostic role of brain natriuretic peptide in hemodialysis patients. Am J Nephrol 2002; 23: 27-39.
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35. Lee SW, Song JH, Kim GA, Lim HL. Plasma brain natriuretic peptide concentration on assessment of hydration status in hemodialysis patient. Am J Kidney Dis 2003; 41: 1257-66.

36. Goto T, Takase H, Toriyama T, et al. Increased circulating levels of natriuretic peptides predict future cardiac events in patients with chronic haemodialysis. Nephron 2002; 92: 610-5.

37. Panigagua R, Ventura MD, Avila-Diaz M, et al. NT-proBNP fluid volume overload and dialysis modality are independent predictors of mortality in ESRD patients. Nephrol Dial Transplant 2010; 25: 551-7.

38. David S, Kümpers P, Seidler V, Biertz F, Haller H, Fliser D. Diagnostic value of N-terminal pro-B-type natriuretic peptide (NT-proBNP) for left ventricular dysfunction in patients with chronic kidney disease stage 5 on haemodialysis. Nephrol Dial Transplant 2008; 23: 1370-7.

39. Choi SY, Lee JE, Jang EH, et al. Association between changes in N-terminal pro-brain natriuretic peptide levels and changes in left ventricular mass index in stable haemodialysis patients. Nephron Clin Pract 2008; 110: 93-100.

40. Kumar S, Khosravi M, Massart A, Davenport A. Is there a role for N-terminal pro-brain type natriuretic peptide in determining volume status in haemodialysis patients? Nephron Clin Pract 2012; 122: 33-7.

41. Ouami S, Bougmiza I, Abroug S, et al. Relationship of brain natriuretic peptide concentrations to left ventricular function and adverse outcomes in children with end-stage renal disease undergoing haemodialysis. Pediatr Cardiol 2011; 32: 568-577.

42. Nalcacioglu H, Ozkaya O, Baysal K, et al. The role of bioelectrical impedance analysis, NT-proBNP and inferior vena cava sonography in the assessment of body fluid volume in children with nephrotic syndrome. Nefrologia 2018; 38: 48-56.

43. Mitsnefes MM, Kimball TR, Border WL, et al. Impaired left ventricular diastolic function in children with chronic renal failure. Kidney Int 2004; 65: 1461-6.

44. Johnstone LM, Jones CL, Grigg LE, Wilkinson JL, Walker RG, Powell HR. Left ventricular abnormalities in children, adolescents and young adults with renal disease. Kidney Int 1996; 50: 998-1006.

45. Haciomeroglu P, Ozkaya O, Gunal N, Baysal K. An echocardiographic assessment of cardiac functions and structure in children on dialysis. Ren Fail 2008; 30: 147-53.