Glomerular filtration decrease after diagnostic cardiac catheterisation in children with congenital cardiac malformation – the role of serum creatinine, cystatin C, neutrophil gelatinase and urine output monitoring

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Abstract

Introduction: Diagnosis of contrast induced-nephropathy (CIN) by a classic renal biomarker such as creatinine concentration can be delayed because of various factors that can influence this marker. Changes in new biomarkers such as neutrophil-gelatinase associated lipocalin (NGAL) and cystatin C are postulated to be more sensitive for recognizing patients prone to CIN-acute kidney injury (AKI).

Aim: To investigate the role of NGAL and cystatin C as early biomarkers in the diagnosis of kidney injury after cardiac catheterisation.

Material and methods: The study group consisted of 50 patients with congenital heart malformation admitted for scheduled cardiac catheterisation. The biomarkers serum creatinine, serum NGAL and serum cystatin C were tested at 5 time-points sequentially from start to 48 h after the procedure.

Results: Significant changes were noted during the research in the serum creatinine concentration ($p < 0.001$) and serum NGAL concentration ($p < 0.001$). CIN-AKI, diagnosed by the modified Schwartz formula, occurred in 16 (32%) patients after 24 h and in 8 (16%) after 48 h. Subsequent analysis showed that serum creatinine significantly rose in the first 2 h of the study with simultaneous reduction in the eGFR. Maximum growth in serum NGAL occurred at 6 h after contrast administration and then returned to the baseline values at 24 h. Serum cystatin C level did not significantly change during the study.

Conclusions: We observed a transient decrease in eGFR and a rise of serum NGAL after 2 h but NGAL was most pronounced at 6 h after the procedure. The potential role of cystatin C as a biomarker of CIN-AKI was not proved.

Key words: children, cardiac catheterization, contrast-induced acute kidney injury.

Introduction

Contrast-induced by nephropathy (CIN) has been identified as the third most common cause of acute kidney injury (AKI) in the population. The incidence of CIN-AKI in the general population was assessed within the range of 2–25% [1, 2], whereas in the paediatric population the data are less precise and available and reported as around 9% [3]. Acute kidney injury is an independent factor for an unfavourable outcome within 12 months from the incident [4]. It has been postulated that early detection of AKI might be essential with regard to chronic kidney disease and cardiovascular episode prevention.

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In the paediatric population AKI is preferably described by RIFLE staging by Akcan-Arikan [5]. This assessment uses estimated glomerular filtration rate (eGFR) calculated from serum creatinine (by the modified Schwartz formula [6]) and urine output. From the epidemiological point of view, both these indices are of comparable value. There is some doubt whether this statement can be supported at the bedside in a selected group of patients. In children with composed cardiac malformation, who often receive chronic diuretic therapy, the role of urine output analysis could be smaller.

Contrast-induced by nephropathy usually is defined as at least 25% rise in serum creatinine with a similar decrease of glomerular filtration within 48–72 h from contrast administration. It has been reported that a significant number of patients with AKI might be missed in early stages because serum creatinine rises later. It might have some clinical significance in a selected group of patients [7]. In the last decade some promising markers of higher sensitivity have been developed. Neutrophil gelatinase-associated lipocalin (NGAL) increases serum concentration earlier, within the first 6 h after kinder injury [8, 9]. The scientific significance of this observation is high with regard to detection of injury, but clinically, it is uncertain whether this should provoke any action in all cases. Still, most popular clinical classifications are based on serum creatinine and urine output.

Presumably, the incidence of CIN-AKI should be higher within selected populations of patients, specifically prone to the development of AKI, due to intrinsic risk factors. Numerous studies show that children with cardiac malformation undergoing cardiac surgery develop AKI with significantly higher frequency than after cardiac catheterisation, with the incidence rate of about 30% [10, 11]. On the other hand, the dose of the contrast dye and high dose of radiation may cause higher than standard risk of CIN of children with cardiac malformations.

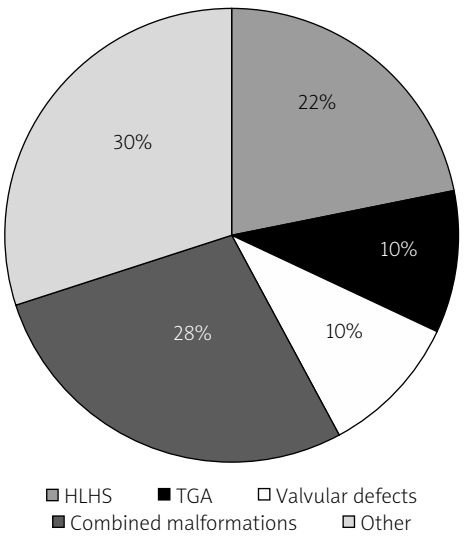

Figure 1. Clinical description of congenital cardiac malformations in the study group
HLHS – hypoplastic left heart syndrome, TGA – translocation of great arteries, combined malformations without HLHS, other: tetralogy of Fallot, persistent arterial duct, aortopulmonary window.

Recent studies raised some doubts about the clinical significance of CIN-AKI in the general population. The US analysis shows that, after standard contrast-enhanced computed tomography, the risk of AKI and its consequences is rather low [12]. However, this study was based on a large emergency department patient group with a low contrast dose per weight. On the other hand, some procedures such as cardiac catheterisation still have high risk for AKI because of intra-aortic contrast infusion, use of high volume of contrast during the procedure, or the situation of cardiogenic shock prior to the procedure [13]. This is valid for both the paediatric and general population.

In the adult population some factors of CIN-AKI are defined. Only some of them are valid in children's organism. We intend to test some of these factors including renal blood flow, dose of contrast dye, administration of diuretics and RAA inhibitors.

Aim

The study aimed to assess the changes in glomerular filtration after cardiac catheterisation in children with complex cardiac malformation as in the group of high risk of development of CIN. The secondary aim was to compare the significance of measurement of serum creatinine, serum cystatin C and serum NGAL in these selected patients.

Material and methods

Study group

The local committee approved the study and all parents/caregivers gave informed consent for participation. The study was designed as a prospective observational one assessing changes of glomerular filtration rate in 50 children (males 35; females 15) with congenital cardiac malformations after diagnostic cardiac catheterisation. The proportions of cardiac defects in the group are presented in Figure 1.

Initial clinical biochemical characteristics of the patients from the study group are presented in Table I. All children had initially normal eGFR by Schwartz according to age. Thirty-two children were cyanotic, 27 children had disturbed renal blood due to congenital heart disease. Inclusion criteria comprised planned contrast angiography in the course of diagnostic or therapeutic procedures in congenital malformations of heart and great vessels and age below 18 years.

Exclusion criteria were as follows: nephrotoxic therapy before and during the procedure, acute cardiac insufficiency, resuscitation or death during the procedure and observation period, urinary tract infection, congeni-

Table I. Clinical and basic biochemical characteristics of the study group

Parameter	Median and interquartile range or number of patients
Age [years]	4.5 (2.0–8.0)
Male/female ratio	35/15
Cyanotic/non-cyanotic malformation, *n*/*n*	32/18
Malformations with normal/disturbed renal parenchymal flow, *n*/*n*	27/23
Estimated glomerular filtration rate [ml/min/1.73 m^2 BSA]	123.04 (109.86–139.04)
Haemoglobin concentration [g/l]	15 (13.1–16.7)
Diagnostic/diagnostic + intervention, *n*/*n*	18/32
Duration of the catheterisation [min]	50 (38–80)
Total dose of the contrast [ml/kg]	2.82 (1.48–5.49)
Total radiation dose [mGy]/time [min]	166.95 (68.00–230.00)/13.27 (7.31–20.09)
RAA blockade before procedure, *n*/*n*	14/36
Proportion of children with diuretic administration before procedure, *n*/*n*	26/24
Heart function by ejection fraction (EF) (%)	62 (57–71)

tal malformation of urinary tract, chronic kidney disease stage 3–5 and AKI before the angiography and blood of plasma transfusion during the procedure.

Study protocol

Children were qualified for the study by cardiologists who were responsible for the cardiac catheterisation. After obtaining consent, baseline assessment was performed. Cardiac echocardiography was done with Philips iE33 machine (EF by single-plane Simpson's). Blood pressure and basic anthropometric parameters were taken as a routine preparation for the catheterisation. Blood test comprised cell blood count, C-reactive protein level, serum creatinine measured by Jaffe method with eGFR calculation by the modified Schwartz formula [6], serum cystatin C (ELISA: Human Cystatin C by R&D Systems, cat No. DCSTC0) with calculation of eGFR by the Filler formula [14], serum NGAL (ELISA: Human Lipocalin-2/NGAL by R&D Systems, cat. No. DLCN20). Clinically, the patients were monitored with regard to blood pressure (oscillometric method) and urine output (hourly) for 48 h.

The clinical and biochemical (eGFR, serum cystatin C, serum NGAL) parameters were assessed prospectively after 2, 6, 24 and 48 h after the first dose of contrast administration. Echocardiography was repeated after 48 h. Acute kidney injury was assessed by the Akcan-Arikan pRIFLE classification, with the first threshold of a 25% decrease in calculated eGFR [5].

Cardiac catheterisation

All patients received standard fluid preparation with normal saline (2–4 ml/kg body weight [b.w.]/h *i.v.*) 6 h before and after the procedure. The initial dye dose (Iomeron 400) was calculated as 1 ml/kg b.w. The final dose range was 1.48–5.49 ml/kg b.w. Median time of the procedure of cardiac catheterisation was 50 min (IQR: 32.5–70) (details in Table I).

For 18 patients the catheterisation was a purely diagnostic procedure, whereas for 32 it was accompanied by invasive cardiology intervention. The interventions included aortic valve balloon valvuloplasty, persistent ductus arteriosus closure, fenestration closure, pulmonary artery balloon angioplasty, veno-venous fistula closure, stent implantation, and valve implantation.

Statistical analysis

All parameters were tested for normal distribution using the Shapiro-Wilk W test. Numerical values were presented as median with 25^{th} and 75^{th} percentiles. Nominal variables were presented as numbers or percentages. The differences in characteristics between groups were verified using Wilcoxon and Friedman's ANOVA tests. The results were regarded as statistically significant if $p < 0.05$ was observed. Statistic package version 13 (StatSoft Inc., Tulsa, OK, USA) was used for all statistical analysis.

Results

After intravascular administration of the ionic contrast we observed significant changes in serum creatinine and eGFR calculated by the Schwartz formula (Figure 2, Table II). Serum creatinine significantly rose in 2 h and decreased to the initial values within 48 h ($p < 0.001$). Estimated GFR which was initially within the normal range for the age of the child significantly decreased in 4 h

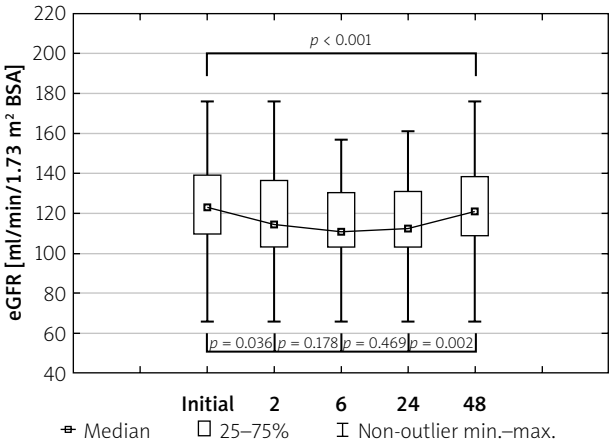

Figure 2. Changes in eGFR calculated by modified Schwartz Formula in the observation period (0–2–6–24–48 h)

and returned to initial values within 48 h of observation. The eGFR decrease met the RIFLE criteria in 16 (15 risk; 1 injury) children (32%) at 24 h and only in 8 (7 risk; 1 injury) children (16%) at 48 h. All of the patients had their diuresis preserved; thus no-one fulfilled the urine output decrease RIFLE criterion. We found that blood pressure (systolic, diastolic and MAP) did not change significantly during the procedure (Table II).

Serum cystatin C did not significantly change within the observation period. However, we observed a tendency to lower eGFR (based on CysC levels) compared to that calculated by serum creatinine (Table II). When we used eGFR by cystatin C, the percentage of children with RIFLE stage R or I was different (24 h –12%; 48 h – 10%) than when the serum creatinine was used.

Serum NGAL significantly changed within the observation period. We noted an abrupt rise of its concentration in two hours after the contrast administration with a subsequent decrease to the initial values after 48 h (Figures 3, 4).

We decided to check whether the selected clinical variables could affect the results of the study. Therefore we compared children younger than 3 years (n = 17) to older ones (n = 33). This comparison showed that serum NGAL was higher in older children at most time-points (2, 24, 48 h) respectively tested (p = 0.01; p = 0.006; p = 0.01). The response to the injury in these groups was comparable – the rise of this parameter was similar.

Later, we checked if possible changes in kidney perfusion might predict higher susceptibility to eGFR decrease. The NGAL was significantly higher at every time-point tested between patients with abnormal (n = 27) and normal (23) renal parenchymal blood flow (Figure 4). This was not confirmed in the case of eGFR by serum creatinine or cystatin C. Additionally we detected no significant differences in eGFR and NGAL between cyanotic congenital and non-cyanotic cardiac malformation.

When we analysed administration of diuretics (n = 27/23) and angiotensin converting enzyme inhibitors (ACEI) (n = 14/36), we found that there were no differences between children receiving these medications and those who did not with regard to serum creatinine, cystatin C or serum NGAL.

When we compared children with AKI by RIFLE criteria and non-AKI children, we found no significant differences in serum NGAL, cystatin C and eGFR by Schwartz formula at the all time-points tested. The changes in time were similar in both analysed groups with statistical significance (Table III).

Table II. Changes in serum creatinine, cystatin C, NGAL, eGFR by Schwartz and Filler and selected clinical values in the observation period. Values presented as median and 25–75 interquartile range

Parameter	Period					Significance (Friedman ANOVA)
	Initial	2	6	24	48	
Serum creatinine [mg/dl]	0.3 (0.3–0.4)	0.4 (0.3–0.4)	0.4 (0.3–0.4)	0.4 (0.3–0.4)	0.3 (0.3–0.4)	< 0.001
eGFR by Schwartz [ml/min/1.73 m² BSA]	123.04 (109.86–139.04)	114.78 (103.25–136.29)	111.17 (103.25–130.10)	112.54 (103.25–131.13)	120.80 (108.76–138.36)	< 0.001
Serum cystatin C [ng/ml]	644.95 (566.9–746.4)	650.85 (552.5–743.6)	646.5 (538.8–781.8)	636.45 (523.4–750.0)	634.05 (485.5–746.4)	0.938
eGFR by Filler [ml/min/1.73 m² BSA]	64.11 (54.41–74.10)	63.46 (54.66–76.27)	63.93 (51.65–78.45)	65.07 (54.11–81.05)	65.35 (54.41–88.19)	0.938
Serum NGAL [ng/ml]	20.42 (21.80–49.60)	21.49 (22.70–51.10)	30.70 (23.00–57.50)	19.08 (18.10–42.20)	21.67 (14.30–40.00)	< 0.001
Mean arterial pressure [mm Hg]	73.33 (65.00–77.67)	69.83 (63.67–78.00)	71.33 (63.67–78.67)	73.67 (65.17–80.50)	77.33 (68.67–81.67)	0.480
Systolic blood pressure [mm Hg]	101 (90–110)	100 (91–108)	99 (89–108)	105 (91–112)	104 (95–116)	0.366
Urine output [ml/kg/h]	X	4.55 (3.46–8.28)	5.38 (3.75–8.88)	1.99 (1.39–2.78)	2.91 (2.01–5.05)	0.161

eGFR – estimated glomerular filtration rate, NGAL – neutrophil gelatinase.

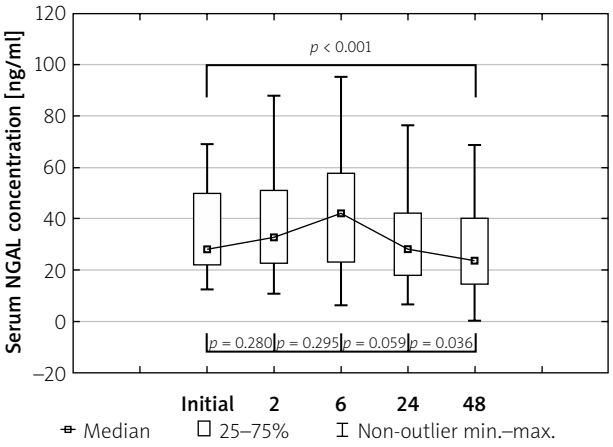

Figure 3. Changes in serum NGAL concentration in the observation period

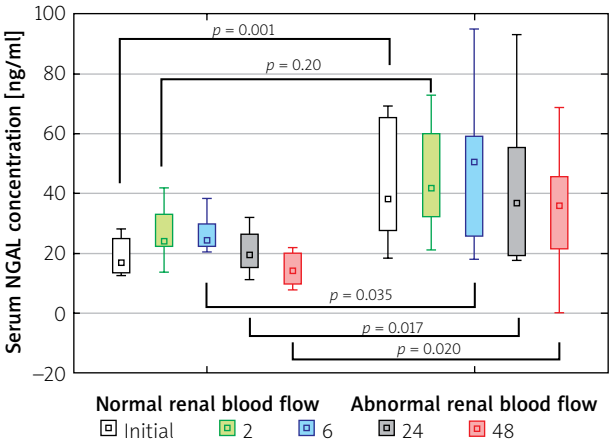

Figure 4. Serum NGAL concentration in children with normal and diminished renal blood flow

We performed a correlation analysis between eGFR (by serum creatinine and cystatin) and cardiac catheterisation and parameters. Serum NGAL (initial and after 24 and 48 h) was positively correlated (significantly) with patient age: $r = 0.4$, $r = 0.5$ and $r = 0.46$ respectively ($p = 0.001$). Similarly, a correlation exists between body weight and height ($p = 0.01$). Initial and 24-h serum NGAL correlated inversely with EF ($r = –0.304$; $r = –0.312$, $p = 0.039$; $p = 0.032$). No other significant correlation with blood pressure, cardiac function or dose of the contrast was detected. Serum creatinine was closely correlated with age of patients at every time-point of analysis with $r \geq 0.65$ ($p = 0.001$).

We detected a borderline inverse correlation of serum cystatin C (initial and after 48 h) and age of patients $r = –027$ ($p = 0.056$), and body height (initial and 48 h) $r = –0.37$; $–0.32$ ($p = 0.022$). Initial cystatin C correlated with mean arterial and systolic blood pressure ($r = –0.31$; $–0.29$, $p = 0.03$). No clinically significant correlations with heart function and dose of contrast or radiation were detected.

Discussion

Our study that eGFR calculated by Schwartz formula decreased after cardiac catherisation with contrast administation in children with congenital heart malformations. These results were mostly comparable to the pilot study performed earlier in a smaller group of patients [15]. Serum creatinine rose within the first 2 h after the procedure and decreased thereafter. This result might be considered as unexpected, because previous studies reported that serum creatinine is a late marker for contrast nephropathy and usually rises within 1–3 days after the procedures [16, 17]. The growth in serum creatinine may not change until 50% of kidney function loss and the levels are variable between age groups, muscle mass, hydration, medication and other modifiable and non-modifiable factors [18]. Although assessing kidney function by serum creatinine (SCr) is still a standard method, it is no longer considered as an early and reliable marker to detect and prevent contrast-induced kidney damage. Surprisingly, in our study serum creatinine rose very ear-

Table III. Comparison of serum NGAL and cystatin C in children with AKI by RIFLE and non-AKI patients

Patients	Parameter	Period					Significance (Friedman ANOVA)
		Initial	2	6	24	48	
Non AKI	Serum cystatin C [ng/ml]	675 (587.1–795)	647.7 (551.75–747.3)	684.6 (545.7–795.6)	677.75 (522.25–802.57)	636.6 (504.5–781.4)	0.956
AKI	Serum cystatin C [ng/ml]	604.3 (535.25–683.25)	635.55 (553.7–719.92)	575.7 (443.1–656.55)	598.05 (514.57–720.07)	613.8 (464.2–670.97)	0.845
	Significance by Mann-Whitney test	NS	NS	NS	NS	NS	
Non AKI	Serum NGAL [ng/ml]	28.3 (19.7–49.6)	40.2 (26.15–55.6)	41.7 (21.8–57.5)	28.7 (18.85–42.72)	22 (11.7–38.9)	< 0.001
AKI	Serum NGAL [ng/ml]	27.4 (23.95–40.15)	29.65 (22.52–46.45)	40.45 (22.8–56)	28.9 (17.9–39.45)	26 (15.05–38.3)	< 0.001
	Significance by Mann-Whitney test	NS	NS	NS	NS	NS	

ly and this observation was similar to the Osman *et al.* study, wherein serum creatinine was elevated > 25% at 4 h after contrast infusion [3]. This can occur because children with congenital heart disorders, especially cyanotic, can be more prone to toxic agents due to chronic hypoxia leading to viscosity and increases in renal vascular resistance and higher intraglomerular pressure [19].

Furthermore, rapid changes in eGFR are expected in patients with glomerular processes or pre-renal causes, when the balance between delivery of oxygen, nutrients and the nephron energy consumption is impaired [20]. Sudden change in renal perfusion due to diminished systematic blood volume or local circulation impairment can result in eGFR decrease. Multiple pre-renal AKI causes such as impaired cardiac function, anti-hypertensive medication (systemic vasodilatation) and increased vascular resistance during anaesthesia combined with intrinsic AKI causes such as nephrotoxic contrast media can lead to sudden renal tubular injury and elevation in serum creatinine [19].

Also, other authors reported that cellular injury occurred within the first 24 h after contrast administration with serum creatinine within the normal range [16, 18, 21]. In our material, serum creatinine fluctuated within the normal ranges for age but significantly increased. This observation looks concordant with Hirsch *et al.*, who also observed an early serum creatinine elevation in the first 24 h after catheterisation [18].

We ascertained the incidence of AKI as 32% of all the group. Most patients reached the Risk stage of RIFLE (13), three of them where in the Injury (I) stage and none of the patients fulfilled the definition of the Failure stage. After 48 h 8 patients still presented depletion in eGFR (by Schwartz formula) > 25% from the baseline values, but calculated levels of eGFR remained in the normal range. Oliguria was not observed in CIN-AKI patients. These data are similar to those presented by Osman *et al.*, who assessed the incidence of AKI as 34.7% and 6.5% of them where in the Injury stage of AKI according to RIFLE [3]. Despite adequate volume expansion and low contrast dose (4.1 mg/kg) they noted high incidence of AKI by creatinine criteria in children with congenital heart malformation. In our study, the median contrast dose was even lower (2.82 ml/kg) and hydration was proper prior to and 6 h after the procedure, but the incidence of CIN-AKI was comparable. Lower AKI incidence was noted by Benzer *et al.*, 19.8% in the 24-hour follow-up [16]. Contrast media dose was similar to our study, but the percentage of cyanotic patients was over two times lower than in our study (31% vs. 64%). The study observation time was shorter (24 h) without follow-up of CIN patients at 48 h after the procedure. Differences in CIN percentage may be caused by alternative choice of CIN diagnostic criteria according to p-RIFLE or other scales. Some authors qualified to the CIN group selected patients who meet at least Injury criteria. In the Hirsch *et al.* study the incidence of CIN-AKI was 12%, but the qualification criteria rose in serum creatinine > 50% from the baseline during the study [18]. Paediatric patients with congenital heart malformation can be more sensitive to contrast infusion even if low dose and low osmolality contrast is used, because of pre-existing viscosity [19, 20, 22].

The clinical significance of this observation is to be established. It raises the question of monitoring of serum creatinine in early diagnosis and prognosis of CIN-AKI. The growth in creatinine is noted when the renal tubular injury already began. Early phases of the injury can be reversible so it is important to assess kidney function by a conservative method. Also the lack of standardized criteria and methods for the diagnosis of CIN-AKI with novel biomarkers limits their use to clinical trials. On the other hand, searching for a novel, early, sensitive and specific marker for prognosing and diagnosing existing or beginning renal injury is crucial. It can lead to lowering the mortality, morbidity and hospital stay due to acute renal injury. The NGAL is postulated to be such a promising marker and some authors postulate that a double or more increase in level of NGAL from the baseline can qualify patients to the group of "subclinical acute kidney injury" even without any changes in serum creatinine or eGFR criteria [21, 23]. In adult studies it was shown that angiography was responsible for more than fifty percent of all CIN altogether [24].

One limitation of the study was the lack of longer observation after the procedure. However, the standard period for the CIN is 48 h and the observation of paediatric patients without complications after angiographic procedures is about 48 h, after which they are discharged. None of the patients needed medical support because of the AKI. At the end of the 48 h observation period the renal function was preserved in all of the children so there were no indications for prolonged hospital stay. Full recovery of decreased eGFR after 48 h raises a question whether elongated monitoring of eGFR is required if there is no significant rise in serum creatinine earlier.

The AKI staging introduced by Akcan-Arikan *et al.* was based on serum creatinine changes and urine output [5]. Our study showed that serum creatinine and eGFR were more sensitive than measurement of urine output. In clinical practice, we often observe an opposite situation, when urine production decreases first as a marker of glomerular hypoperfusion. In the case of CIN after cardiac catheterisation urine production is preserved by high fluid administration and maintained cardiac function, whereas the contrast toxicity concerns mostly mesangial and tubular cells; it does not affect glomeruli directly [24]. According to clinical practice and recent guidelines, CIN could be prevented by adequate hydration with normal saline, low dosage and low osmolarity of the dye [24]. Our centre procedure requires iv hydration before and after catheterisation and low-osmotic, non-ionic contrast

(iomeprol) usage in a dose of 1–2 ml/kg, considered as a low dose of contrast medium. It showed its efficacy.

The NGAL serum concentration is a recognised marker of AKI after cardiac surgery [10, 25]. It has been postulated that it could also be used in contrast nephropathy. The NGAL expression rises in response to hypoxia or toxic injury. Increased NGAL concentration can be detected in acute bacterial infections, chronic inflammatory conditions, cancers, chronic kidney diseases and chronic hypertension [21]. Presence of these conditions can influence measurements of plasma NGAL and urinary NGAL if the process occurs in the kidney or urinary tract. However, the rise in serum NGAL is much lower during the above-mentioned conditions than during AKI. Our study provided evidence that changes in NGAL serum concentration after cardiac catheterisation are more sensitive than serum creatinine and cystatin C in detection of AKI. They occurred earlier, but resolved at the same time as the other markers. This observation is similar to the data of Hirsch *et al.*, who performed a comparable study in children [18]. They found that serum NGAL rose shortly after the procedure and preceded the increase in creatinine. This was observed in children who developed AKI with a 50% eGFR decrease. They reported higher absolute NGAL increase than in our study but with the same tendency. This could be explained by different inclusion criteria – 50% vs. 25% increase of creatinine, and consequently deeper kidney injury. In the Bachorzewska-Gajewska *et al.* study, performed in a large adult patient group after percutaneous coronary interventions, the baseline serum NGAL was higher than in our study [9]. Absolute growth in serum NGAL during the study was comparable to growth in our study. They confirmed statistically significant changes in serum NGAL within 2, 4 and 8 h during the procedure with a subsequent drop in 24 h and return to the baseline in 48 h. Our study revealed a related trend in the serum NGAL concentration. A meta-analysis published by Zhou *et al.* clearly described NGAL as a promising and more predictive marker of AKI infants, children and adults with normal kidney function [11]. Benzer *et al.* reported similar results with a serum NGAL increase up to 6 h with subsequent decrease to 48 h after catheterisation with comparable values of serum NGAL [16].

We detected no significant changes in serum cystatin C and eGFR by the Filler formula in the whole examined group. In the group with AKI diagnosed by serum creatinine the level of cystatin C was significantly increased in the 24 h and then it dropped to a normal level compared to the group without CIN-AKI ($p < 0.05$). Cystatin C was previously suggested to substitute serum creatinine as a marker of kidney function, but it has not happened yet. The half-life of cystatin C is 3 times shorter than creatinine so a rise after acute kidney injury could be observed prior to or at the same time as changes in the creatinine but will decline in advance [16]. In our study we observed a significant rise in serum cystatin C in the CIN-AKI group at 2 h (Me 680.66 ng/ml, IQR: 553.7–724.8 ng/ml, $p < 0.05$) of the study compared to the baseline values (Me 571.2 ng/ml, IQR: 518.62–667.42 ng/ml) and then gradual reduction. A similar observation was made by Osman *et al.*, who detected normal serum cystatin C in all periods of the study, but in the CIN group the level of cystatin C was significantly higher compared to the baseline [3].

We decided to compare children younger and older than 3 years. We expected to find significant differences in incidence of AKI and degree of kidney injury and significantly lower levels of serum NGAL concentration. The results we obtained might have occurred because the younger group received a double dose of dye compared to older children and the median contrast dose exceeded 4 ml/kg, regarded as a safe dose for kidneys. Although younger children could be more prone to toxic kidney injury while basal serum NGAL concentration is lower compared to the older group, this observation needs further evaluation.

Conclusions

Diagnostic cardiac catheterisation with contrast media administration induced a significant but transient decrease in eGFR (Schwartz formula) and a significant rise of serum neutrophil gelatinase. The potential role of cystatin C as a biomarker of CIN-AKI was not proved.

The incidence of procedure-related acute kidney injury was relatively high, and significantly more frequent than after standard radiology examinations.

Preceding pharmacotherapy with ACEI or diuretics did not influence the degree of contrast injury. Amongst clinical factors, only diminished renal blood flow might have an unfavourable defect on the risk of contrast-induced nephropathy.

In this selected group of patients with complicated cardiac malformations, when administration of diuretics before and after the procedure is a clinical practice, serum markers of acute kidney injury should be preferred over the urine output measurement.

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Conflict of interest

The authors declare no conflict of interest.

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