Incidence and factors associated with acute kidney injury in neonatal non-cardiac surgery☆

Incidencia y factores asociados a daño renal agudo en cirugía no cardíaca neonatal

Dear Editor:

Acute kidney injury (AKI) is a frequent complication of major surgery in newborn infants, especially those with congenital heart defects, which are associate with an increased morbidity and mortality and incidence of chronic kidney disease (CKD).[1] There is little evidence on AKI in association with neonatal non-cardiac surgery (NNCS), for which the incidence has been estimated at 30%.[2] To analyse the incidence of AKI in the context of NNCS and potential factors associated with its development and its impact on patient outcomes, we carried out a retrospective and cross-sectional study including patients who underwent NNCS in our hospital between 2014 and 2019, excluding those with pre-existing kidney failure or who developed AKI more than 7 days post surgery. We defined AKI and classified it into 3 stages applying the neonatal modified Kidney Disease Improving Global Outcome (KDIGO) criteria.[3] We established two groups (AKI and no AKI) and compared them in terms of their demographic, clinical and laboratory characteristics and their outcomes. We performed a multivariate analysis adjusted for gestational age (GA) and birth weight (BW) as confounders to study factors associated with the development of AKI and to assess whether AKI could be a risk factor for mortality. We analysed the association of different variables with the duration of AKI with the Spearman corre-

Table 1 Descriptive analysis of the sample and comparison based on the development of acute kidney injury after surgery.

Variable	Total (N = 181)	No AKI (n = 160; 88.5%)	AKI (n = 21; 11.5%)	*P*[a]
Clinical and demographic characteristics				
GA (weeks)[b]	35^{+6} (27^{+2}-39)	36 (27^{+5}-39)	29^{+1} (25^{+6}-38)	.045
BW (g)[b]	2310 (1000–3150)	2382 (1027–3175)	1055 (800–2900)	.049
Sex (male)[c]	77 (42%)	70 (43%)	7 (33%)	.364
Antenatal disease	46 (25.5%)	44 (27.5%)	2 (10%)	.140
1-minute Apgar score[d]	7.4 ± 2.2	7.4 ± 2.2	6.8 ± 2.1	.122
Nephrotoxic medication[c]	150 (83%)	129 (80%)	21 (100%)	.027
Timing of surgery (days post birth) [b]	15 (3–33)	15.5 (4–36)	13 (3–16)	.252
Preoperative laboratory characteristics				
Urea (mg/dL)[b]	24 (14–42)	22 (14–40)	35 (20–51)	.081
Creatinine (mg/dL)[b]	0.48 (0.3–0.7)	0.4 (0.3–0.7)	0.6 (0.4–1)	.135
Electrolyte abnormalities[c]	44 (24.3%)	39 (24.3%)	5 (23.8%)	.878
Hyponatremia (Na < 135)[c]	29 (16%)	27 (17%)	2 (10%)	.908
Hyperkalaemia (K > 5.5)[c]	23 (13%)	21 (13%)	2 (10%)	.908
Characteristics of surgery				
Setting (in NICU)[c]	39 (21.5%)	31 (19.5%)	8 (38%)	.052
Type				
Neurosurgery[c]	55 (30%)	54 (33%)	1 (5%)	.017
Abdominal surgery[c]	108 (60%)	92 (57%)	16 (76%)	.017
Other[c]	18 (10%)	14 (8.5%)	4 (19%)	.017
Duration (minutes)[d]	119 ± 79	119 ± 82	115 ± 53	.429
HR[d]	138 ± 22	138 ± 22	137 ± 26	.420
$SatO_2$[d]	97 ± 2.5	97 ± 2.3	97 ± 1.1	.374
MAP[d]	49 ± 14	51 ± 13	38 ± 13	< .001
Complications[c,e]	16 (9%)	13 (8%)	3 (14%)	.035
Outcomes				
Death[c]	27 (15%)	19 (12%)	8 (38%)	.002

BW, birth weight; GA, gestational age; HR, heart rate; MAP, mean arterial pressure; NICU, neonatal intensive care unit; $SatO_2$, oxygen saturation.

[a] Qualitative variables compared by means of the χ^2 test and quantitative variables by means of the Mann-Whitney *U* test.

[b] Results expressed as median and interquartile range.

[c] Results expressed as absolute frequency and percentage.

[d] Results expressed as mean and standard deviation.

[e] Preoperative complications: hypotension, bradycardia, oxygen desaturation, cardiac arrest, tension pneumothorax, haemorrhage.

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Table 2 Characteristics of patients with acute kidney injury after surgery.

Variable		KDIGO AKI stage[a]		
	Total (n = 21)	1 (n = 8; 38%)	2 (n = 7; 33%)	3 (n = 6; 29%)
Clinical and laboratory characteristics				
Postoperative urea (mg/dL)[b]	95 (61–165)	70 (51–165)	143 (83–176)	95 (72–132)
Postoperative creatinine (mg/dL)[b]	1.2 (0.8–1.5)	0.9 (0.7–1.4)	1.2 (0.7–1.47)	1.4 (1.2–1.6)
Urine output (mL/kg/h)[b]	0.3 (0–1)	1 (0–1)	0 (0–0.05)	0 (0–0)
Time of AKI onset after surgery (hours)[b]	2 (0–12)	2 (0–12)	6 (0–24)	0 (0–8)
Time of poorest renal function (day)[b]	5 (3–7.5)	6.5 (4–8)	3 (2–5)	5 (3–10)
Treatment				
Fluid restriction (days)[b]	6.5 (2.5–11)	4 (1–7)	6 (2–9)	12 (11–37)
Furosemide[a]	20 (95%)	7 (88%)	7 (100%)	6 (100%)
Duration of furosemide (days)[b]	5 (3–8)	5.5 (4.5–8)	3 (2–6)	10 (5–15)
Theophylline[a]	4 (19%)	0 (0%)	1 (14%)	3 (50%)
Duration of theophylline (days)[b]	4.5 (3.5–6)	0 (0–0)	3.5 (3–4)	6 (5–7)
Antihypertensive medication[a]	1 (5%)	0 (0%)	1 (14%)	0 (0%)
RRT[a]	2 (10%)	0 (0%)	0 (0%)	2 (33%)
Duration of RRT (days)[b]	14.5 (5–24)	0 (0–0)	0 (0–0)	14.5 (5–24)
Outcomes				
Improvement (days)[b]	6.5 (3–11)	6.5 (5–10)	5 (3–8)	11 (10–13)
Duration (days)[b]	15 (9–26)	14.5 (7–16)	9 (9–14)	25.5 (20–33)
Recovery from AKI[c]	14 (66%)	5 (62%)	6 (85%)	3 (50%)
Associated postoperative complications[a]	7 (33%)	0 (0%)	3 (43%)	4 (80%)
Death[a]	8 (38%)	3 (37%)	2 (28%)	3 (50%)
Follow-up in nephrology department after discharge[a]	4 (24%)	0 (0%)	2 (28%)	2 (33%)

AKI, acute kidney injury; KDIGO, Kidney Disease: Improving Global Outcomes; RRT, renal replacement therapy.
[a] Results expressed as absolute frequency and percentage.
[b] Results expressed as median and interquartile range.
[c] Creatinine levels normalised in 13/13 survivors at hospital discharge and in 1/8 deceased patients before death.

lation coefficient and by means of multiple linear regression adjusted for GA and BW. The statistical analyses were performed with the software STATA version 16.0 (Stata Corp, College Station, Texas, USA), and we considered *P* values of less than 0.05 statistically significant.

A total of 21/181 patients (11.6%) developed AKI. Table 1 presents the characteristics of the overall sample and the results of the univariate analysis comparing both groups, and Table 2 presents the characteristics of patients with AKI based on the KDIGO stage. Abdominal surgery (OR, 12.36; 95% CI, 1.6–96.8; = .017) and a lower intraoperative mean arterial pressure (MAP) (OR, 0.91; 95% CI, 0.86–0.97; *P* = .007) were associated with an increased incidence of AKI in the analysis adjusted for GA and BW. All patients with AKI received nephrotoxic drugs and 20/21 (95%) had received furosemide in continuous intravenous infusion at a mean dose of 2 mg/kg/h.[1,2] In addition, AKI was associated with an increase in mortality (OR, 4; 95% CI, 1.2–12; *P* = .017) adjusted for GA and BW. The main causes of death were refractory shock and multiple organ failure. In 14/21 of patients (66.6%), including all survivors at discharge and 1 deceased patient, there was evidence of recovery from AKI with normalization of creatinine levels. Increased duration of AKI was associated with longer duration of treatment with furosemide ($\rho = 0.50$; *P* = .036) and a lower intraoperative MAP ($\rho = 0.55$; *P* = .030), although this association did not persist in the multivariate analysis. Of the 13 survivors with AKI, only 4 (30%) were referred to the outpatient paediatric nephrology department for post-discharge follow-up: two who had stage 2 AKI, and two who had stage 3 AKI.

The development of AKI is a complication to be considered in NNCS due to its frequency and associated morbidity and mortality, as reflected by the results for the primary outcome in our study, a significantly increased mortality in neonates with AKI (38%) compared to those without AKI (12%). Mortality in infants with AKI was lower in the study conducted by Wu et al. (18%),[2] which could be due to the exclusion of patients with characteristics that could be associated with greater severity. The factors associated with the development of AKI in the context of NNCS in our hospital, such as smaller GA, smaller BW, the use of nephrotoxic medication, abdominal surgery, a lower MAP during surgery and intraoperative complications, were consistent with the findings of previous studies and make sense from a pathophysiological standpoint.[4,5] Therefore, patients with these risk factors would benefit from closer monitoring of renal function for early detection and treatment of AKI. Although the design of our study did not allow us to assess causality, the univariate association between longer duration of AKI and longer duration of treatment with furosemide found in our study, given the known nephrotoxicity of this drug, suggests the need to optimise the duration of treatment with furosemide in this clinical scenario. It is also worth noting that even if the creatinine level reverts to baseline, a follow-up by a paediatric nephrologist is recommended at 3 months to evaluate recovery from AKI and assess for hypertension

and proteinuria in order to establish the risk of progression to CKD.[6]

The main limitations of the study were those intrinsic to its retrospective design and it having been conducted in a single centre, in addition to the lack of consensus regarding the monitoring of postoperative creatinine levels, on account of which some patients may not have been included in the sample if they maintained an adequate urine output. Due to the above, we think that prospective longitudinal studies in larger samples and with a standardised renal function protocol during the hospital stay and nephrological follow-up after discharge are required to determine the prognosis of these patients more accurately.

Ethical considerations

The study adhered to the World Medical Association International Code of Ethics (Declaration of Helsinki).

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Conflicts of interest

The authors have no conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.anpede.2023.05.011.

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Atrial standstill, debut of a muscular dystrophy

Aurícula silente, inicio de una distrofia muscular

Dear Editor:

Emery-Dreifuss muscular dystrophy (EDMD) is a rare disease with an incidence of 1 per 400 000 live births associated with sudden death in the first decades of life. It is characterised by the triad of joint contractures (chiefly elbows, neck and Achilles tendon), muscular dystrophy (progressive wasting of scapulohumeral and peroneal muscles) and heart disease (atrial arrhythmias, conduction disorders and cardiomyopathy).[1]

Cardiac involvement usually manifests in the second or third decade of life in the form of atrial arrhythmias (flutter, fibrillation, atrial standstill) and atrioventricular block, and determines the prognosis.[1,2]

We present the case of a boy aged 13 years who was previously asymptomatic and presented with sharp, stabbing, nonradiating, intense and intermittent right-sided chest pain at rest, not triggered by physical activity, with no other symptoms. His maternal grandmother, who carried a pacemaker, had undergone tricuspid and mitral valvuloplasty. In addition, a maternal uncle who suffered from a muscular disorder that had not been identified precisely had died suddenly at age 35 years in his sleep.

The patient had normal breathing and bradycardia, with detection of a grade II/VI murmur best heard at the level of the tricuspid valve. The salient findings of the neurologic examination were mild contracture of the Achilles tendon

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