ORIGINAL ARTICLE

https://doi.org/10.1590/1806-9282.20220837

A retrospective analysis: the outcome of renal replacement therapies in critically ill children

Kübra Çeleğen[1]*, Mehmet Çeleğen[2]

SUMMARY

OBJECTIVE: A few pediatric studies were present which focused on renal replacement therapy used for critically ill children. This research aimed to determine the ratio of utilization of intermittent hemodialysis, continuous renal replacement therapy, and peritoneal dialysis, and to study the properties and outcomes of critically ill pediatric patients who underwent renal replacement therapy.

METHODS: Critically ill children admitted to the intensive care unit and received renal replacement therapy from February 2020 to May 2022 were included. The children were divided into three groups: hemodialysis, continuous renal replacement therapy, and peritoneal dialysis.

RESULTS: A total of 37 patients (22 boys and 15 girls) who received renal replacement therapy met the criteria for this study. Continuous renal replacement therapy was used in 43%, hemodialysis in 38%, and peritoneal dialysis in 19%. In all, 28 (73%) children survived and 9 (27%) died in intensive care unit. The mean systolic blood pressure was significantly lower among children who received continuous renal replacement therapy ($p<0.001$). The need for inotropic medications and a higher PRISM III score were found to be the greatest indicators of mortality.

CONCLUSION: The outcome of children receiving renal replacement therapy seems to be related to their needs for vasoactive drugs and the severity of the underlying disease in the continuous renal replacement therapy group relative to the other groups.

KEYWORDS: Acute kidney injury. Continuous renal replacement therapy. Renal dialysis. Peritoneal dialysis. Pediatrics.

INTRODUCTION

Despite technological progressions in intensive care units (ICU) and the presence of different renal replacement modalities in recent years, acute kidney injury (AKI) is associated with high mortality and morbidity in critically ill patients[1]. The prevalence of AKI in pediatric and adult patients in ICU has been regarded at 5% to over 80% depending on the definition, although only around 5% of patients need renal replacement therapy (RRT)[2]. Although increased consciousness and the agreement on consensus descriptions for the AKI diagnosis have increased physicians' focus on milder renal dysfunction and allowed them to make decisions earlier, sometimes it is uncertain which patients are convenient for RRT, which procedures might be more beneficial, what pulls the trigger for beginning, how many ''doses" should be prescribed, and how long therapy should sustain. There is a common agreement that RRT should be started in cases of AKI, which is complicated by serious metabolic disturbances such as uremia, acidosis, and hyperkalemia[3]. Even though there is no definite indication of RRT in ICU, it is usually preferred for fluid overload and sepsis[4]. Typically, different RRTs are used: intermittent hemodialysis (HD), continuous RRT (CRRT), or peritoneal dialysis (PD)[5]. Although PD and HD are still important treatment options in AKI management, advanced CRRT machines capable of balanced fluid volume control have led to an increased preference for CRRT in pediatric ICU patients[1,2]. In particular, the choice of RRT is frequently arranged by several variables, such as the decision of the doctor, the familiarity with the technique, and the hemodynamic status of the patient.

The main purpose of this research was to define the relative ratio of utilization of HD, CRRT, and PD among critically ill pediatric patients admitted to ICU and to represent patient survival parameters based on the RRT technique as well as their sickness course.

METHODS

This retrospective study was enforced to determine the distribution of different RRT in pediatric patients with AKI who were admitted to the ICU from February 2020 to May 2022. Children aged 1 month to 18 years with the diagnosis of acute renal failure (ARF), volume overload, electrolyte abnormality,

[1]Afyonkarahisar Health Sciences University, Faculty of Medicine, Department of Pediatrics, Division of Pediatric Nephrology – Afyonkarahisar, Turkey.
[2]Afyonkarahisar Health Sciences University, Faculty of Medicine, Department of Pediatrics, Division of Pediatric Intensive Care Unit – Afyonkarahisar, Turkey.
*Corresponding author: kubractf@hotmail.com

Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.
Received on January 11, 2023. Accepted on January 13, 2023.

metabolic diseases of inborn, and intoxication that needed any type of RRT during their ICU stay were included. Exclusion criteria contained all stages of chronic renal disease, acute chronic kidney disease, fluid-responsive prerenal situation, and urinary tract obstruction caused by ARF.

A disposable, pediatric-size, semi-rigid PD catheter was placed into the peritoneal cavity to perform PD. Initially, 5–10 mL/kg of commercially available PD fluid were used to control the filling and drainage of fluid. Afterward, 15–20 mL/kg fluid volume with glucose concentration was preferred, and the fill volume was increased to 20–30 mL/kg in the case of insufficient ultrafiltration. Hemodiafiltration or continuous RRT was achieved using a Gambro Prisma membrane (AN-69). The blood flow rate was adjusted according to the patients' weight. Replacement or dialysate fluid was prescribed between 2,000 and 8,000 mL/h/1.73 m^2 [6,7]. Systemic heparin was used for anticoagulation, and the target pre-RRT activated clotting time (ACT) was between 170 and 220 s[8].

Intermittent HD was accomplished with Fresenius Medical Care 2008® series HD machines. Fresenius Polysulfone® dialyzer was selected. The dialysate bath was adjusted for sodium and potassium. The blood flow rate was set at 4–5 mL/kg/min. The length and frequency of each dialysis period were decided based on the requirements of the patients. Heparin was used to extend the usage of hemofiltration filter. If there is no coagulopathy, 20 units/kg of intravenous heparin are administered. After the loading dose, 10 units/kg/h of heparin infusion is started, and the heparin dose is adjusted to keep the target ACT level between 180 and 220 s.

The children were divided into three groups: HD, CRRT, and PD. The selection of modality was primarily associated with the choice of the physician and the patient's hemodynamic status. Initially, the ratio of the usage of CRRT, HD, and PD groups among seriously ill patients was described. Second, the results contain a comparison of demographic parameters and patient outcomes (mortality ratio, length of ICU stay, duration of RRT treatment, inotropic drug requirements [dopamine, dobutamine, epinephrine, norepinephrine, vasopressin, and milrinone], ventilator days, and complications) between different RRT groups.

Statistical analysis

The variables were investigated using the histogram, Q-Q plots, and analytic methods for normal distribution. Normally distributed data were reported as mean±standard deviation and non-normal distribution as median. Statistical testing of the three RRT groups was undertaken using the chi-square test for categorical variables or one-way analysis of variance with Tukey post-hoc pairwise tests for continuous variables to identify differences between pairs of data. Levene's test was used to assess the homogeneity of variances. Kruskal-Wallis test was performed to analyze the nonparametric data. Mann-Whitney U test was performed to analyze the significance of pairwise differences. Bonferroni correction was used to adjust for multiple comparisons. An overall p-value of less than 0.05 was considered statistically significant. The multivariate logistic regression analysis was performed to identify the most significant parameters.

RESULTS

A total of 37 patients who received RRT were included. A comparison of demographic and clinical parameters in children is shown in Table 1. CRRT was used in 43%, HD in 38%, and PD in 19%. In all, 28 (73%) patients survived and 9 (27%) died. At the time of starting RRT, although the median age of patients who received PD was 5 months (3–9 months), patients who underwent HD was 132 months (3–170 months), and this difference was significant (p=0.049). RRT was used more frequently in males (p=0.76). The median weight was 13.6 kg (3–65 kg). The weight of children who received PD was lower than that of patients who received CRRT or HD (p=0.07). The systolic blood pressure was significantly lower among CRRT patients (69.6±6.1 mmHg) (p<0.001). The admission diagnoses included sepsis (n=15), acute tubular necrosis (n=12), hemolytic uremic syndrome (n=4), metabolic disease (n=3), intoxication (n=2), and bone marrow transplant (n=1). There was no significant difference between the groups in terms of comorbidity (p=0.32). The median length of ICU stay was 18 days (2–62 days). The duration of ICU stay was insignificantly longer in children undergoing PD than in children who received other RRT modalities (p=0.3). The duration of RRT for the sum of 37 cases was 5.8±3.1 days on HD, 3.4±1.8 days on CRRT, and 6.7±5.9 days on PD. There was no difference between the duration of RRT modalities (p=0.52). Overall, 26 patients needed mechanical ventilation. Conventional mechanical ventilation was the most commonly used ventilation modality. The PRISM III score was significantly greater in patients undergoing CRRT 18 (12–21) compared with HD 6 (2–22) and PD 9.5 (6–12) (p=0.02). Depending on the clinical requirements, 85.7% of patients undergoing CRRT, 22.2% of patients requiring HD, and 50% of patients undergoing PD needed vasoactive inotropic drugs (CRRT versus HD or PD, p=0.01).

The total mortality ratio was 24.3% (n=9) (Table 2). The survival ratio was higher in males (p=0.95). The survival rate of children who needed inotropic drugs was significantly lower than that of patients who needed no inotropic drugs (p=0.03).

At admission, nonsurvivors had significantly lower systolic pressure (p<0.001). The systolic blood pressure was described by the percentiles[9]. The PRISM III scores were significantly higher in nonsurvivors (p<0.001). Nonsurvivors required mechanical ventilator support more commonly than survivors (p=0.52).

Multivariate regression analysis was performed to detect independent risk factors. The requirement for inotropic drugs and a higher PRISM III score were found to be the greatest indicators of mortality (odds ratio [OR] 1.8; 95% confidence interval [CI] 1.05–2.1; p=0.04, OR 2.3; 95%CI 1.25–3.2; p=0.03, respectively) (Table 3).

DISCUSSION

RRT is preferred for critically ill pediatric patients for improving clinical outcome[10]. The major outcomes of this study are as follows: First, when we compared our results, we found that CRRT is the most frequently used RRT type, and mortality was higher in children undergoing CRRT. Second, mortality was higher in children who used vasoactive inotropic drugs. Finally, a higher PRISM III score was associated with mortality.

Although different studies have been performed to find the survival advantage of CRRT over HD, the superiority of one modality over the other has not been demonstrated[11,12].

Table 1. Comparison of demographic and clinical parameters of children who received renal replacement therapy.

Variables	HD (n=14)	CRRT (n=16)	PD (n=7)	p-value
Age at admission (month)	132 (3–170)	13 (3–172)	5 (3–9)#	0.049
Sex (female n/%, male n/%)	6 (42.8%), 8 (57.2%)	6 (37.5%), 10 (62.5%)	3 (42.8%), 4 (57.2%)	0.76
Weight at admission (kg)	20 (3–65)	10 (4–63)	5.5 (3–7)	0.07
Systolic blood pressure at admission (mmHg)	109.2±8.3#	69.6±6.1	82.7±8.7	<0.001
Hearth rate	133.6±28.6	137.7±22.8	144.2±21.5	0.09
Primary diagnosis				
Sepsis	1 (7.1%)	11 (68.8%)	3 (42.8%)	0.06
ATN	7 (50%)	4 (25%)	1 (14.2%)	
HUS	3 (21.4%)	–	1 (14.2%)	
Metabolic disease	1 (7.1%)	–	2 (28.4%)	
Intoxication	2 (14.2%)	–	–	
Bone marrow transplantation	–	1 (6.2%)	–	
Comorbidity				
Respiratory disorders	–	2	–	0.32
Neurological disorders	1	1	–	
Renal disorders	1	–	–	
Metabolic disorders	1	–	2	
Hematological-oncological disorders	–	1	–	
Duration of ICU (day)	16 (2–45)	12 (2–48)	33 (12–62)	0.3
Duration of RRT (day)	5.8±3.1	3.4±1.8	6.7±5.9	0.52
Mechanical ventilation support				
CMV	5 (35.7%)	10 (62.5%)	3 (42.8%)	0.27
HFOV	–	5 (31.3%)	1 (14.2%)	
NIV	1 (7.1%)	1 (6.2%)	–	
PRISM III score	6 (2–22)	18 (12–21)#	9.5 (6–12)	0.02
Vasoactive inotropic drug	2 (22.2%)	6 (85.7%)#	2 (50%)	0.01
Outcome				
Survived	13 (92.8%)	9 (56.25%)	6 (85.7%)	0.02
Died	1 (7.2%)	7 (43.75%)#	1 (14.3%)	

The parameter of the group with (#) sign is significantly higher than those in the other groups.

The survival ratio of pediatric patients requiring RRT is mostly not accurately associated with the RRT modality, but rather with the severity of the underlying disease of patients[7]. Similar findings are shown in adult studies, which define underlying conditions requiring RRT and symptoms of multi-organ failure as the most important predictors of survival[13]. A randomized prospective trial showed an increased survival ratio in HD, but the CRRT group had a higher severity of disease despite the randomization[14]. In a meta-analysis trial comparing HD and CRRT, no superiority of either dialysis treatment over the other could be demonstrated[15]. Different studies were performed to determine the efficacy and outcome of PD in comparison to HD. The outcomes of Noshad et al. suggested that patients' quality of life and survival ratio were higher on PD than on HD[16]. Liberek et al. showed that the survival rate was similar when comparing the PD and HD[17]. In this present study, the increased mortality in patients undergoing continuous RRT can be explained by the fact that the intensity of the disease is more severe, and patients are hemodynamically unstable and need more inotropic support.

It has been shown that critically ill patients undergoing HD need much less vasopressor use than other modalities, and the survival ratio was lower in patients who required vasopressor than in patients who required no vasopressor[7]. Smoyer et al. showed that patients with multi-organ failure requiring vasopressors have an increased risk of mortality[18]. This current study found that the requirement for vasopressor drugs was higher in patients receiving CRRT, and the survival rate was lower in children who needed vasopressor drugs. The rationale for why vasopressor drugs are more commonly used in the CRRT mode is that CRRT is preferred in patients with hemodynamic instability.

In infants, vascular access for CRRT or HD is quite complex, and also infants are more sensitive to hemodynamic fluctuations associated with CRRT and HD[19]. For these causes, PD is the first choice of RRT modality among infants[1]. AKI is common after

Table 3. Multivariate logistic regression analysis of survivors versus nonsurvivors.

Variables	Odds ratio	95%CI	p-value
The requirement for inotropic drugs	1.8	1.05–2.1	0.04
PRISM III score	2.3	1.25–3.2	0.03
Systolic blood pressure at admission	0.98	1.12–1.5	0.09

Table 2. Comparison of demographic and clinical parameters between survivors and nonsurvivors.

Variables	Survivors (n=28)	Nonsurvivors (n=9)	p-value
Age at admission (month)*	63 (3–172)	6 (5–84)	0.42
Sex (female n/%, male n/%)	10 (35.7%), 18 (64.3%)	3 (33.3%), 6 (66.7%)	0.95
Weight at admission (kg)*	15 (3–65)	6 (5–24)	0.56
Systolic blood pressure at admission (mmHg)	94.5±18.1	65.0±6.2	<0.001
Primary diagnosis			
Sepsis	9 (32.1%)	6 (66.7%)	0.14
ATN	11 (39.3%)	1 (11.1%)	
HUS	4 (14.2%)	–	
Metabolic disease	2 (7.1%)	1 (11.1%)	
Intoxication	2 (7.1%)	0	
Bone marrow transplantation	–	1 (11.1%)	
Duration of ICU (day)*	15 (2–62)	5 (2–18)	0.2
MV requirement	17 (60.7%)	9 (100%)	0.52
Mechanical ventilation support			
CMV	12 (42.9%)	6 (66.6%)	0.35
HFOV	3 (10.7%)	3 (33.3%)	
NIV	2 (7.1%)	0	
PRISM III score	10.3±6.6	18.3±0.57	<0.001
Duration of RRT (day)	5.6±3.6	2.6±1.1	0.18
Vasoactive inotropic drug	7 (41.2%)	3 (100%)	0.03

*Indicates median (min–max).

complex congenital heart surgery, and PD is a frequently preferred method of RRT in these patients[20,21]. Although CRRT was more frequently chosen as RRT among whole patients, PD was the most commonly preferred RRT model for those with low body weight children and infants in this study. Hemodynamic instability is one of the main reasons for the preference for CRRT in a considerable number of ICU patients with ARF[22]. Augustine et al. showed that mean arterial pressure and vasopressor support were similar between intermittent and continuous dialysis methods in patients with ARF just before starting the dialysis modality[23]. A study showed that the incidence of circulatory failure and inotropic support did not differ between the continuous venovenous hemodiafiltration and intermittent hemodialysis groups[24]. In this current study, the initial systolic blood pressure was significantly lower in the CRRT group.

Bunchman et al. found that the duration of RRTs was similar among critically ill children[7]. A research presented that the duration of RRT was similar between CRRT and HD patients[24]. In the current study, there was no difference between the duration of the RRT modalities.

Beltramo et al. showed that children who received CRRT stayed in the hospital 7 days longer than those who received HD[1]. In a study conducted by D. E. Uehlinger et al., although the length of hospital stay was longer in the HD group, there was no statistically significant difference between CRRT and HD groups[1,24]. This study showed that the ICU stay was insignificantly longer in the PD group.

A study interested in RRT modalities in critically ill children claimed that requiring mechanical ventilation was associated with higher mortality on multivariate logistic regression analysis[1]. In a study comparing the effects of continuous and intermittent RRTs on acid-base balance, no difference was found in terms of mechanical ventilation need[25].

In this current research, mechanical ventilation support was insignificantly more common in the CRRT group.

This research had some limitations. First, this is a retrospective study performed by using records gathered from the hospital's electronic data system. Second, the timing of renal-replacement therapy initiation was not standardized. Finally, the amount of inotropic drug support was not evaluated, while the inotropic drug requirement was found to be an independent risk factor in regression analysis.

CONCLUSION

The outcome of patients receiving RRT seems to be associated with their requirements for vasoactive drugs and the severity of the underlying disease. CRRT is the most prevalent therapy for RRT in critically ill pediatric patients in ICU. The utilization of CRRT mode is related to raising mortality. Additionally, prospective studies are needed to determine the ideal RRTs in critically ill children.

ETHICAL ASPECTS

This research was approved by University Medical Faculty Ethical Committee (date: April 01, 2022, decision no: 2022/4).

AUTHORS' CONTRIBUTIONS

KÇ: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Validation, Writing – original draft. **MÇ:** Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

REFERENCES

1. Beltramo F, DiCarlo J, Gruber JB, Taylor T, Totapally BR. Renal replacement therapy modalities in critically ill children. Pediatr Crit Care Med. 2019;20(1):e1-9. https://doi.org/10.1097/PCC.0000000000001754
2. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. Nephron Clin Pract. 2012;120(4):c179-84. https://doi.org/10.1159/000339789
3. Bagshaw SM, Darmon M, Ostermann M, Finkelstein FO, Wald R, Tolwani AJ, et al. Current state of the art for renal replacement therapy in critically ill patients with acute kidney injury. Intensive Care Med. 2017;43(6):841-54. https://doi.org/10.1007/s00134-017-4762-8
4. Barbar SD, Clere-Jehl R, Bourredjem A, Hernu R, Montini F, Bruyère R, et al. Timing of renal-replacement therapy in patients with acute kidney injury and sepsis. N Engl J Med. 2018;379(15):1431-42. https://doi.org/10.1056/NEJMoa1803213
5. Bagshaw SM, Berthiaume LR, Delaney A, Bellomo R. Continuous versus intermittent renal replacement therapy for critically ill patients with acute kidney injury: a meta-analysis. Crit Care Med. 2008;36(2):610-7. https://doi.org/10.1097/01.CCM.0B013E3181611F552
6. Lai YC, Huang HP, Tsai IJ, Tsau YK. High-volume continuous venovenous hemofiltration as an effective therapy for acute management of inborn errors of metabolism in young children. Blood Purif. 2007;25(4):303-8. https://doi.org/10.1159/000106102

7. Bunchman TE, McBryde KD, Mottes TE, Gardner JJ, Maxvold NJ, Brophy PD. Pediatric acute renal failure: outcome by modality and disease. Pediatr Nephrol. 2001;16(12):1067-71. https://doi.org/10.1007/s004670100029
8. Maxvold NJ, Bunchman TE. Renal failure and renal replacement therapy. Crit Care Clin. 2003;19(3):563-75. https://doi.org/10.1016/s0749-0704(03)00010-1
9. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, et al. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. Pediatrics. 2017;140(3):e20171904. https://doi.org/10.1542/peds.2017-1904
10. Basu RK, Wheeler DS, Goldstein S, Doughty L. Acute renal replacement therapy in pediatrics. Int J Nephrol. 2011;2011:785392. https://doi.org/10.4061/2011/785392
11. Jakob SM, Frey FJ, Uehlinger DE. Does continuous renal replacement therapy favourably influence the outcome of the patients? Nephrol Dial Transplant. 1996;11(7):1250-5. PMID: 8672018
12. Swartz RD, Messana JM, Orzol S, Port FK. Comparing continuous hemofiltration with hemodialysis in patients with severe acute renal failure. Am J Kidney Dis. 1999;34(3):424-32. https://doi.org/10.1016/s0272-6386(99)70068-5
13. Fiaccadori E, Lombardi M, Leonardi S, Rotelli CF, Tortorella G, Borghetti A. Prevalence and clinical outcome associated with preexisting malnutrition in acute renal failure: a prospective cohort study. J Am Soc Nephrol. 1999;10(3):581-93. https://doi.org/10.1681/ASN.V103581
14. Mehta RL, McDonald B, Gabbai FB, Pahl M, Pascual MT, Farkas A, et al. A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure. Kidney Int. 2001;60(3):1154-63. https://doi.org/10.1046/j.1523-1755.2001.0600031154.x
15. Tonelli M, Manns B, Feller-Kopman D. Acute renal failure in the intensive care unit: a systematic review of the impact of dialytic modality on mortality and renal recovery. Am J Kidney Dis. 2002;40(5):875-85. https://doi.org/10.1053/ajkd.2002.36318
16. Noshad H, Sadreddini S, Nezami N, Salekzamani Y, Ardalan MR. Comparison of outcome and quality of life: haemodialysis versus peritoneal dialysis patients. Singapore Med J. 2009;50(2):185-92. PMID: 19296035
17. Liberek T, Renke M, Skonieczny B, Kotewicz K, Kowalewska J, Chmielewski M, et al. Therapy outcome in peritoneal dialysis patients transferred from haemodialysis. Nephrol Dial Transplant. 2009;24(9):2889-94. https://doi.org/10.1093/ndt/gfp132
18. Smoyer WE, McAdams C, Kaplan BS, Sherbotie JR. Determinants of survival in pediatric continuous hemofiltration. J Am Soc Nephrol. 1995;6(5):1401-9. https://doi.org/10.1681/ASN.V651401
19. Tomar A, Kumar V, Saha A. Peritoneal dialysis in children with sepsis-associated AKI (SA-AKI): an experience in a low- to middle-income country. Paediatr Int Child Health. 2021;41(2):137-44. https://doi.org/10.1080/20469047.2021.1874201
20. Zhang L, Jin Y, Zhang F, Li H, Wu Q. Modified peritoneal dialysis for treatment of acute renal failure after complex congenital heart surgery in infants. Heart Surg Forum. 2018;21(4):E286-9. https://doi.org/10.1532/hsf.1915
21. Baskin E, Gulleroglu KS, Saygili A, Aslamaci S, Varan B, Tokel K. Peritoneal dialysis requirements following open-heart surgery in children with congenital heart disease. Ren Fail. 2010;32(7):784-7. https://doi.org/10.3109/0886022X.2010.493980
22. Jones CH, Richardson D, Goutcher E, Newstead CG, Will EJ, Cohen AT, et al. Continuous venovenous high-flux dialysis in multiorgan failure: a 5-year single-center experience. Am J Kidney Dis. 1998;31(2):227-33. https://doi.org/10.1053/ajkd.1998.v31.pm9469492
23. Augustine JJ, Sandy D, Seifert TH, Paganini EP. A randomized controlled trial comparing intermittent with continuous dialysis in patients with ARF. Am J Kidney Dis. 2004;44(6):1000-7. https://doi.org/10.1053/j.ajkd.2004.08.022
24. Uehlinger DE, Jakob SM, Ferrari P, Eichelberger M, Huynh-Do U, Marti HP, et al. Comparison of continuous and intermittent renal replacement therapy for acute renal failure. Nephrol Dial Transplant. 2005;20(8):1630-7. https://doi.org/10.1093/ndt/gfh880
25. Uchino S, Bellomo R, Ronco C. Intermittent versus continuous renal replacement therapy in the ICU: impact on electrolyte and acid-base balance. Intensive Care Med. 2001;27(6):1037-43. https://doi.org/10.1007/s001340100953