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ORIGINAL RESEARCH

Correlation Between the Inferior Vena Cava/ Aorta (Ivc/Ao) Ratio and Serum Lactate Levels in Children With Renal Disorder

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Background: Acute kidney injury (AKI) is common in critically ill children in the PICU, with incidence rates from 2.5% to 58%, impacting mortality and hospital duration. Early AKI detection is vital, but conventional hemodynamic monitoring often lacks specificity. This study investigates the relationship between the inferior vena cava/aortic (IVC/Ao) ratio and serum lactate levels as non-invasive indicators of renal hemodynamics and tissue perfusion in children. Understanding these parameters could improve early diagnosis, aid clinical decisions, and enhance outcomes for pediatric AKI patients, offering an accessible monitoring method for clinicians.

Methods: This cross-sectional study involved 48 pediatric patients aged 5–18 years showing Pediatric Early Warning Score (PEWS) ≥3 and diagnosed with renal disorders. Patients were admitted to the emergency department, high care unit, PICU, and pediatric ward at Dr. Hasan Sadikin Hospital, Bandung, between May and August 2023. AKI was diagnosed using pRIFLE or KDIGO criteria. The IVC/Ao ratio was assessed via transabdominal USG, and serum lactate levels were measured. Spearman correlation analysis was conducted to assess their relationship.

Results: The median (IQR) IVC/Ao ratio was 0.91 (0.70–1.10), and serum lactate levels were 1.5 (1.1–2.4) mmol/L. Spearman correlation analysis revealed a negative correlation between the IVC/Ao ratio and serum lactate (rho = −0.65, $p < 0.001$).

Conclusion: A decrease in the IVC/Ao ratio correlates with an increase in serum lactate levels in children with AKI.

Keywords: acute kidney injury, children, IVC/Ao, serum lactate

Introduction

Children who are critically ill and admitted to the pediatric intensive care unit (PICU) face a risk of developing acute kidney injury (AKI), with the incidence rate varying between 2.5% and 58%. AKI is characterized by decreasing kidney function, leading to impaired elimination of waste products, electrolyte imbalances, and disrupted fluid homeostasis.[1,2] This condition is associated with adverse outcomes, including increased use of assisted ventilation, prolonged hospital stays, and elevated mortality rates.[3,4] Recognizing the importance of early diagnosis and preventive assessment becomes necessary in addressing all the potential challenges.

Hemodynamic monitoring, consisting of blood pressure, heart rate, respiratory rate, temperature, and oxygenation status, aids in identifying patients at an elevated risk of AKI. However, all the parameters lack specificity in stratifying the risk for kidney injury. Modern ultrasound examinations offer insights into renal hemodynamics, particularly regarding vascular changes in AKI and fluid tolerance. This guidance aids in selecting prompt and appropriate management.[5] To achieve such guidance, there are two ultrasound methods for assessing hemodynamics and predicting fluid therapy

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response. The methods include the dynamic method used in measuring stroke volume, cardiac output (CO), and the inferior vena cava/aortic (IVC/Ao) ratio) and the static aspect, which measures central venous pressure (CVP). The dynamic method outperforms the static aspect, specifically in predicting fluid therapy response in the context of hemodynamic disturbances.[6] Within the dynamic aspect, the IVC/Ao ratio is regarded as a readily available and accessible non-invasive method. During expiration, the maximum diameter of the IVC is measured, and during systole, the diameter of Ao is measured.[7] The Ao diameter, remaining relatively constant with circulating fluid changes, serves to assess volume status.[8]

Elevated blood lactate levels (hyperlactatemia) function to be a marker of tissue hypoperfusion, as seen in shock patients. Clinical signs of tissue hypoperfusion may not always be present, making lactate levels valuable in such conditions. Additionally, blood lactate levels serve as a prognostic predictor.[9] A previous study on adults showed that the initial lactate value had the highest accuracy in predicting mortality in non-traumatic critical illness patients compared to the IVC and cardiac output. In the context of kidney disorders, the IVC/Ao ratio provides insights into hemodynamic status, aiding in assessing intravascular volume in patients at risk of acute kidney injury (AKI). Elevated blood lactate levels are often indicative of tissue hypoperfusion, including in the kidneys, potentially exacerbating renal dysfunction through ischemia or oxidative stress. Studies highlight that combining the IVC/Ao ratio with serum lactate levels could serve as a predictive tool for assessing AKI risk and enabling earlier, more effective interventions in pediatric patients with kidney disorders. The relationship between the IVC/Ao ratio and serum lactate levels in critically ill pediatric patients is currently limited.[10]

This study aims to investigate the correlation between the IVC/Ao ratio and serum lactate levels in children with renal disorders, providing insights into their potential role in early AKI diagnosis and risk stratification beyond general PICU settings. By focusing on the interplay between these parameters, the study seeks to enhance our understanding of hemodynamic changes and improve patient outcomes in pediatric renal care.

Material and Methods

Study Design and Participants

This cross-sectional study included 50 pediatric patients with renal disorder admitted to Dr. Hasan Sadikin Hospital, Bandung, in various units, particularly emergency department (ED), high care unit (HCU), PICU, and pediatric ward. Patients without lactate serum levels (n = 2) were excluded, resulting in a total of 48 patients for the analysis. The research took place in May–August 2023. Approval for the study protocol was obtained from the Health Research Ethics Committee of Dr. Hasan Sadikin Hospital and the Research Ethics Committee of Universitas Padjadjaran, and all participants provided written informed consent.

BMI-for-age was evaluated using the WHO growth standards to determine the nutritional status of children. The BMI-for-age z-score compares a child's BMI to the median BMI of reference data for their age and sex, categorizing as underweight (<-2 SD), normal weight (−2 to +1 SD), overweight (+1 to +2 SD), and obesity (>+2 SD). This approach provides an age-appropriate measure essential for accurate growth and health monitoring in pediatric populations.[11] The pediatric hypertension classification criteria are based on the Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children.[12]

The inclusion criteria comprised patients with pediatric early warning scores (*P*EWS) ≥3, oliguria (urine output <1 mL/kg/hour), and/or renal disorder following the criteria from the kidney disease, particularly improving global outcomes (KDIGO) and pediatric risk, injury, failure, loss, and end-stage renal disease (pRIFLE). The classification system using the criteria of risk, injury, failure, loss, and end-stage renal disease, known as "RIFLE", has been widely applied. Experts have modified the RIFLE criteria for children, referred to as pRIFLE, to define AKI in children, particularly critically ill children, as a diagnostic criterion.[13]

In addition to the pRIFLE classification system, the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 proposed a standardized and validated definition for the pediatric population. The KDIGO criteria identify AKI in three stages based on changes in serum creatinine from baseline or urine output. The baseline creatinine is defined as the lowest serum creatinine value in the preceding three months, which estimates the baseline glomerular filtration rate

(GFR) using the Schwartz equation.[14] Meanwhile, the exclusion criteria comprised the condition of massive ascites, chest and abdominal defects preventing ultrasound examination, congenital heart disease, and structural heart abnormalities.

The selection of research subjects was carried out using consecutive sampling, that is, all patients who came in order and met the research criteria were used as research samples until they met the minimum research sample size. The laboratory examination was conducted using blood samples from pediatric patients at the Clinical Pathology Laboratory of Hasan Sadikin Hospital, Bandung. Patient characteristics, including age, sex, basic signs, anthropometric measurements, laboratory test results, main disease diagnosis, and comorbid conditions, were directly collected during the initial patient assessment. Subsequently, consultant pediatric cardiologists conducted a screening assessment for cardiac structural abnormalities. This study included 14 pediatric patients who underwent hemodialysis. Pediatric patients with normal intracardiac structures were further evaluated for IVC/Ao ratio and serum lactate levels.

Ultrasound Examination

The IVC/Ao ratio was assessed through transabdominal ultrasonography using a Philips Type EPIQ linear probe (1–5 MHz). IVC/Ao ratio diameter using transabdominal ultrasound brand Ultrasound Philips Type Lumify with Linear probe 4–12 MHz.[15] Ultrasound data was collected using a Philips EPIQ 7G ultrasound system with shear wave elastography and a C5-1 curvilinear transducer (Philips Healthcare, Andover, MA). A skilled pediatrician, routinely performing the examination, conducted the ultrasound. The pediatric patient was positioned in the supine posture after the removal of clothing, and the probe was then applied to the epigastric region. The marking line of the probe was directed toward the cardiac area and then transversely positioned to visualize the Ao and IVC. The diameter of the IVC/Ao was measured in B-Mode, and the ultrasound results for each patient were recorded (Figure 1) to calculate ratio of the two parameters.

Statistical Analysis

Data were presented as mean (standard deviation [SD]) or median (interquartile range [IQR]) or median (minimum–maximum) based on data distribution. The Shapiro–Wilk test was used to assess data normality. The correlation between the IVC/Ao ratio and serum lactate levels was analyzed using the Spearman correlation. Statistical significance was set at a *p-value* <0.05. Analysis using the Statistical Product and Service Solution (SPSS) for Windows version 25.0 program.

Results

The median age was 12 years (min of 5 to max of 17), with 62.5% (N = 30) being male, and malnutrition affected half of children (50%, N = 24). The blood pressure distribution was uniform, with equal percentages of hypotension, normotension, and hypertension, each at 33.3% (N = 16). The mean hemoglobin was 9.7 g/dL (SD of 2.3), and the median

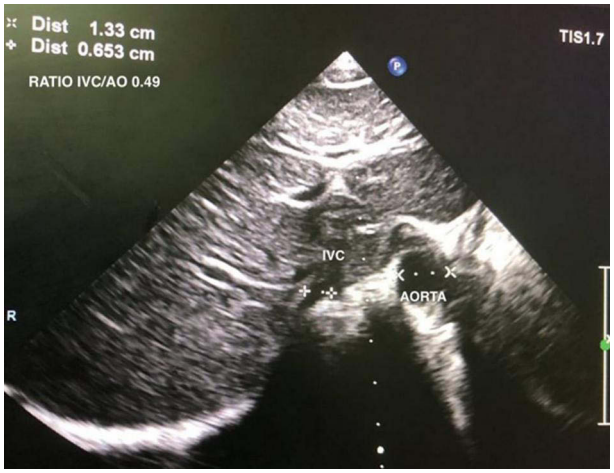

Figure 1 Ultrasound examination of IVC/Ao ratio.

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C-reactive protein was 1.52 mg/dL (min of 0.10 to max of 31.00). Hematological abnormalities were prevalent comorbidities (66.7%, N = 32), followed by infectious diseases (64.6%, N = 31), and neurological abnormalities (43.8%, N = 21). Urinary protein +3 was detected in 47.9% (N = 23), and urine erythrocytes +3 were found in 43.8% (N = 21) of the patients. During the study, 20.8% (N = 10) of the patients passed away (Table 1).

Table 1 Characteristics of Pediatric Patients with Acute Kidney Injury (AKI) (N = 48)

Characteristics	N (%)	Mean (SD)/Median (Min–Max)
Age (years)		12 (5–17)
Sex		
Male	30 (62.5)	
Female	18 (37.5)	
Weight (kg)		32 (12–68)
Height (cm)		137 (19)
BMI/Age		−0.95 (1.67)
Nutritional status		
Malnutrition (BMI/Age <-1)	24 (50.0)	
Normal	20 (41.7)	
Overweight (BMI/Age >1)	4 (8.3)	
Blood pressure (mmHg)[a]		
Hypotension	16 (33.3)	
Normotension	16 (33.3)	
Hypertension	16 (33.3)	
Blood analysis		
Haemoglobin (g/dL)		9.7 (2.3)
Hematocrit (%)		29.2 (7.0)
Leucocyte (sel/mm^3)		10,480 (130–127,550)
Thrombocyte (sel/mm^3)		293,021 (171,510)
Renal function		
Ureum (mg/dL)		89.2 (41.9–385.0)
Creatinine (mg/dL)		2.9 (1.5–21.20)
Albumin (mg/dL)		2.97 (0.67)
C-reactive protein (mg/L)		1.52 (0.10–31.00)
Comorbidities		
Respiratory disorder	9 (18.8)	
Neurological disorder	21 (43.8)	
Gastrointestinal disorder	17 (35.4)	
Hematological disorder	32 (66.7)	
Infectious disease	31 (64.6)	
Endocrinological disorder	4 (8.3)	
Allergy-immunology disorder	10 (20.8)	
Sepsis	12 (25.0)	
Outcomes		
Dead	10 (20.8)	
Alive	38 (79.2)	
Urinary protein		
0	0 (0)	
+1	3 (6.3)	
+2	6 (12.5)	
+3	23 (47.9)	
+4	16 (33.3)	

(*Continued*)

Table 1 (Continued).

Characteristics	N (%)	Mean (SD)/Median (Min–Max)
Urinary erythrocyte		
0	4 (8.3)	
+1	12 (25.0)	
+2	11 (22.9)	
+3	21 (43.8)	

Notes: [a]Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents, American Academy of Pediatric, 2017. This study included 14 pediatric patients who underwent hemodialysis.
Abbreviations: BMI, Body mass index; SD, standard deviation; Min, minimum; Max, maximum.

Several factors contribute to the kidney disorders or types of kidney diseases experienced by the study participants, including: Rapid Progressive Glomerulonephritis (RPGN), Glomerulonephritis with Acute Phase (GNAPS), Minimal Change Nephrotic Syndrome, Non-Minimal Change Nephrotic Syndrome, Lupus Nephritis, Urosepsis, IgA Nephropathy, and Nephrolithiasis. The IVC/Ao ratio with the median (IQR) IVC/Ao ratio remains within the normal range at 0.91 (0.70–1.10). The median (IQR) serum lactate level is 1.5 (1.1–2.4) mg/dL. The Spearman correlation coefficient showed that a decrease in the IVC/Ao ratio would possibly increase serum lactate levels (*rho*= −0.65, *p-value* <0.001) (Figure 2). The Spearman correlation coefficient between the IVC/Ao ratio and serum lactate levels is −0.65, indicating the direction and strength of the relationship between these variables. The negative value (−0.65) suggests an inverse relationship, meaning that as the IVC/Ao ratio decreases, serum lactate levels tend to increase, and vice versa. The p-value of <0.001 signifies the statistical significance of this observed correlation.

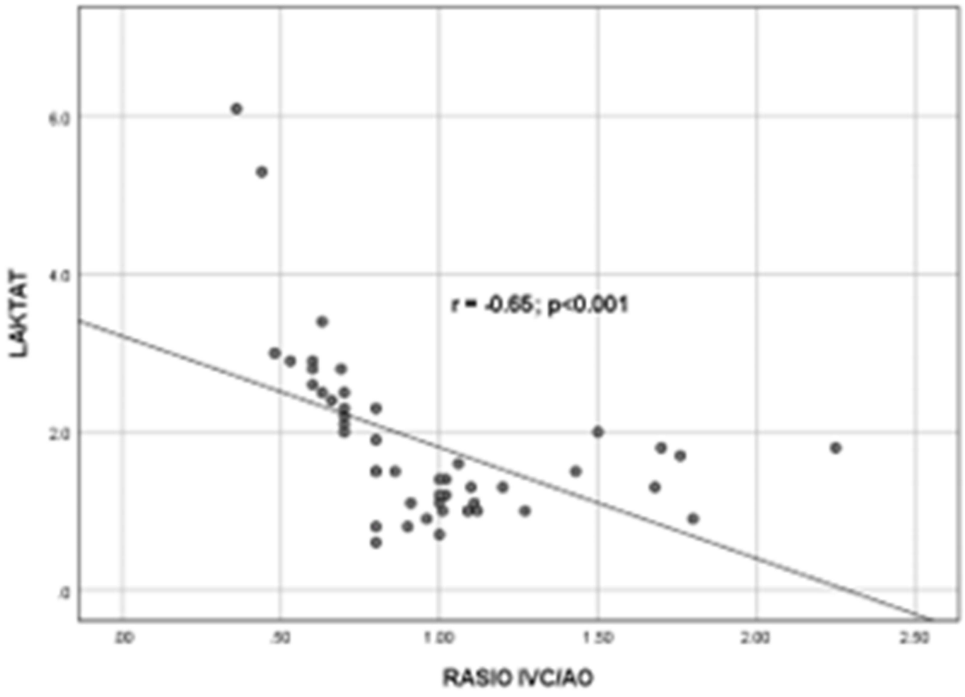

Figure 2 Scatter plot of IVC/Ao Ratio Correlation with Lactate (mmol/L).

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Discussion

The IVC/Ao ratio represented a non-invasive method for evaluating intravascular volume. Previous reviews showed its utility as a parameter for detecting the early phases of hypovolemia and monitoring fluid therapy.[16] In this study, the median IVC/Ao ratio (IQR of 0.91 (0.70–1.10)) was similar to the analysis conducted in Italy, where the median range value in children aged 4–16 years was 0.93–1.12. The first quartile range was 0.79–0.93, and the third quartile range was 1.06–1.30.[17] An Indonesian analysis comprising 3682 children in the emergency room and PICU of Cipto Mangunkusumo Hospital showed that the mean (SD) IVC/Ao ratio before fluid challenge in the responsive subject group was significantly lower at 0.70 (0.05) compared to 0.86 (0.09) after fluid challenge ($p = 0.000$).[18] Similarly, an investigation conducted in Turkey with 124 pediatric patients showed an increase in the IVC/Ao ratio after fluid therapy in the groups of mildly and moderately to severely dehydrated children.[19] It suggested a potential benefit for patients with a low IVC/Ao ratio to receive fluid therapy. Assessing changes in the IVC/Ao ratio values after fluid administration was crucial for evaluating therapeutic response.

Hemodynamic monitoring plays a vital role in managing children with sepsis, especially when kidney involvement is present. Sepsis-associated acute kidney injury (S-AKI) is strongly associated with unfavorable outcomes. Patients with S-AKI demonstrate impaired hemodynamic performance, as observed through IVC/Ao ratio assessment via two-dimensional ultrasonography and USCOM evaluation. Measuring the IVC/Ao ratio offers comparable accuracy to USCOM and serves as a practical, low-cost alternative for hemodynamic monitoring.[20]

In this study, the median serum lactate levels (IQR of 1.5 (1.1–2.4) mmol/L) were found within normal limits (0.2–2.0 mmol/L).[21] Spearman Rank correlation testing showed a negative relationship between the IVC/Ao ratio and serum lactate levels ($rho = -0.65$, $p < 0.001$). The results showed that conditions with a low IVC/Ao ratio correlated with elevated blood lactate levels. However, the underlying pathomechanism explaining such correlation remained poorly understood. A low ratio was significantly influenced by changes in the IVC diameter rather than the Ao diameter due to higher compliance of the IVC.[6] In hypovolemic conditions, a low IVC diameter resulted from vasoconstriction as a direct response to low volume status. Additionally, hypovolemic conditions could lead to inadequate oxygenation of all body organs, contributing to hypoxia. Lactate served as a crucial and rapidly available source of energy in hypoxia conditions. Hypovolemia can lead to kidney disorders by reducing blood volume, resulting in decreased renal perfusion. This insufficient blood flow can trigger acute kidney injury (AKI), marked by damage to renal tubular cells due to hypoxia and a lack of essential oxygen and nutrients necessary for normal cellular function. Previous reviews identified lactate levels to be a marker of tissue hypoperfusion, a risk stratification tool, and a progression indicator in AKI patients.[9]

Elevated lactate levels had a vasodilatory effect and may induce acidosis. Surprisingly, acidosis stimulated catecholamine production to maintain relatively constant peripheral vascular resistance, thereby attenuating the peripheral vasodilatory effect. Acidosis also had a direct vasoconstrictive effect on the venous system, further augmented by catecholamine production. This may explain the venoconstrictor effect of lactate on the IVC.[22] Another study reported that patients with elevated lactate levels had higher concentrations of endothelin-1 on admission, with a subsequent significant reduction within 48 hours. The results suggested a more pronounced endothelin-mediated vasoconstriction in the peripheral vascular. Moreover, endothelin-mediated vasoconstriction may be present in patients with higher lactate serum levels, showing inadequate perfusion and serving as a marker of organ injury.[23] This could represent another possible mechanism for the vasoconstrictor properties of lactate on the IVC.

Higher lactate levels were reported in a cohort analysis of sepsis patients with acute renal failure (mean (SD) 29.9 (25.7) vs 18.6 (9.3) mmol/L, $p = 0.001$). The mean lactate levels increased with the severity of renal failure. Serum lactate levels at ICU admission were associated with a higher risk of acute renal failure (adjusted OR 1.03 (95% CI 1.01–1.06), $p = 0.024$).[24] Lactate levels, serving as a parameter for tissue hypoperfusion, have been subjected to extensive examination. Increased lactate levels unresponsive to fluid therapy might have arisen from heightened aerobic glycolysis in the muscle compared to hypoperfusion.[25,26] Therefore, measuring lactate levels upon ICU admission and subsequently assessing the risk of organ damage and death was crucial. The therapeutic target was to reduce lactate levels by ≥20% every 2 hours in the first 8 hours.[27]

This study indicated that the most common comorbidities were hematologic disorder (66.7% (N = 32)) and infectious diseases (64.6% (N = 31)). The results showed that the primary hematologic comorbidity was anemia, with a mean (SD) hemoglobin level of 9.7 (2.3) g/dL, falling below the normal limits for the median pediatric age.[21] Anemia predisposed to acute renal failure or exacerbated factors during hospitalization. Malhotra et al found that anemia increased the risk of acute renal impairment in critically ill patients [OR 1.477 (0.891–2.449), $p = 0.13$].[28] Anemia was a factor predisposing to hypoxia, while infectious diseases included inflammatory processes and immune dysregulation potentially leading to renal hypoperfusion. Pediatric patients with multiple comorbidities, particularly those related to hematological issues and perfusion abnormalities, should be considered at higher risk for acute kidney injury and mortality. This highlights the need for targeted risk assessment and management strategies in this population.[29,30] Anemia in this population may result from chronic inflammation, nutritional deficiencies (such as iron, vitamin B12, or folate), blood loss, or underlying hematological disorders, all of which are common in critically ill pediatric patients. Correction of accompanying clinical conditions, such as blood pressure abnormalities, anemia, and infection, needed simultaneous attention.[13,29]

The findings of this study align with established principles that reduced effective intravascular volume can lead to decreased tissue perfusion, a condition indicated by elevated serum lactate levels. However, the importance of correlating the IVC/Ao ratio with serum lactate lies in its potential clinical application. The IVC/Ao ratio, assessed through non-invasive transabdominal ultrasonography, can serve as an accessible and cost-effective alternative to serum lactate measurements. This could be especially valuable in emergency scenarios or low-resource environments where immediate access to laboratory testing is limited. By establishing the utility of the IVC/Ao ratio as a reliable proxy for serum lactate, clinicians can have an efficient tool for rapid hemodynamic assessment and decision-making, potentially improving patient outcomes in critical care settings.[6,19,20]

This study had limitations, including firstly, the sample size did not allow for categorization analysis of vessel volume based on ultrasonography. Secondly, pediatric patients with renal impairment had diverse laboratory features, potentially influencing variations in the IVC/Ao ratio and serum lactate levels due to underlying clinical conditions.

Conclusion

In conclusion, this study demonstrates a negative correlation between the IVC/Ao diameter ratio and serum lactate levels in children with kidney disorders. A decrease in the IVC/Ao ratio is associated with an increase in serum lactate levels. Assessing the IVC/Ao ratio alongside blood lactate levels can help evaluate the risk of acute kidney injury (AKI) and its progression. This evaluation is recommended upon initial admission to the Pediatric Intensive Care Unit (PICU) and should be repeated after fluid therapy.

Institutional Review Board Statement

This study was performed in accordance with the recommendations of the Institutional Review Board of Hasan Sadikin Hospital (Bandung, Indonesia) with number LB.02.01/X.6.5/149/2023. The study protocol, patient information sheet, and consent forms were submitted to the Ethics Committee for consideration and approval. Approval was obtained before the enrolment of the participants. This research was conducted according to the protocol and following the latest Edinburgh, Scotland revision of the Declaration of Helsinki, ICH Good Clinical Practice guidelines, and local regulatory requirements.

Informed Consent Statement

The parent or legal guardian of patient provided written informed consent in accordance with Declaration of Helsinki and Good Clinical Practice guidelines.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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