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Evaluation of Fluid Status of Children in Pediatric Intensive Care Unit by Measuring Inferior Vena Cava Diameter

Pediatrik Yoğun Bakım Ünitesindeki Çocukların Sıvı Durumunun Inferior Vena Cava Çapı Ölçülerek Değerlendirilmesi

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Abstract

Introduction: The aim of this study was to determine the correlation between Inferior Vena Cava (IVC) diameter, vena cava inferior collapsibility (cIVC) and vena cava inferior distensibility (dIVC) with other hemodynamic parameters to determine the fluid requirement or volume load of patients hospitalised in the pediatric intensive care unit.

Methods: Sixty-two patients aged 1 month-18 years were included in this study. IVC diameters were measured, collapsibility and distensibility were calculated to predict the fluid status of the patients. Physical examination findings, biochemical markers, perfusion indices (PI), pleth variability indices (PVI) were also evaluated.

Results: There were 33 girls and 29 boys, aged between 3-211 months. IVC minimum diameter (D_{min}) varied between 0.27 and 2.10 cm, while IVC maximum diameter (D_{max}) varied between 0.56 and 2.90 cm and there was a very strong relationship between D_{max} and D_{min} in the same direction (r=0.956, p<0.001). There was a positive correlation between D_{min} and cIVC or dIVC among patient groups according to mechanical ventilation (MV) support status. In contrast, there was a negative correlation between PI and PVI and cIVC in patients without MV support (r=-0.355, p=0.040; r=-0.404, p=0.018). There was a positive correlation between D_{min} and D_{max} (r=0.928, p<0.001). There was also a positive correlation between PVI and PI and a negative correlation between lactate (r=0.393, p=0.02; r=-0.272, p=0.033).

Conclusion: The high cIVC in spontaneously breathing patients may be associated with intravascular fluid loss. However, more patients are needed to comment on patients receiving MV support.

Keywords: Distensibility, collapsibility, fluid status, Inferior Vena Cava diameter

Öz

Giriş: Bu çalışmanın amacı çocuk yoğun bakım ünitesinde yatan hastaların sıvı gereksinimi veya hacim yükünü belirlemek için Inferior Vena Cava (IVC) çapı, vena kava inferior kollapsibilitesi (cIVC) ve vena kava inferior distansibilitesi ile diğer hemodinamik parametreler arasındaki korelasyonu belirlemektir.

Yöntemler: Bu çalışmaya 1 ay-18 yaş arası 62 hasta dahil edildi. Hastaların sıvı durumlarını tahmin etmek için IVC çapları ölçüldü, kollapsibilite ve distansibiliteleri hesaplandı. Fizik muayene bulguları, biyokimyasal parametreleri, perfüzyon indeksi (PI), pleth variyabilite indeksi (PVI) de değerlendirildi.

Bulgular: Üç-211 ay arasında değişen yaşlarda 33 kız, 29 erkek çocuk vardı. IVC çaplarından minimum çap (D_{min}) 0,27 ile 2,10 cm arasında değişirken, maksimum çap (D_{maks}) 0,56 ile 2,90 cm arasında değişiyordu ve D_{min} ile D_{maks} arasında aynı yönde çok güçlü bir korelasyon vardı (r=0,956, p<0,001). D_{min} ile cIVC veya dIVC arasında, mekanik ventilasyon (MV) desteği alma durumuna göre hasta grupları arasında pozitif bir korelasyon vardı. Buna karşın, MV desteği almayan hastalarda PI ve PVI ile cIVC arasında negatif korelasyon mevcuttu (r=-0,355, p=0,40; r=-0,404, p=0,018). D_{min} ve D_{maks} arasında pozitif bir korelasyon vardı (r=0,928, p<0,001). PVI ve PI arasında da pozitif korelasyon ve laktat arasında negatif korelasyon vardı (r=0,393, p=0,02; r=-0,272, p=0,033).

Sonuç: Spontan soluyan hastalarda yüksek cIVC, intravasküler sıvı kaybı ile ilişkili olabilir. Ancak, MV desteği alan hastalar hakkında yorum yapabilmek için daha fazla sayıda hastaya ihtiyaç vardır.

Anahtar Kelimeler: Distansibilite, kollapsibilite, sıvı durumu, Inferior Vena Cava çapı

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Introduction

Ensuring hemodynamic stabilization is of vital importance in the management of critically ill patients admitted to the pediatric intensive care unit (PICU). The fluid, electrolyte, and acid-base equilibria must be maintained. If any of these three balances is disrupted, the body will not function normally. Maintaining hemodynamic balance reduces mortality and morbidity, especially for patients in PICU. In dehydration or shock, inadequate fluid resuscitation can cause tissue hypoperfusion and end-organ damage, while excessive fluid resuscitation can cause central venous pressure, hypertension, polyuria, peripheral oedema, hypoalbuminaemia, intracranial pressure, and mortality.[1-3]

Before making fluid management decisions in these individuals, clinicians should assess their hemodynamic condition. Dynamic methods like body weight loss, skin turgor, capillary refill time (CRT), systolic pressure change, heart rate, heart rate volume change, urine output, serum bicarbonate, lactate levels, and passive leg lift test can assess patients' hemodynamic status.[1,4,5] Recent studies have also employed perfusion index (PI), pleth variability index (PVI), and inferior vena cava (IVC) diameter measurement.[4] Measured IVC diameters and vena cava inferior distensibility (dIVC) in mechanically ventilator-dependent patients, and collapsibility in spontaneously breathing patients without mechanical ventilator (MV) support, can guide fluid management.[1,6] The aim of this study was to determine the correlation of IVC diameter, vena cava inferior collapsibility (cIVC), and dIVC with other hemodynamic parameters to assess the hemodynamic status, fluid requirement, or volume load of patients admitted to the PICU.

Materials and Methods

Selection of Patients

Between January 1, 2020, and June 1, 2020, pediatric patients aged 1 month to 18 years who were hospitalised in the PICU were included in the study. Among these patients, those with congenital heart disease, congenital vascular anomalies, pulmonary hypertension, pneumothorax/hemothorax, or cardiac tamponade; those who started inotropic therapy before hospitalisation; those who received MV support and had a positive end-expiratory pressure >8 cm H_2O; and those who had conditions that hindered ultrasonography (obesity, burns, wounds in the anterior chest dura, drains secondary to chest surgery) were not included in the study.

In addition, IVC diameters were measured collapsibility and distensibility were calculated, and physical examination findings and biochemical markers were also recorded. According to this information, it would be sufficient to reach at least 30% of the population for the best estimation. However, the aim is to reach at least 50% of the population in case of missing data. Accordingly, a minimum of 60 pediatric patients was calculated to be included in this study.[7] In accordance with these calculations, a total of 62 patients were included in the study.

Ethics Committee approval was obtained from Mersin University Clinical Research Ethics Committee, with the board (decision date: 08.01.2020 and decision no: 2020/26).

Assessment of Patients

The IVC diameter of the patients was measured during inspirium and expirium by a faculty member of the division of pediatric intensive care at the time of admission to the PICU. This was done using GE Logiq e ultrasound system ultrasonography device with the GE convex 4C-RS probe in our PICU. All measurements were performed by the same faculty member. The ultrasound probe was placed perpendicular to the long axis of the body just below the xiphoid bone level, and a cross-sectional image of the IVC and the aorta was obtained in B-mode. Afterwards, the junction of the IVC and right atrium, and the area where the hepatic veins join were visualised by turning the probe clockwise towards the patient's right shoulder. Switching to M-mode, IVC diameter was measured from the image taken 1-2 cm distal to the opening of the IVC into the right atrium in both inspiration and expiration. dIVC: [vena cava inferior maximum diameter (D_{max})-vena cava inferior minimum diameter (D_{min})/D_{min}]x100 and cIVC [cIVC: (D_{max}-D_{min})/D_{max}]x100 were calculated and recorded. Simultaneously, fever, pulse rate, blood pressure, oxygen saturation, and CRT, PI, PVI, blood count, blood biochemistry, blood gas parameters, ventilator parameters, demographic characteristics, and clinical problems of the patients were recorded.

Statistical Analysis

The data were analysed with Statistical Package for the Social Science (SPSS) 22. The mean, standard deviation, median, 1st and 3rd quartiles, number, and percentage were shown. The chi-square test determined the relationships between categorical variables. Normality was tested with Shapiro-Wilk. The Student t-test was employed for variables that satisfied the normality assumption, and the Mann-Whitney U test for variables that did not. The statistical significance level was set at $p<0.05$.

Patients were categorized by diagnosis, chronic disease state, ventilation status, and pre-hospitalization fluid therapy. Results were compared between patient groups.

Results

There were 33 girls and 29 boys, aged between 3 and 211 months (median 70.5, interquartile range: 18.25-135.75). 17.7% of patients were 1-12 months old, 29% were 13-59 months old, 17.7% were 60-119 months old, and 35.5% were 120-216 months old. Patients who couldn't be included in all four diagnostic groups (electric shock, corrosive substance ingestion, drug intoxication, intrathecal treatment hospitalization) were defined as "other". Patients were hospitalized in the PICU for the following reasons: 16.1% due to neurological disease, 14.5% due to trauma, 43.5% due to infection/sepsis, 12.9% for surgery or for follow-up, and 12.9% for other reasons.

Table 1 presents the analysis from the study of physical examination findings of patient groups. There was no statistically significant difference between groups in terms of MV support and chronic illnesses. However, CRT and blood pressure values were significantly different in the group, identified as having an intravascular volume deficit during the clinical evaluation before hospitalization, fluid loaded compared to those who were not. CRT was prolonged in 53% of those who received fluid loading (p=0.025), and blood pressure was lower than the age-adjusted norm in 53.8% of the cases (p=0.039). A significant difference was found between the groups by diagnosis, only in terms of the pulse rate, according to age. Pulse rate increased with age in 40.7% of the patient group hospitalised due to infection/sepsis (p=0.029) (Table 1).

In terms of biochemical parameters, there was no significant difference between chronic disease status groups, but lactate levels differed between patients with and without MV support and between patients who received fluid loading before hospitalisation in the PICU and who didn't (p=0.018, p=0.022) (Table 2).

A statistically significant correlation was found between prolonged CRT and increased lactate (p<0.001), decreased pH (p<0.001), increased urea (p=0.021), increased creatinine (p=0.011), increased sodium (p=0.025), and urine density (p<0.001). A significant difference was shown among blood pressure value, lactate (p=0.02), pH (p=0.02), CO_2 (p=0.032), creatinine (p=0.032), sodium (p=0.030), and urine density (p<0.001) (Table 3).

IVC diameter D_{min} varied between 0.27 and 2.10 cm, while D_{max} varied between 0.56 and 2.90 cm, and there was a very strong relationship between D_{max} and D_{min} in the same direction (r=0.956, p<0.001). A linear correlation was found between patient age and IVC diameters (r=0.724, p<0.001 for D_{max}; r=0.646, p<0.001 for D_{min}).

Table 4 compares ultrasonographic and pulse oximetric data between groups based on concomitant chronic disease and MV support. D_{max}, D_{min}, and PVI differed significantly between chronic illness groups (p=0.003; p=0.12; p=0.030). The study compared patient groups based on MV supports for IVC measures, PVI, and PI. Significant differences were found mainly in respiratory variations of IVC (p<0.001).

Table 1. Distribution of physical examination findings between patient groups

Patient groups		CRT					Pulse rate (according to age)					$Ta_{systolic}$ (according to age)						
		Normal		Increased		p	Normal		Increased		p	$Ta_{systolic}$ normal		$Ta_{systolic}$ d decreased		$Ta_{systolic}$ increased		p
		N	%	N	%		N	%	N	%		N	%	N	%	N	%	
Mechanical ventilator support	Yes (n=28)	17	60.7	11	39.3	0.410	23	82.1	5	27.9	0.448	15	53.6	10	35.7	3	10.7	0.512
	None (n=34)	29	85.3	5	14.7		24	70.6	10	29.4		23	67.6	8	23.5	3	8.8	
Fluid loading before hospitalization	Done (n=13)	6	46.2	7	53.8	0.025*	8	61.5	5	38.5	0.324	6	46.2	7	53.8	0	0.0	0.039*
	Not done (n=49)	40	81.6	9	18.4		39	79.6	10	20.4		32	65.3	11	22.4	6	12.2	
Diagnosis groups	Neurological (n=10)	10	100	0	0.0	0.060	10	100	0	0.0	0.029*	7	70.0	1	10.0	2	20.0	0.313
	Trauma (n=9)	7	77.8	2	22.2		8	88.9	1	11.1		6	66.7	3	33.3	0	0.0	
	Infection/sepsis (n=27)	17	63.0	10	37.0		16	59.3	11	40.7		15	55.6	10	37.0	2	7.4	
	After surgery (n=8)	7	87.5	1	12.5		7	87.5	1	12.5		5	62.5	1	12.5	2	25.0	
	Others (n=8)	5	62.5	3	37.5		6	75.0	2	25.0		5	62.5	3	37.5	0	0.0	
Chronic diseases	Yes (n=39)	28	71.8	11	28.2	0.574	30	75.8	9	23.1	0.789	23	59.0	11	28.2	5	12.8	0.515
	None (n=23)	18	78.3	5	21.7		17	73.9	6	26.1		15	65.2	7	30.4	5	12.8	

CRT: Capillary refill time, $Ta_{systolic}$: Systolic blood pressure, *: Statistically significant

In addition, D_{min} was positively correlated with cIVC or dIVC in both groups, according to MV support status. Only the MV-supported group had a positive correlation between D_{max} and dIVC. However, PI and PVI were negatively correlated with cIVC in patients without MV support (r=-0.355, p=0.040; r=-0.404, p=0.018) (Table 5).

As a result, cIVC of patients with low PI and PVI measurements were high, which may be associated with intravascular volume loss.

Table 6 shows the correlations between IVC diameters, respiratory variability, PI, PVI, and biochemical parameters. A significant positive correlation exists between D_{min} and D_{max} (r=0.928, p<0.001). D_{min} is negatively correlated with cIVC and/or dIVC (r=-0.416, p=0.001). Creatinine is the only laboratory parameter that correlates positively with D_{min} and D_{max} (r=0.326, p=0.010 for D_{min}; r=0.340, p=0.005 for D_{max}).

Table 2. Evaluation of laboratory parameters of the patient groups according to fluid loading and MV support status before hospitalization

	Fluid loading before hospitalization			MV support		
	Yes (n=13)	No (n=49)	p	Yes (n=28)	No (n=34)	p
Lactate	7.462±5.807	4.302±3.834	0.789	6.554±5.833	3.658±2.238	0.018*
pH	7.368±0.098	7.383±0.066	0.975	7.372±0.091	7.386±0.054	0.484
CO_2 (mmHg)	44.323±10.702	42.276±10.785	0.771	44.954±11.804	40.853±9.503	0.135
HCO_3 (mmol/L)	24.169±6.498	23.559±4.504	0.283	24.039±5.985	23.397±3.932	0.614
BE (mmol/L)	-0.615±6.751	-0.514±3.980	0.885	-0.918±5.581	-0.221±3.729	0.559
Hemoglobin (g/dL)	16.885±24.426	9.657±1.917	0.433	12.600±18.744	9.997±2.121	0.424
Hematocrit (%)	28.38±5.32	29.51±5.59	0.839	28.04±4.11	30.29±6.31	0.096
White blood cell (x1/µL)	8680.00±4910.38	9506.80±4492.18	0.995	9124.64±5024.28	9505.38±4196.66	0.746
Urea (mg/dL)	75.31±112.03	23.06±1724	0.874	34.657±24.469	33.407±72.609	0.936
Creatinine (mg/dL)	1.244±1.756	0.446±0.566	0.149	0.815±1.081	0.448±0.875	0.155
Sodium (meq/L)	139.62±12.28	140.00±6.16	0.818	143.18±8.170	137.24±6.24	0.002*
Urine density	1018.69±8.85	1015.84±8.54	0.432	1018.61±9.27	1014±7.71	0.071

MV: Mechanical ventilation, BE: Base deficit, *: Statistically significant

Table 3. Relationship between physical examination findings and laboratory parameters

	CRT			Pulse rate (according to age)			$Ta_{systolic}$ (according to age)			
	Normal (n=46)	Elongated (n=16)	p	Normal (n=47)	Increased (n=15)	p	Ta normal (n=38)	Ta decreased (n=18)	Ta increased (n=6)	p
Lactate	3.2±1.9	10.1±5.6	<0.001*	4.4±3.9	6.9±5.6	0.058	3.1±2.8	9.1±5.2	4.0±2.6	0.002*
pH	7.40±0.07	7.33±0.07	<0.001*	7.38±0.07	7.35±0.07	0.109	7.39±0.06	7.33±0.06	7.43±0.06	0.002*
CO_2 (mmHg)	41.5±9.7	46.1±12.7	0.148	41.8±9.9	45.4±13.0	0.268	41.1±10.3	47.9±11.0	37.0±7.4	0.032*
HCO_3 (mmol/L)	24.1±4.4	22.5±6.2	0.283	23.8±8.1	23.4±5.4	0.835	23.6±5.0	23.4±5.4	25.1±3.6	0.752
BE (mmol/L)	0.1±4.0	-2.4±5.9	0.125	-0.4±4.7	-0.9±4.6	0.748	-0.1±4.3	-1.7±5.4	0.4±4.0	0.434
Hemoglobin (g/dL)	9.7±1.8	15.4±6.1	0.370	11.9±14.4	9.0±2.6	0.455	12.3±1.6	9.4±2.1	9.5±2.5	0.692
Hematocrit (%)	29.6±5.3	28.4±6.1	0.453	29.7±4.9	28.1±7.2	0.334	29.9±4.7	28.4±6.5	27.8±7.2	0.530
White blood cell (x1/µL)	9388±4524	9175±4782	0.874	9120±4530	10001±4721	0.519	10212±4640	8040±4249	7646±4115	0.150
Urea (mg/dL)	17.9±10.4	80.5±97.1	0.02*	23.0±17.8	68.5±105.2	0.117	17.3±9.8	72.3±94.1	25.2±16.2	0.067
Creatinine (mg/dL)	0.31±0.19	1.50±1.64	0.01*	0.54±0.80	0.85±1.42	0.423	0.28±0.16	1.36±1.59	0.49±0.35	0.032*
Sodium (meq/L)	138.1±5.1	145.2±11.2	0.025*	140.0±7.6	139.7±8.3	0.886	139.2±6.0	142.9±10.8	135.7±3.0	0.030*
Urine density	1012±5.9	1027±5.9	<0.001*	1015±7.8	1020±9.8	0.028*	1013±6.8	1025±6.5	1012±2.2	<0.001*

CRT: Capillary refill time, $Ta_{systolic}$: Systolic blood pressure, BE: Base deficit, *: Statistically significant

Table 4. Evaluation of D_{max}, D_{min}, dIVC/cIVC, PVI, PI parameters of patients according to chronic disease and mechanical ventilator support status

	No chronic disease (n=23)		Chronic illness present (n=39)		p	MV is not available (n=34)		MV is available (n=28)		p
	Min-max	Median (25-75%)	Min-max	Median (25-75%)		Min-max	Median (25-75%)	Min-max	Median (25-75%)	
D_{max} (cm)	0.67-2.90	1.23 (0.92-1.64)	0.56-2.90	0.9 (0.77-1.12)	0.003*	0.62-2.90	1.02 (0.86-1.35)	0.56-2.90	0,91 (0.77-1.57)	0.336
D_{min} (cm)	0.34-2.10	0,67 (0.47-0.82)	0.27-1.90	0.45 (0.38-0.67)	0.012*	0.30-2.10	0.55 (0.41-0.68)	0.27-2.00	0.49 (0.38-0.78)	0.655
dIVC/cIVC (%)**	27.6-133.3	49.2 (44.6-56.9)	34.3-165.0	54.3 (49.2-100.0)	0.070	27.6-59.2	49.2 (44.6-51.6)	34.3-165.0	96.2 (57.8-107.3)	<0.001*
PVI	12-40	26 (21-32)	10-44	21 (15-25)	0.030*	10-40	23.50 (18.00-30.25)	12-44	22.00 (14.00-26.50)	0.181
PI	0.14-8	1.80 (0.58-3.10)	0.12-12	1.4 (0.8-2.3)	0.867	0.12-12	1.20 (0.59-2.45)	0.35-8.00	1.50 (0.92-2.80)	0.151

**: In all analyses, dIVC value was analyzed for patients receiving mechanical ventilator support and cIVC value was analyzed for patients who did not receive mechanical ventilator support but breathed spontaneously.
D_{max}: Vena cava inferior maximum diameter, D_{min}: Vena cava inferior minimum diameter, dIVC: Vena cava inferior distensibility, cIVC: Vena cava inferior collapsibility, PI: Perfusion index, PVI: Pleth variability index, MV: Mechanical ventilator, *: Statistically significant

Table 5. Correlations of vena cava inferior measurements, PI and PVI with each other in patient groups formed according to mechanical ventilator support

			D_{min}	cIVC/dIVC	PVI	p
Mechanical ventilation is not available	D_{max}	r	0.954	-0.363	-0.091	-0.026
		p	<0.001*	0.035*	0.608	0.886
	D_{min}	r		-0.588	0.013	0.081
		p		<0.001*	0.942	0.650
	cIVC	r			-0.404	-0.355
		p			0.018*	0.040*
	PVI	r				0.194
		p				0.271
Mechanical ventilation is available	D_{max}	r	0.961	-0.303	0.048	0.369
		p	<0.001*	0.116	0.809	0.053
	D_{min}	r		-0.520	-0.012	0.449
		p		0.005*	0.953	0.017
	dIVC	r			<0.001	-0.300
		p			0.999	0.121
	PVI	r				0.043
		p				0.828

**: In all analyses, dIVC value was analyzed for patients receiving mechanical ventilator support and cIVC value was analyzed for patients who did not receive mechanical ventilator support but breathed spontaneously.
D_{max}: Vena cava inferior maximum diameter, D_{min}: Vena cava inferior minimum diameter, dIVC: Vena cava inferior distensibility, cIVC: Vena cava inferior collapsibility, PI: Perfusion index, PVI: Pleth variability index, *: Statistically significant

Table 6. Correlations between vena cava inferior measurements, PI, PVI and biochemical parameters

		D_{min} (cm)	cIVC/ dIVC	PVI	PI	Lactate	pH	CO_2 (mmHg)	HCO_3 (mmol/L)	BE (mmol/L)	Hgb (g/dL)	Hct (%)	WBC (x1/ µL)	Urea (mg/ dL)	Creatinine (mg/dL)	Na (mEq /L)	Urine density
D_{max} (cm)	r	0.928	-0.228	0.113	0.037	0.092	0.137	0.047	0.167	0.001	0.042	0.004	0.018	0.028	0.349	-0.001	0.059
	p	<0.001*	0.075	0.381	0.778	0.478	0.287	0.715	0.196	0.993	0.745	0.975	0.889	0.831	0.005*	0.995	0.650
D_{min} (cm)	r		-0.416	0.162	0.115	0.096	0.167	-0.021	0.155	-0.028	0.060	0.010	0.101	0.010	0.326	0.107	0.038
	p		0.001*	0.210	0.375	0.460	0.194	0.874	0.228	0.830	0.644	0.937	0.437	0.941	0.010*	0.408	0.772
cIVC/dIVC**	r			-0.157	-0.136	0.174	-0.309	0.324	-0.056	-0.106	-0.206	-0.152	-0.330	0.269	0.064	0.041	0.190
	p			0.223	0.293	0.176	0.014*	0.010*	0.666	0.413	0.108	0.238	0.009*	0.034*	0.620	0.752	0.139
PVI	r				0.393	-0.272	0.005	-0.003	-0.228	-0.192	0.105	0.040	-0.060	-0.147	-0.139	0.010	-0.127
	p				0.002*	0.033*	0.971	0.979	0.075	0.134	0.415	0.758	0.643	0.254	0.280	0.938	0.326
PI	r					-0.088	0.061	0.078	-0.149	-0.054	-0.035	-0.047	-0.061	-0.056	-0.042	-0.009	-0.032
	p					0.495	0.635	0.546	0.246	0.675	0.785	0.717	0.640	0.665	0.744	0.946	0.805

**: In all analyses, dIVC value was analyzed for patients receiving mechanical ventilator support and cIVC value was analyzed for patients who did not receive mechanical ventilator support but breathed spontaneously.
D_{max}: Vena cava inferior maximum diameter, D_{min}: Vena cava inferior minimum diameter, dIVC: Vena cava inferior distensibility, cIVC: Vena cava inferior collapsibility, PI: Perfusion index, PVI: Pleth variability index, BE: Base deficit, Hgb: Hemoglobin, Hct: Hematocrit, WBC: White blood cell, *: Statistically significant

Unlike creatinine, urea was positively correlated with cIVC or dIVC (r=0.269, p=0.034). There is a positive correlation between PVI and PI, and a negative correlation between lactate and these parameters (r=0.393, p=0.02; r=-0.272, p=0.033). Thus, PVI is directly proportional to PI and inversely proportional to lactate. The study found no statistically significant association between PI and any laboratory parameter (p>0.005).

The study found significant correlations between lactate and pH, urea, creatinine, sodium, and urine density. Lactate and pH correlated negatively (r=-0.38, p=0.002). This is because lactic acidosis is the major component of metabolic acidosis in intravascular volume loss. Additionally, lactate levels are significantly correlated with increases in urea, creatinine, sodium, and urine density (respectively r=0.454, p<0.001; r=0.380, p=0.002; r=0.326, p=0.010; r=0.640, p<0.001). Although there was a significant negative correlation between pH and urea, sodium, and urine density (r was negative for each of them and p<0.05), the correlation with creatinine was not statistically significant, even though creatinine increased as pH decreased (r=-0.223, p=0.081).

Discussion

In PICU patients, fluid status should be determined and appropriate fluid resuscitation initiated without delay. However, inadequate or forceful fluid treatment may cause fatal outcomes. Therefore, assessing patients' fluid status and starting appropriate treatment are vital.[8,9]

To date, IVC diameter and respiratory variability in adult patients have been studied extensively.[9,10] Compared to adult patients, pediatric research is more limited and has more inconsistent outcomes. Age-related changes in IVC diameter may be a major cause of this paradox. Mannarino et al.[11] found that IVC diameters increased with age in healthy Caucasian children, but there was a weak correlation between cIVC and age. In another study involving 63 healthy, normovolemic children, it was shown that the measured IVC diameter increased with age, and this increase was statistically significant (p<0.001) in all pediatric ages.[12] Similar to previous studies in pediatric ages, in our study of 62 pediatric patients hospitalized in the PICU, a linear relationship was found between age and D_{min}, D_{max}. It was observed that these diameters increased with increasing age (r=0.646, p<0.001 for D_{min}; r=0.724, p<0.001 for D_{max}).

Positive pressure ventilation increases intrathoracic pressure during inspiration, decreases systemic venous return, and causes a rise in IVC diameter. Therefore, dIVC is more reflective of preload dependency.[13,14] In contrast, in spontaneously

breathing patients, intrathoracic pressure decreases during inspiration, increasing venous return and causing IVC collapse. Thus, inspiratory IVC diameter is smaller than expiratory IVC diameter, and hypovolaemia may increase respiratory variability. This makes cIVC a more appropriate parameter for spontaneously breathing patients.[13]

In a literature review published by Ciozda et al.[14] in 2016, data from a total of 1430 patients receiving MV support were combined, and the usefulness of IVC diameters for the estimation of central venous pressure (CVP) was evaluated. The results indicated that the reported correlations between IVC size and CVP in patients receiving MV support were weak and inconsistent. In approximately half of the studies in this population of 1430 patients, no statistically significant correlation was found between CVP and IVC diameters; and in those in which significance was found, correlations were mostly weak and moderate in strength. Weber et al.[15] confirmed the low degree of predictability of respiratory variation of IVC diameter in determining fluid sensitivity during MV in a pediatric patient population.

In a prospective study conducted in the PICU of a clinic in which 50 patients aged 5-18 years with a diagnosis of shock were evaluated, a statistically significant correlation was found between IVC diameters measured at the end of expiration and inspiration, and CVP measured at the same stage. In addition, it was observed that respiratory variability of IVC decreased as CVP and IVC diameters increased during effective fluid resuscitation. This study concluded that ultrasonographic evaluation of the IVC is a good guide for the assessment of fluid status in children with shock, contrary to many studies with contradictory results in the literature.[16] However, Zhang et al.[17] suggested in their study that the distensibility of IVC diameter in mechanically ventilated patients can only be used with moderate reliability in patients with low CVP, i.e., hypovolaemia, whereas it is not reliable in estimating CVP in patients with normal or high CVP.

In a study conducted on children with spontaneously breathing sepsis, contrary to many studies in the literature, cIVC had very poor test properties in predicting fluid sensitivity. The authors suggested that this was due to the fact that in sepsis, that is, in the presence of systemic inflammation, fluid outflow from the vein is prominent due to marked endothelial dysfunction, and the effect size and duration of the fluid therapy applied are reduced.[18]

Previous studies evaluating the usefulness of IVC diameters and respiratory variability to assess intravascular volume status have been conducted in either spontaneously breathing patients or mechanically ventilated patients, and most of them have been compared with CVP measurement, which is an invasive method. Unlike these studies, we included patients from both groups in our study without making a distinction between spontaneously breathing and mechanically ventilated patients. Therefore, we had the opportunity to conduct a comparison of these two groups. In order to make these comparisons, we needed data other than IVC diameters.

Indeed, in a study of 100 PICU patients aged 1-12 years, a moderate positive correlation was found between PI and blood pressure, while a strong positive correlation was found with pulse rate. Based on the obtained data analysis, they suggested that a 57% decrease in PI could predict shock in children aged 1-12 years. Therefore, they concluded that PI can detect hypovolemia and/or shock long before cardiovascular deterioration occurs.[19]

Based on this information, we preferred to record non-invasive data, including physical examination findings, biochemical markers, PI and PVI, which we use in clinical practice to assess the fluid status of patients, rather than using an invasive method like CVP measurement, which may have complications. Our main starting point was to predict fluid status and fluid responsiveness without resorting to an invasive method unless patients required it.

In our study, 45.2% of patients were receiving MV support in synchronized intermittent mandatory ventilation/pressure support mode accompanied by sedation, while 54.8% were spontaneously breathing in room air without MV support. We found a strong negative correlation between D_{min} and cIVC or dIVC in both groups (r=-0.588, p<0.001; r=-0.520, p=0.005). Both groups had a negative correlation with D_{max}, but only spontaneously breathing patients without MV support had a statistically significant negative correlation with cIVC (r=-0.363, p=0.035). However, PI and PVI were negatively correlated with cIVC in patients without MV support (r=-0.355, p=0.040; r=-0.404, p=0.018). Patients with low PI and PVI had high cIVC values, which may indicate intravascular volume loss. In the mechanically ventilated group, PI, PVI, IVC ultrasonography, and dIVC did not show a statistically significant correlation. Positive pressure may affect IVC diameter and respiratory variability in mechanically ventilated patients.

Miller et al.[13] found that while cIVC isn't better for diagnosing acute heart failure in spontaneously breathing patients with dyspnea, the IVC/aortic ratio can be used with higher specificity in combination with other physical examination findings and laboratory parameters to assess hemodynamic status. In our study, CRT and blood pressure were statistically significantly different in the group that needed fluid loading before hospitalization, and received it, according to the analyses in which physical examination findings were evaluated by patient groups (p=0.025; p=0.039). Compared to a control group, the blood pressure in the fluid-loaded group was lower, and CRT was longer. In addition to physical examination

results, laboratory measures are used to assess peripheral perfusion, organ hypoperfusion, and intravascular status. The lactate level is the most sensitive of these parameters to perfusion disorder. In the presence of hypovolemia, lactate levels increase because lactate clearance decreases. A study found that reduced lactate clearance is a good indication of shock and resuscitation.[20]

Our study related lactate levels to other parameters. Patients with and without chronic disease showed similar lactate levels. MV-supported patients had significantly higher lactate levels than others. For patients who needed and received fluid loading before hospitalization, the volume administered was higher. Lactate levels were higher in patients with fluid deficit and decreased peripheral perfusion (p=0.022), as previously reported. In patients with prolonged CRT and low blood pressure for age, lactate levels were significantly higher than in patients with normal or high blood pressure (p<0.001; p=0.002). Elevated pulse rate patients showed higher lactate levels than normal patients, although not significantly. In conclusion, decreased intravascular volume status led to lactate levels and physical examination findings being similarly affected. Our investigation found similar results for lactate and urea; creatinine; salt; and urine density, all of which should increase with kidney hypoperfusion. This shows that lactate level and IVC diameter are more sensitive fluid status indicators. Lactate level was positively correlated with D_{min}, D_{max}, dIVC/cIVC and negatively correlated with PI and PVI. Only the PVI-lactate correlation was significant (r=-0.272, p=0.033). D_{min}, D_{max}, and dIVC/cIVC are positively associated with urea, creatinine, sodium, and urine density, although only D_{min} and D_{max} were significantly correlated with creatinine (r=0.326, p=0.010; r=0.349, p=0.005). It is thought that this may be due to the limited number of patients in our study.

Study Limitations

Our study contains flaws. The number of patients was insufficient because the study was conducted at one center over a short period. However, ultrasonographic measurements were often performed throughout the day by a single PICU faculty member specialized in this discipline to ensure reproducibility. Another major drawback is that patients who were under 2 years old, spontaneously breathing, and not sedated were prone to *valsalva* during measurements, which took longer and may have compromised dependability.

Conclusion

In our study, IVC diameters were measured ultrasonographically and respiratory variability was calculated. After analyzing these data, we found that cIVC can predict fluid status in spontaneously breathing pediatric patients because IVC diameters don't have a fixed cut-off value. We found that patients with lower blood pressure; prolonged CRT; higher lactate; or lower PI and PVI had higher cIVC. When these results are considered, spontaneously breathing patients with high cIVC (closer to 100%) may have intravascular volume loss.

In contrast, mechanically ventilated patients had statistically significant but modest relationships with various variables, although none were as robust as those of freely breathing patients. We can conclude that positive pressure may affect IVC diameter and respiratory variability in mechanically ventilated patients.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained from Mersin University Clinical Research Ethics Committee, with the board (decision date: 08.01.2020 and decision no: 2020/26).

Informed Consent: Written informed consent was obtained from all the parents before the participants were enrolled in the study.

Footnotes

Authorship Contributions

Concept: A.E.A., Design: A.M.A., A.E.A., M.A., Data Collection or Processing: A.M.A., M.A., Analysis or Interpretation: A.M.A., A.E.A., M.A., S.E., Literature Search: A.M.A., A.E.A., S.E., Writing: A.M.A., A.E.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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