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RESEARCH

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Prognostic value of combined central venous oxygen saturation and lactate in pediatric patients after cardiac surgery

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Abstract

Objectives This study assessed the value of measuring both arterial lactate levels and central venous oxygen saturation (ScvO2) in predicting cardiac surgery outcomes in pediatric patients.

Methods A prospective cohort study was conducted on 73 patients who underwent surgery for congenital heart disease. Vasoactive-inotropic score (VIS), serial mean arterial blood pressures (MAP), lactate levels, and $ScvO_2$ were measured immediately and 3, 6, 12, 18, and 24 h after admission to the pediatric intensive care unit (PICU). To test the prognostic values of these markers, we calculated the areas under the receiver operating characteristic curves (AUCs). Binary logistic regression was used to identify the determinants of postsurgical complications.

Results The most common complications after cardiac surgery were the prolonged need for mechanical ventilation (38.36%), chest infection (30.14%), prolonged stay in the PICU (24.66%), and sepsis (9.59%). ScvO2 6 h after admission was most predictive of complications ($AUC=85.5\%$), followed by ScvO2/lactate ($AUC=83.0\%$), lactate level 12 h after admission ($AUC=75.0\%$), MAP ($AUC=73.6\%$), and VIS ($AUC=63.4$). In multivariate analysis, body weight and ScvO2 6 h after PICU admission were the main predictors of complications ($OR=0.01$, 95% CI 0.001–0.689, $p=0.033$), and ($OR=0.87$, 95% CI 0.798–0.948, $p=0.002$) respectively.

Conclusions To predict complications after pediatric cardiac surgery, lactate measurement does not add value to ScvO2 measurement 6 h after admission.

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Keywords Central venous oxygen saturation, Lactate, Cardiac surgery, Pediatric, PICU stay, Global tissue hypoxia

Background

In humans, oxygen is vital for proper aerobic metabolism. The key metabolic reactions that take place in the mitochondria of cells involve the combination of a fuel (e.g., sugars, fats) with oxygen to create energy, as well as carbon dioxide (CO_2) and water (H_2O) [1]. Hypoxemia is characterized by a drop in the partial pressure of oxygen in the blood, whereas hypoxia is characterized by a decrease in tissue oxygenation [2]. In hypoxia, oxygen is not available sufficiently at the tissue level to maintain proper homeostasis. This can be caused by insufficient

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oxygen transport to tissues due to poor blood supply or low oxygen concentration in the blood as in hypoxemia [3]. Hypoxemia occurs frequently during the early postoperative period in infants who have undergone surgical repair of congenital heart defects. If hypoxemia is not corrected early, it can result in the need for prolonged mechanical ventilation (MV) support, intensive care unit (ICU) stay, and hospital stay. Additionally, uncorrected postoperative hypoxemia can cause multiple organ dysfunction [4]. Hypoperfusion resulting from circulatory deficiencies is characterized by inadequate oxygen delivery to tissues. The degree and duration of hypoperfusion are linked strongly to the development of organ failure [3]. It should be noted that global tissue hypoxia (GTH) is not detected through conventional monitoring of vital signs, such as heart rate, blood pressure, central venous pressure, and urine output [5].

Identifying patients at risk for postoperative complications is challenging, but it would assist physicians and nurses in monitoring and allocating additional resources to certain patients to prevent or quickly address and treat anticipated complications. Low central venous oxygen saturation ($ScvO_2$) and high arterial lactate levels, which are indicators of circulatory problems, have been utilized by clinicians to initiate and improve early hemodynamic treatment [6]. The balance of oxygen supply and demand is measured by $ScvO_2$; it decreases when cardiac output, hemoglobin, or arterial oxygen saturation decreases or when oxygen demand increases due to fever, shivering, agitation, or hypercatabolic state. GTH and lactic acidosis may be the result of disruption of this balance, which may manifest itself with clinical symptoms of hypoperfusion, such as hypotension or oliguria [6, 7]. In surgical patients at high risk for complications, elevated lactate levels have been linked to an increased risk of morbidity and mortality. Lactic acidosis is usually caused by systemic hypoperfusion in severely ill patients; however, it can also be caused by liver disease, thiamine deficiency, epinephrine, other drugs/toxins, or inborn metabolic abnormalities. These causes can affect the specificity of lactate levels to predict circulatory problems [8].

In patients undergoing general and cardiac surgery who are at high risk for complications, the association between low $ScvO_2$ or elevated lactate levels and morbidity/mortality has been extensively explored. The critical values for $ScvO_2$ and lactate in these studies were 60–70% and 2–4 mmol/L, respectively [9–11]. Serial blood lactate levels and the ScvO2/lactate ratio are useful predictors of death within 7 days after laparotomy [12]. Rivers et al. [13] used an increase in lactate levels to identify a subset of patients with severe sepsis and septic shock; this subset was treated early with medications aimed at improving ScvO2, and morbidity and mortality rates were reduced as a result. However, few researchers have investigated the prognostic significance of the combination of low $ScvO_2$ and elevated lactate levels, especially in pediatric patients. We examined whether this combination could better predict complications after cardiac surgery in pediatric patients.

Methods

Sample size

We assumed that the area under the curve (AUC) of lactate levels and $ScvO_2$ that would help predict GTH after cardiac surgery was 0.75 [10]; therefore, the minimal sample size using MedCalc software was 73 (on the basis of a significance level of 95%, a dropout rate of 20%, an alpha error of 0.05, 80% power, and null hypothesis of 50%). We randomly selected 73 children who underwent surgery at a cardiac tertiary referral center in Aswan, Egypt.

Study population and study setting

This prospective cohort study was conducted at a cardiac tertiary referral center in Aswan, Egypt, from August 2020 to March 2021. All patients aged 18 years or younger, on or off cardiopulmonary bypass, and with a central venous catheter in the internal jugular position after cardiac surgery were eligible for inclusion. To ensure that hemodynamic compromise was the only cause of a decrease in $ScvO_2$ or an increase in lactate level, we excluded all children with the following conditions: diseases and conditions that cause impaired lactate metabolism, such as liver failure and sepsis; conditions that cause a high lactate level, such as high adrenaline dose or inotropic support before surgery; conditions that affect oxygen delivery, such as preexisting congestive cardiac failure, cardiomyopathy, hemodynamic instability, or cardiac arrest; conditions that affect oxygen content of the blood, such as perioperative bleeding; preoperative elevation of any laboratory value that indicated systemic hypoperfusion; conditions affecting outcomes of surgery, such as preexisting renal or organ failure; or the need for extracorporeal membrane oxygenation.

Study procedures

Sociodemographic data and anthropometric measures were collected from all study participants. The children's ages were categorized as 1 month or younger, more than 1 month to 1 year, or older than 1 year. Weights of children were plotted on the Egyptian growth chart (weight for age) as being below the 5th percentile; in the 10th, 25th, 50th, or 75th percentile; and above the 95th percentile. After admission to the pediatric intensive care unit (PICU), all patients underwent a complete clinical examination, and the extensive medical history was collected from their caregivers or relatives. Information about operative details and events was obtained from surgeons and anesthesiologists. Routine laboratory data were obtained at PICU admission and every 24 h: complete blood cell count, coagulation profile, kidney function test and urinary output, liver function test, and C-reactive protein level. Serial lactate levels and $ScvO_2$ were measured from arterial and central venous lines, respectively, immediately and 3, 6, 12, 18, and 24 h after PICU admission. Serial mean arterial blood pressure (MAP) was measured immediately and 3, 6, 12, 18, and 24 h after PICU admission. The vasoactive-inotropic score (VIS) was calculated for each patient according to the following formula [14]: VIS = dopamine (μg/kg/min) + dobutamine (μg/kg/min) + 100 × epinephrine (μg/kg/min) + 100 × norepinephrine (μg/kg/min) + 10 × milrinone (μg/kg/min) + 10,000 × vasopressin (mU/kg/min). Moderate GTH was defined as $ScvO_2$ of < 70% and lactate level between ≥ 2 and < 4 mmol/L, and severe GTH was defined as $ScvO_2$ of < 70% and lactate level of ≥ 4 mmol/L). Cryptic hypoperfusion was defined as moderate or severe GTH with normal macrohemodynamic parameters [15].

Outcomes

Complications included the need for prolonged PICU stay (≥ 14 days), prolonged MV (≥ 72 h), major adverse events (chest infection, sepsis, cardiac arrest, neurological deficit, acute kidney injury, and the need for surgical re-exploration), the need for extracorporeal membrane oxygenation, and inhospital mortality. Therefore, the patients were classified as those with and without complications.

Statistical analysis

Data for continuous numerical variables were calculated as means and standard deviations. In case of skewed data, medians and interquartile ranges were calculated instead. Categorical data were presented in the form of numbers and percentages. To predict postoperative complications, we used receiver operating characteristic curve (ROC) analysis and the Youden index to examine the prognostic value of serum lactate level, $ScvO_2$, MAP, and inotropic score [16]. To assess the relationship between $ScvO_2$, lactate level and complications, we performed Pearson's correlation analysis. The chi-square test (χ^2) was used to evaluate the associations between categorical variables. We performed binary logistic regression analysis to calculate odds ratio (OR) and 95% confidence interval (CI) for each variable to assess the variables that predicted complications (outcome); weight, lactate level, MAP, inotropic score, and $ScvO_2$ were examined as independent covariates (predictors). We considered p-values of < 0.05 statistically significant. We created nomograms to allow for a preliminary visual assessment of the risk and severity of postoperative complications. For data analysis, we used SPSS Statistics, version 26 (IBM Corporation, Armonk, NY, USA), and Stata 17.0 (Stata Corp. LLC, College Station, TX, USA).

Results

Sociodemographic and laboratory findings

Of the 73 children included in this study, 51 (69.86%) were male, 33 (45.21%) were 1 month old or younger, 15 (20.55%) were older than 1 month and younger than 1 year, and 25 (34.24%) were older than 1 year. The weights of 25 (34.25%) were below the 5th percentile (Table 1).

The complete blood cell count was within normal except for the mean platelet count ($117.51 \pm 9.25 \times 10^3$/μL), which was below the normal range. Similarly, the biochemical profile was normal except for the mean level of aspartate aminotransferase (121.29 ± 8.26 U/L), which was above the normal range. The mean complexity score was 8.86 ± 2.67, and the mean inotropic score was 12.73 ± 8.20. Total surgical repair was performed in 59 patients (90.8%), and 14 (19.2%) underwent palliative surgical intervention (Supplementary Table S1).

Complications after cardiac surgery

Complications developed in 35 patients (49.95%). The most common complication after cardiac surgery was the need for prolonged MV (38.36%), chest infection (30.14%), prolonged stay in the PICU (24.66%), and sepsis (9.59%) (Supplementary Figure S1).

Table 1 Patients' sociodemographic features ($n = 73$)

Variable (total $n = 73$)	Number
Sex	
Male	51 (69.86%)
Female	22 (30.14%)
Age	
≤ 1 month	33 (45.21%)
> 1 month to ≤ 1 year	15 (20.55%)
> 1 year	25 (34.25%)
Weight (kg), mean ± SD	8.32 ± 0.90
Below 5th percentile	25 (34.25%)
10th percentile	13 (17.81%)
25th percentile	12 (16.44%)
50th percentile	16 (21.92%)
75th percentile	5 (6.85%)
Above 95th percentile	2 (2.74%)
Height (cm), mean ± SD	70.3 ± 3.2

Correlation between $ScvO_2$, arterial lactate level, and complications after cardiac surgery

To study the correlation between lactate levels and different outcomes, different measures of lactate were compared with hospital stay (LOS), PICU LOS, MV duration, and inotropic duration. Baseline lactate levels were significantly and positively correlated with MV duration ($r=0.24$, $p<0.5$) and inotropic score ($r=0.25$, $p<0.05$) (Supplementary Tables S2, S3).

Role of $ScvO_2$, arterial lactate level, vasoactive-inotropic score, and mean arterial blood pressure in predicting complications after cardiac surgery

$ScvO_2$ measured 6 h after PICU admission had the highest AUC (85.5%; $p<0.001$), with 81.6% sensitivity and 82.9% specificity for predicting complications, a positive predictive value (PPV) of 83.8%, and a negative predictive value (NPV) of 80.6%. Lactate measured 12 h after PICU admission had an AUC of 75.0% ($p<0.001$), with 63.2% sensitivity and 82.0% specificity, a PPV of 80.0%, and an NPV of 67.4%. The ratio of $ScvO_2$ 6 h after admission to lactate level 12 h after admission had a sensitivity of 68.4% and specificity of 80.0% in predicting complications (*AUC* 83.0%, $p<0.001$). MAP 18 h after admission had an AUC of 73.6% ($p<0.001$), with 42.1% sensitivity, 97.1% specificity, a PPV of 94.1%, and an NPV of 60.7%. The inotropic score had the lowest AUC of (63.4%; $p<0.001$), with 92.1% sensitivity, 40.0% specificity, a PPV of 62.5%, and a NPV of 82.4% (Table 2). The ROC showed that the best predictors were central venous oxygen saturation (ScvO2) 6 h after admission to the PICU (ScvO2_6) followed by arterial lactate level 12 h after admission to the PICU (Lactate_12), ScvO2/lactate ratio, mean arterial pressure (MAP) 18 h after admission to the PICU (MAP_18), and VIS (Fig. 1).

Predictors of complications after cardiac surgery

The incidence of complications was highest among children between the ages of one month and one year (78.79%) in comparison with children between the ages of one month and one year (33.33%) and children older than 1 year (16.00%; $p<0.001$). The mean $ScvO_2$ measured 12 h after admission was significantly higher among patients with complications (64.74 ± 11.74) than among those without complications (49.14 ± 11.74; $t=5.86$, $p<0.001$). Furthermore, the mean arterial blood pressure measured after 18 h from admission (66.42 ± 13.33 mm Hg) was higher in patients without complications than in those with complications (56.06 ± 8.10 mm Hg; $t=4.03$, $p=0.001$). The mean inotropic score was lower in patients without complications (0.29 ± 0.46) than in those with complications (0.54 ± 0.51; $t = -2.24$ $p=0.029$), as was the mean lactate level (1.87 ± 0.90 mmol/L vs 2.62 ± 1.49 mmol/L, respectively; $t = -2.58$, $p=0.012$). Neither sex nor patient weight was significantly associated with complications between the studied groups (Table 3).

The regression model was well-calibrated (Table 4). The Hosmer–Leeshawn chi-square value was 4.61 ($p=0.59$), and the overall model was statistically significant ($\chi^2=48.29$, $p<0.001$). The predictive capacity of the model increased from 52.80 to 86.10%. $ScvO_2$ measured 6 h after admission was a significant predictor of complications. The OR decreased by 0.87 (95% *CI* 0.798–0.948, $p = 0.002$) for each increase in $ScvO_2$ by 1%. Weight was a statistically significant predictor of the incidence of complications (*OR* 0.01; 95% *CI* 0.001–0.689; $p=0.033$). The AUC of the developed logistic regression

Table 2 Validity and performance of specific measurements and vasoactive-inotropic score in predicting complications after cardiac surgery in pediatric patients

Measurement	AUC	Cutoff	*p*-value	Sensitivity	Specificity	PPV	NPV	PLR	NLR
$ScvO_2$ 6 h after PICU admission	85.5	58.0	< 0.001	81.6% (65.7–92.3%)	82.9% (66.4–93.4%)	83.8% (67.8–93.3%)	80.6% (64.2–92.4%)	4.75% (2.26–10.01%)	22.2% (11.2–44.1%)
Lactate level 12 h after PICU admission	75.0	1.3	< 0.001	63.2% (46.0–78.2%)	82.0% (66.4–93.4%)	80.0% (62.0–89.3%)	67.4% (50.7–85.9%)	3.68% (1.71–7.93%)	44.5% (28.6–69.2%)
$ScvO_2$/lactate ratio	83.0	38.3	< 0.001	68.4% (51.3–82.5%)	80.0% (63.1–91.6%)	78.8% (61.3–89.0%)	70.0% (53.2–86.4%)	3.42% (1.7–6.9%)	0.40% (0.2–0.7%)
VIS	63.4	15.0	< 0.001	92.1% (78.6–98.3%)	40.0% (23.9–57.9%)	62.5% (43.9–89.4%)	82.4% (59.5–90.6%)	1.54% (1.2–2.0%)	19.7% (6.2–62.9%)
MAP 18 h after PICU admission	73.6	72.0	< 0.001	42.1% (26.3–59.2%)	97.1% (85.1%–99.9%)	94.1% (72.9–97.0%)	60.7% (43.1–98.4%)	14.74% (2.1–105.4%)	59.6% (45.2–78.6%)

AUC area under the curve, *PPV* positive predictive value, *NPV* negative predictive value, *PLR* positive likelihood ratio, *NLR* negative likelihood ratio, *VIS* vasoactive-inotropic score, *$ScvO_2$* central venous oxygen saturation, *PICU* pediatric intensive care unit, *MAP* mean arterial pressure

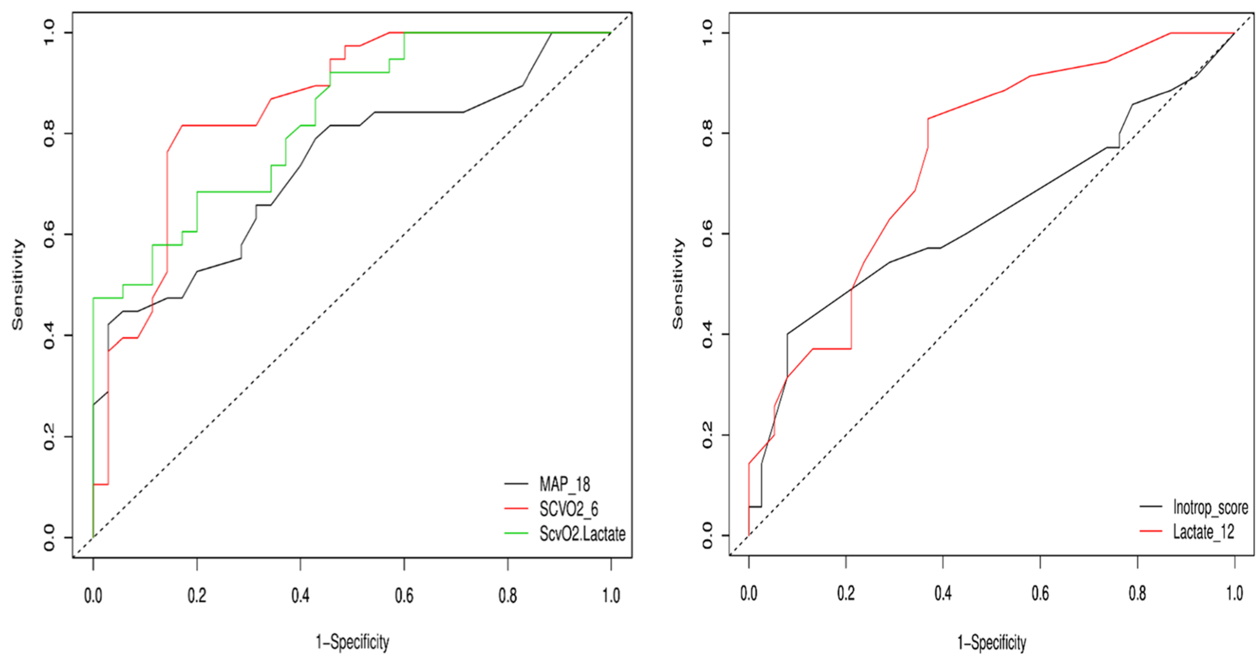

Fig. 1 Receiver operating characteristic curves of predictors of complications after cardiac surgery. The best predictors were central venous oxygen saturation (ScvO2) 6 h after PICU admission (ScvO2_6) followed by arterial lactate level 12 h after PICU admission (Lactate_12), ScvO2/lactate ratio, mean arterial pressure (MAP) 18 h after PICU admission (MAP_18), and VIS

Table 3 Baseline laboratory findings as predictors of complications

Variable ($n = 73$)	Patients with complications ($n = 35$)	Patients without complications ($n = 38$)	Test statistic	*p-value*
Sex (*n*)			0.053	0.817
Male ($n = 51$)	24 (47.06%)	27 (52.94%)		
Female ($n = 22$)	11 (50.00%)	11 (50.00%)		
Age (*n*)			24.08	< 0.001
≤ 1 month ($n = 33$)	26 (78.79%)	7 (21.21%)		
1 month to 1 year ($n = 15$)	5 (33.33%)	10 (66.67%)		
> 1 year ($n = 25$)	4 (16.00%)	21 (84.00%)		
Weight, kg (*n*)			6.05	0.262
Below 5th percentile ($n = 15$)	12 (48.00%)	13 (52.00%)		
10th percentile ($n = 13$)	9 (69.23%)	4 (30.77%)		
25th percentile ($n = 12$)	6 (50.0%)	6 (50.0%)		
50th percentile ($n = 16$)	4 (25.00%)	12 (75.00%)		
75th percentile ($n = 5$)	3 (60.00%)	2 (40.00%)		
Above 95th percentile ($n = 2$)	1 (50.00%)	1 (50.00%)		
$ScvO_2$ 12 h after PICU admission (mean ± SD)	49.14% ± 11.74%	64.74% ± 11.74%	5.86	< 0.001
Lactate level 6 h after PICU admission (mean ± SD)	2.62 ± 1.49 mmol/L	1.87 ± 0.90 mmol/L	− 2.58	0.012
MAP 18 h after PICU admission (mean ± SD)	56.06 ± 8.10 mm Hg	66.42 ± 13.33 mm Hg	4.03	0.001
Vasoactive-inotropic score (mean ± SD)	0.54 ± 0.51	0.29 ± 0.46	− 2.24	0.029
Aortic clamp time (mean ± SD)	89.60 ± 52.26 min	84.76 ± 50.80 min	0.4	0.690

CVP central venous pressure, *MAP* mean arterial pressure, *PICU* pediatric intensive care unit, $ScvO_2$ central venous oxygen saturation, *SD* standard deviation

Table 4 Multivariable regression analysis of predictors of postoperative complications

Predictor	*p*-value[a]	OR	95% *CI* (lower–upper)
Constant	0.042	5826.02	
Inotropic score	0.127	1.10	0.974–1.237
$ScvO_2$ 6 h after PICU admission	**0.002**	0.87	0.798–0.948
Weight	0.267		
Above 95th percentile[R]		1	
Below 5th percentile	0.200	0.08	0.002–3.872
10th percentile	0.334	0.13	0.002–8.070
25th percentile	0.235	0.09	0.002–4.631
50th percentile	**0.033**	0.01	0.0001–0.689
75th percentile	0.237	0.04	0.000–7.884
Age	0.300		
> 1 year[R]		1	
≤ 1 month	0.210	4.91	0.408–59.159
1 month to 1 year	0.852	0.82	0.105–6.433
Lactate level 6 h after PICU admission	0.719	0.86	0.391–1.911
MAP 18 h after PICU admission	0.899	1.01	0.912–1.110

$ScvO_2$ central venous oxygen saturation, *PICU* pediatric intensive care unit, *MAP* mean arterial blood pressure. [a]significant values are in boldface

[R] Reference

model was 92%, $p<0.001$ (Supplementary Figure S2). The nomogram for calculating the probability that complications would develop after cardiac surgery is depicted in (Supplementary Figure S3).

Discussion

We evaluated whether measuring arterial lactate level in addition to $ScvO_2$ would improve the prediction of complications after pediatric cardiac surgery among 73 patients admitted to a cardiac tertiary referral center in Aswan, Egypt. In this study, 35 patients (49.95%) developed complications. The most common complications after cardiac surgery were prolonged MV, chest infection, prolonged PICU LOS, and sepsis. In addition to age, $ScvO_2$ measured 6 h after PICU admission, blood lactate level measured 12 h after PICU admission, and MAP measured 18 h after PICU admission were significantly associated with complications. Furthermore, all of these markers had good validity in predicting complications after cardiac surgery. However, multivariate regression analysis revealed that $ScvO_2$ and weight were the only predictors of complications after cardiac surgery.

The demand for tools to predict complications after cardiac surgery is not new. Research has focused on lactate clearance, duration of high lactate levels, duration of cardiopulmonary bypass, inflammatory markers, and other indicators, with an emphasis on predicting low cardiac output syndrome; however, no optimal prognostic method has been established [17]. A study of the role of pro-inflammatory cytokines in inducing cardiac injury after arterial switch procedure in 63 newborns revealed that cardiac troponin T, interleukin-6, and interleukin-8 levels were higher in patients who developed low cardiac output syndrome [18].

In our study, we observed that all measured lactate levels and $ScvO_2$ during the first 24 h after admission were significantly correlated with hospital LOS, PICU LOS, duration of MV, and duration of inotropic support. To best predict clinical outcomes, the optimal times to measure lactate levels and $ScvO_2$ are 12 and 6 h after admission to the PICU, respectively. Maillet et al. [19] found that compared to patients whose lactate levels were < 3 mmoL/L, those with lactate levels > 3 mmoL/L on ICU had considerably longer durations of both MV and LOS of the ICU, as well as an increased mortality rate. In a large study ($n=1820$), Kogan et al. [20] found that a maximum lactate level of 4.4 mmol/L during the first 10 h after admission to the ICU was associated with prolonged MV, prolonged LOS in the ICU, and an increased rate of mortality. Similarly, Pearse et al. [9] found that the rate of complications was considerably higher among patients with a $ScvO_2$ of < 64.4% during the first 8 h after surgery than among those with a higher $ScvO_2$. On the other hand, lactate levels in patients with and without complications were < 2 mmoL/L; the two groups did not differ significantly. Of note, $ScvO_2$ and lactate measurements play an important role in the diagnosis of occult hypoperfusion. In individuals with normal macrohemodynamics, occult hypoperfusion is characterized as moderate to severe GTH with a mean arterial pressure of 65 mmHg, a mean central venous pressure of 8 mmHg, and mean urine output of 0.5 mL/kg/h [15]. Hu et al. [10] found that on admission to the ICU, 19 patients (32%) had occult hypoperfusion. GTH was found in 21 individuals (35%): 13 (22%) had moderate GTH and 8 (13%) had severe GTH.

In our study, arterial lactate level 12 h after PICU admission had 63.2% sensitivity and 82.0% specificity for predicting postsurgical complications, $ScvO_2$ had 81.6% sensitivity and 82.9% specificity, VIS had 92.1% sensitivity and 40.0% specificity, and MAP measured 18 h after PICU admission had 97.1% sensitivity and 94.1% specificity. Similarly, Gaies et al. [20] reported that the maximum VIS estimated during the first 24 h after cardiac PICU admission was significantly associated with morbidity and death. A maximum VIS of ≥ 20 indicates a higher risk of a bad composite clinical outcome. Seear and his colleagues [21] found that arterial lactate and ScvO2 levels were the only postoperative measures that could predict serious adverse outcomes after cardiac operations in pediatric patients. Moreover, the $ScvO_2$/lactate ratio appeared to have better predictive value: when the ratio was < 5, the PPV for complications was 93.8%, with 78.9% sensitivity and 90.5% specificity. Each measurement separately had high specificity but limited sensitivity. Single-measure predictive power was of only fair quality, but it could have been increased for patients at high risk of complications by tracking repeated measures over time 0.986.

Rocha et al. (2021) [22] found that, overall, the $ScvO_2$/lactate ratio distinguished patients with and without major adverse events very effectively ($AUC = 84\%$), outperforming either variable alone, with 48% sensitivity, 94% specificity, 60% PPV, and 91% NPV. However, when we calculated the ratio of $ScvO_2$ 6 h after PICU admission and lactate level 12 h after PICU admission, the AUC did not improve. Moreover, when we included all significant variables in the bivariable analysis, in addition to weight, the regression model showed that $ScvO_2$ and weight were the only significant predictors of complications, with an AUC of 92%. This finding may be attributable to the correlation between $ScvO_2$ and lactate. Bisaya and his colleagues [23] found that when ScvO2 was 65%, arterial lactate level was weakly correlated with $ScvO_2$ ($r^2 = 0.0431$, $p < 0.001$), whereas they were strongly correlated in individuals with an O_2 extraction ratio of 50% ($r^2 = 0.93$, $p = 0.0019$). Of note, about one-third of patients studied by Bisarya et al. had a $ScvO_2$ of 50% or less. In our study, approximately one-third of the patients had a $ScvO_2$ 6 h after PICU admission of ≤ 50 which explains the high correlation between arterial lactate and $ScvO_2$.

In this study, we found that one of the main predictors of postoperative complications was the weight of the patient. Similarly, an examination of demographic data, preoperative results, and surgical details of the population, patients with serious postoperative morbidity: they were considerably with younger age, weighed less, and had higher Aristotle scores [24]. This finding can be explained by the fact that these conditions are associated with poor growth and development. In contrast, Seear et al. [21] reported that both body weight and duration of circulatory arrest were weak predictors of complications, but they were not predictors at every measured time point.

Strengths and limitations

To the best of our knowledge, this study is one of the first in pediatrics to determine the prognostic value of using combined markers in the prediction of complications after cardiac surgery. In this study, we obtained serial measurements of both markers and determined measurement times that were most strongly correlated with the outcomes. Additionally, the prospective nature of the study reduces the bias of missing data and allows intensive clinical and laboratory follow-up of the patients. However, this study had limitations. First, the significant heterogeneity of heart conditions and surgeries limits generalizability to other centers and populations; as a result, our findings must be interpreted with care. Actually, we included patients with different categories of congenital heart disease: some were acyanotic (VSD, ASD, coarctation of the aorta), and others were cyanotic of whom some have total correction (as arterial switch for patients with TGA and total correction of tetralogy of Fallot), and the others had only palliative repair (shunt for patients with complex congenital heart and Glenn for patients with single ventricle physiology); all these would have different baseline saturation and different oxygen delivery and consequently different ScVo2 and lactate owing to different degrees of mixing due to residual shunting, or amount of shunting is dependent on the patient's hemodynamics as MAP and pulmonary vascular resistance PVR that are continuously changing according to different conditions and other variables (fever, sedation, over or under shunting). Another limitation was the different age categories; we had different age groups with different physiology, age, weight, and hemodynamic parameters as blood pressure that could not be accounted for, so we strongly recommend further research in every age category to avoid these limitations. Finally, this study was a single-center observational study; future multicenter studies are mandatory to provide more robust evidence.

Conclusion

In pediatric patients admitted to the PICU after cardiac surgery, $ScvO_2$ measured 6 h after admission can predict the risk of complications and allow early initiation of therapy to achieve better outcomes. In this study, monitoring of lactate levels and $ScvO_2$ facilitated rapid identification of hypoperfusion in pediatric patients after cardiac surgery. Our findings support the use of $ScvO_2$ levels to detect hypoperfusion that would otherwise go unnoticed by conventional monitoring, thereby preventing the worsening of hypoperfusion and the development of organ failure. However, more research is necessary to determine the efficacy of lactate levels and $ScvO_2$ in guiding hemodynamic management and their effect on morbidity and mortality in pediatric patients after cardiac surgery.

Abbreviations

AUC	Area under the curve
CI	Confidence interval
CPB	Cardiopulmonary bypass
CVP	Central venous pressure
GTH	Global tissue hypoxia
LCOS	Low cardiac output syndrome
LOS	Length of stay
MAP	Mean arterial blood pressure
MV	Mechanical ventilation
NPV	Negative predictive value
OR	Odds ratio
PICU	Pediatric intensive care unit
PPV	Positive predictive value
ROC	Receiver operating characteristic
$ScvO_2$	Central venous oxygen saturation
VIS	Vasoactive-inotropic score

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s43054-023-00230-6.

Additional file 1: Fig. S1. Complications that developed after cardiac surgery. ECMO, extracorporeal membrane oxygenation; LOS, length of stay; MV, mechanical ventilation; PICU, pediatric intensive care unit. **Fig. S2.** Receiver operating characteristic (ROC) curve of the developed logistic regression model. **Fig. S3.** Nomogram of the predictors of postoperative complication after cardiac surgery in pediatric patients. **Table S1.** Laboratory results in 73 children with cardiac diseases. **Table S2.** Correlation between serial measurements of lactate levels and $ScvO_2$ and complications (n = 73). **Table S3.** Complication across different age groups.

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Authors' contributions

All authors contributed to the study's conception and design. Material preparation and data collection were performed by AH and review and editing AA, RG, MH, and AH. The first draft of the manuscript and statistical analysis were performed by RG, conceptualization and supervision by FE and AA, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data are available by request from first author.

Declarations

Ethics approval and consent to participate

The study was approved by the ethical committee of the Faculty of Medicine, Menoufia University Ethical Committee. Date 08/2020, no. PEDI-27 Written informed consent was obtained from the parents of all individual participants included in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

1. West JB. Respiratory physiology: the essentials. 2012: Lippincott Williams & Wilkins.
2. Sarkar M, Niranjan N, Banyal P (2017) Mechanisms of hypoxemia. Lung India Off Organ Indian Chest Soc 34(1):47
3. Bhutta BS, Alghoula F, Berim I. Hypoxia. In: StatPearls. 2022, StatPearls Publishing.
4. Wang Y, Xue S, Zhu H (2013) Risk factors for postoperative hypoxemia in patients undergoing Stanford A aortic dissection surgery. J Cardiothorac Surg 8(1):1–7
5. Martin ND et al (2020) Contemporary hemodynamic monitoring, fluid responsiveness, volume optimization, and endpoints of resuscitation: an AAST critical care committee clinical consensus. Trauma Surg Acute Care Open 5(1):e000411
6. Shanmukhappa C, Lokeshwaran S. Venous oxygen saturation. 2020.
7. Futier E et al (2010) Central venous O_2 saturation and venous-to-arterial CO_2 difference as complementary tools for goal-directed therapy during high-risk surgery. Crit Care 14(5):R193
8. Kraut JA, Madias NE (2014) Lactic acidosis. N Engl J Med 371(24):2309–2319
9. Pearse R et al (2005) Changes in central venous saturation after major surgery, and association with outcome. Crit Care 9(6):1–6
10. Hu BY et al (2012) Combined central venous oxygen saturation and lactate as markers of occult hypoperfusion and outcome following cardiac surgery. J Cardiothorac Vasc Anesth 26(1):52–57
11. Mohammadien HA, El-Shafay MM, Hossien MT (2017) Study of the predictive role of central venous oxygen saturation in acute type I respiratory failure patients. Sohag Med J 21(3):469–476
12. Salem G et al (2021) Central venous oxygen saturation/lactate ratio: a novel predictor of outcome following emergency open laparotomy. Eur J Trauma Emerg Surg 47(2):353–363
13. Rivers E et al (2001) Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 345(19):1368–1377
14. Gaies MG et al (2010) Vasoactive–inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. Pediatr Crit Care Med 11(2):234–238

15. Rivers EP et al (2007) The influence of early hemodynamic optimization on biomarker patterns of severe sepsis and septic shock. Crit Care Med 35(9):2016–2024
16. López-Ratón M et al (2014) Optimalcutpoints: an R package for selecting optimal cutpoints in diagnostic tests. J Stat Softw 61:1–36
17. Attanà P et al (2012) Lactate and lactate clearance in acute cardiac care patients. Eur Heart J Acute Cardiovasc Care 1(2):115–121
18. Hövels-Gürich HH et al (2002) Production of proinflammatory cytokines and myocardial dysfunction after arterial switch operation in neonates with transposition of the great arteries. J Thorac Cardiovasc Surg 124(4):811–820
19. Maillet J-M et al (2003) Frequency, risk factors, and outcome of hyperlactatemia after cardiac surgery. Chest 123(5):1361–1366
20. Gaies MG et al (2014) Vasoactive-inotropic score (VIS) is associated with outcome after infant cardiac surgery: an analysis from the Pediatric Cardiac Critical Care Consortium (PC4) and virtual PICU system registries. Pediatr Crit Care Med 15(6):529
21. Seear MD, Scarfe JC, LeBlanc JG (2008) Predicting major adverse events after cardiac surgery in children. Pediatr Crit Care Med 9(6):606–611
22. Rocha VHS, Manso PH, Carmona F (2021) Central venous oxygen saturation/lactate ratio and prediction of major adverse events after pediatric heart surgery. Braz J Cardiovasc Surg 36:736–742
23. Bisarya R et al (2019) Serum lactate poorly predicts central venous oxygen saturation in critically ill patients: a retrospective cohort study. J Intensive Care 7(1):1–8
24. Ranucci M et al (2010) Central venous oxygen saturation and blood lactate levels during cardiopulmonary bypass are associated with outcome after pediatric cardiac surgery. Crit Care 14(4):1–10

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