Associations between oxygen delivery and cardiac index with hyperlactatemia during cardiopulmonary bypass

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ABSTRACT

Objective: Metabolism management plays an essential role during cardiopulmonary bypass (CPB). There are different metabolic management devices integrated to heart-lung machines; the most commonly used and accepted metabolic target is indexed oxygen delivery (DO2i) (280 mL/min/m²) and cardiac index (CI) (2.4 L/min/m²), which can be managed independently or according to other metabolic parameters. Our objective was to compare lactate production during CPB procedures using different metabolic management: DO2i in relation to indexed oxygen extraction ratio (O2ERi) and CI in relation to mixed venous oxygen saturation (SvO2).

Methods: Data on 500 CPB procedures were retrospectively collected in a specialized regional tertiary cardiac surgery center in Italy between September and 2012 and November 2019. In group A, the DO2i with 280 mL/min/m² target in relation to O2ERi 25% was used; in group B, CI with 2.4 L/min/m² target in relation to SvO2 75% was used. During CPB, serial arterial blood gas analyses with blood lactate and glucose determinations were obtained. Hyperlactatemia (HL) was defined as a peak arterial blood lactate concentration $>$ 3 mmol/L. The postoperative outcome of patients with or without HL was compared.

Results: Eight pre- and intraoperative factors were found to be significantly associated with peak blood lactate level during CPB at univariate analysis. HL ($>$ 3 mmol/L) was detected in 15 (6%) patients of group A and in 42 (16.8%) patients of group B ($P = .022$); hyperglycemia ($>$ 160 mg/dL) was found in 23 (9.2%) patients of group A and in 53 (21.2%) patients of group B ($P = .038$). Patients with HL during CPB had a significant increase in serum creatinine value, higher rate of prolonged mechanical ventilation time and intensive care unit stay. A cutoff of DO2i $<$ 270 mL/min/m² in relation to O2ERi $>$ 35% in group A and a cutoff of CI $<$ 2.4 L/min/m² in relation to SvO2 $<$ 65% in group B were found to have a positive predictive value of 80% and 75% for HL, respectively. A cutoff of DO2i $>$ 290 mL/min/m² in relation to O2ERi 24% in group A and a cutoff of CI $>$ 2.4 L/min/m² in relation to SvO2 $>$ 75% in group B were found to have a negative predictive value of 78% and 62% for HL, respectively.

Conclusions: This retrospective observational analysis showed that management of DO2i in relation to O2ERi was 16% more specific in terms of negative predictive value for HL during CPB compared with the use of CI in relation to SvO2. Group A reported a significant reduction in the incidence of intraoperative lactate peak, correlated with postoperative reduction of serum creatinine value, mechanical ventilation time, and intensive care unit stay, compared with group B. (JTCVS Techniques 2020;2:92-9)

CENTRAL MESSAGE

This study showed that management of indexed oxygen delivery in relation to indexed oxygen extraction ratio was more specific in terms of negative predictive value for hyperlactatemia during cardiopulmonary bypass compared with cardiac index and mixed venous oxygen saturation.

PERSPECTIVE

The management of indexed oxygen delivery in relation to indexed oxygen extraction ratio follow the cardiopulmonary bypass was more specific in terms of negative predictive value for hyperlactatemia compared to the use of cardiac index in relation to mixed venous oxygen saturation. That management can correlate with postoperative better outcome especially in terms of serum creatinine, mechanical ventilation time, and intensive care unit stay.

See Commentaries on pages 100 and 102.

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During cardiac surgery with cardiopulmonary bypass (CPB) in adult patients, hyperlactatemia (HL) is detectable at a considerable rate (10%-20%)\(^1,2\) and is associated with postoperative morbidity and mortality.\(^3\) At present, the nature of HL during and after cardiac operations is not totally clear, but the majority of authors\(^3-6\) tend to attribute this finding to tissue hypoxia (type A HL) even if type B HL (without tissue hypoxia) has been advocated in some cases.\(^7-9\) The main factors leading to a possible organ dysxia during CPB are the hemodilution degree\(^10\) and a low peripheral oxygen delivery.\(^1,2,4-6,10-12\) In the state of perfusion, there are different metabolic management devices integrated to the heart–lung machine (eg, Quantum Spectrum [Spectrum Medical, Cheltenham, England], Connect Livanova [London, England], CDI Terumo Medical, Vaughan, Ontario, Canada), Landing Eurosets [Medolla, Italy]), with multiple measured and calculated parameters; the most commonly used and accepted metabolic target for the scientific community is the value of indexed oxygen delivery (DO\(_{2i}\)) (280 mL/min/m\(^2\)) and the cardiac index (CI) (2.4 L/min/m\(^2\)). These parameters can be managed independently or according to other metabolic parameters (eg, hemoglobin [Hb], vascular resistance, temperature, and diuresis), resulting in wide variability in CPB management of each center.

This study has the objective to compare lactate production during CPB procedures using different metabolic management: DO\(_{2i}\) in relation to indexed oxygen extraction ratio (O\(_2\)ER\(_i\)) (group A), and CI in relation to mixed venous oxygen saturation (SvO\(_2\)) (group B) (Video 1).

**MATERIALS AND METHODS**

**Population and Study Design**

This study presents a comparative retrospective analysis that has been carried out between 2 historical times: the first historical period (2012-2015) used conventional extracorporeal circulation with blood gas test for metabolic management during CPB; the second historical period (2016-2019) used conventional extracorporeal circulation with blood gas test and the integration with metabolic parameter monitoring system. Between September 2012 and November 2019, 500 adults aged >28 to 80 years were collected for elective cardiac surgery procedures, without chronic kidney failure and with calculated European System for Cardiac Operative Risk Evaluation II score (mean value, 4.1%±4.5%). At our institution (Department of Cardiothoracic Surgery, Anthea Hospital, Bari, Italy), the study protocol was approved by the local ethics committee and all patients provided written consent to scientific treatment of their data. Patients were divided into 2 groups for CPB metabolic management: in group A (study group, n = 250), the DO\(_{2i}\) target with a target of 280 mL/min/m\(^2\) was used in relation to O\(_2\)ER\(_i\); in group B (control group, n = 250), the CI target with a target of 2.4 L/min/m\(^2\) was used in relation to SvO\(_2\).

**Data Collection**

Patients were selected according to the following criteria:

- Elective, primary cardiac surgery: complete CPB and cardioplastic arrest had to be foreseen with an expected CPB duration >90 minutes.
- Patients were excluded if they presented abnormal plasma lactate levels (>2 mmol/L) before entering CPB, renal or liver failure, obesity, uncompensated diabetes, autoimmune disease, active infection, any immunosuppressant therapy, or coagulation disorder. Patients undergoing surgery with circulatory arrest or having preoperative hematocrit (Hct) <27% were also excluded.

The cardiac surgery procedures that were analyzed for this study are coronary artery bypass graft (n = 200), isolated aortic valve replacement (n = 100) and mitral valve repair with minimally invasive approach (n = 200).

Preoperative data included patient demographic characteristics, baseline serum creatinine levels, ventricular ejection fraction, comorbidities (eg, chronic obstructive pulmonary disease or previous cerebrovascular accident), baseline Hb, logistic European System for Cardiac Operative Risk Evaluation II score and New York Heart Association functional class.\(^2\)

Perioperative data included type of operation, CPB duration, nadir body temperature during CPB, nadir Hct and Hb values (measured at the start of the CPB operation and every 20 minutes thereafter), nadir DO\(_{2i}\), nadir DO\(_2\)/O\(_2\)ER\(_i\) ratio during CPB, nadir CI, nadir CI/SvO\(_2\), peak serum lactate, and glucose during CPB. Postoperative data included peak serum creatinine, mechanical ventilation time, and days spent in the intensive care unit (ICU).

The primary end points were specificity and sensitivity, positive and negative predictive value for HL between target DO\(_{2i}\) in relation to O\(_2\)ER\(_i\) during CPB with the control group in terms of
intraoperative lactate and glycemia trends. Secondary end points were peak postoperative serum creatinine level, mechanical ventilation time, and length of ICU stay.

Anesthetics and Surgical Procedures

Patients were monitored with 5-lead electrocardiography, a left radial artery catheter, capnography, pulse oximetry, and rectal/urine bladder temperature sensors. Transesophageal echocardiography was performed in all patients. Anticoagulant therapy consisted of heparin sodium before CPB at a dose of 300 IU/kg to give an activated clotting time of >250 seconds. The surgical procedures were performed as routine by 2 surgeons. Pericardial blood was collected separately and could be processed or reinjected, if needed. The hard shell and soft shell resuscitation, and surgical procedures were performed as routine by 2 surgeons. Concentrated red blood cells were transfused whenever Hb concentrations fell below 6 g/dL during surgery or below 8 g/dL during ICU stay.

**CPB Setting**

Both open (Admiral; Remo-well Eurosets; EOS Dideco; Mirandola, Italy; Inspire 6F; LivaNova) and closed circuits (Closed Eurosets) were used for CPB. Pericardial blood was collected separately and could be processed or reinjected, if needed. The hard shell and soft shell resuscitation, and surgical procedures were performed as routine by 2 surgeons. Concentrated red blood cells were transfused whenever Hb concentrations fell below 6 g/dL during surgery or below 8 g/dL during ICU stay.

**Metabolic Management During CPB in Group A**

In group A, DO₂ with a target of 280 mL/min/m² was managed in relation to O₂ER, the cutoff for increase in DO₂ was >25% O₂ER, the cutoff for decrease in DO₂ was <25% O₂ER. DO₂ and O₂ER-related measurements were performed using a Landing system provided by Eurosets. Data were collected every 5 seconds during CPB. Data required to calculate bypass graft procedures were performed in median sternotomy with central cannulation, MVR in right minithoracotomy approach with peripheral cannulation, and surgical procedures were performed as routine by 2 surgeons. Concentrated red blood cells were transfused whenever Hb concentrations fell below 6 g/dL during surgery or below 8 g/dL during ICU stay.

**TABLE 1. Preoperative profile and operative data**

| Characteristic                      | Group A (n = 250) | Group B (n = 250) |
|------------------------------------|------------------|------------------|
| Mean age (y)                       | 69.6             | 71.3             |
| Male sex                           | 60 (44)          | 61 (48)          |
| Mean body surface area (m²)        | 1.75             | 1.79             |
| Mean left ventricular ejection fraction (%) | 46               | 48               |
| Median NYHA functional class       | 2                | 2                |
| EuroSCORE (mean)                   | 4.1              | 4.7              |
| Pre-CPB hematocrit (%)             | 32.4 ± 1.2       | 32.6 ± 1.9       |
| Pre-CPB Hb (g/dL)                  | 10.4 ± 1.1       | 10.8 ± 1.2       |
| No. of chronic obstructive pulmonary disease cases (mean) | 23               | 24               |
| Creatinine (mg/dL)                 | 1.09 ± 0.6       | 1.06 ± 0.9       |
| Obstructive coronary artery disease (%) | 23              | 24               |

Values are presented as mean ± standard deviation. NYHA, New York Heart Association; EuroSCORE, European System for Cardiac Operative Risk Evaluation; CPB, cardiopulmonary bypass; Hb, hemoglobin.

**TABLE 2. Operative data**

| Parameter                           | Group A (n = 250) | Group B (n = 250) | P value |
|-------------------------------------|------------------|------------------|--------|
| CPB time (min)                      | 125 ± 13.2       | 120 ± 8.37       | .92    |
| Aortic crossclamp time (min)        | 61 ± 4           | 68 ± 7           | .75    |
| Nadir temperature (°C) during CPB   | 34.9 ± 1.1       | 34.7 ± 2.1       | .75    |
| Nadir hemoglobin value (mg/dL) during CPB | 8.73 ± 1.53      | 8.89 ± 1.25      | .88    |
| Nadir hematocrit (%) during CPB     | 25.6 ± 3.8       | 25.9 ± 3.1       | .89    |
| Nadir DO₂ (mL/min/m²) during CPB    | 290 ± 29         | 278 ± 14         | .039   |
| O₂ER (%) during CPB                 | 24 ± 1           | 29 ± 5           | .0029  |
| Nadir CI (L/min/m²) during CPB      | 2.6 ± 0.2        | 2.4 ± 0.1        | .0032  |
| Nadir SvO₂ (%)                      | 81 ± 2           | 70 ± 5           | .0029  |

Values are presented as mean ± standard deviation. CPB, Cardiopulmonary bypass; DO₂, indexed oxygen delivery; O₂ER, indexed oxygen extraction ratio; CI, cardiac index; SvO₂, mixed venous oxygen saturation.
DO$_2$ and O$_2$ERi were arterial Hb; measured parameters included arterial 
saturation, SvO$_2$, blood pump flow, Hb, arterial and venous temperature, 
mean arterial pressure, body surface area, and CI.

DO$_2$ was calculated using the following equation:

$$DO_2 = (CaO_2 - CvO_2) / Vo_2$$

where arterial O$_2$ content was calculated as follows: $(CaO_2)$ arterial O$_2$ content $(mL/100 mL) = Hb (mg/dL) \times 1.34 \times Hb$ saturation $(\%) + 0.003 \times O_2$ tension (mm Hg).

O$_2$ERi $(\%)$ was calculated using the following equation:

$$O_2ER_i = VO_2 / DO_2 = (CaO_2 - CvO_2) / CaO_2$$

**Metabolic Management During CPB in Group B**

In group B, CI with a target of 2.4 L/min/m$^2$ was managed in relation to 
SvO$_2$ (the cutoff for increase in CI was $<$75% SvO$_2$, the cutoff for decrease 
in CI was $>$75% SvO$_2$). Related measurements were performed using a 
Flowmeter probe in arterial line to measure the real flow of the roller 
pump and the blood gas analyzer (GEM Premier 3000 IQM; Instrumenta-
tion Laboratory, Werfen Group IVD company) set to measure at 37°C for 
mixture.

**TABLE 3. Univariate analysis (correlation matrix)**

| Factor                          | Correlation coefficient | $P$ value |
|---------------------------------|-------------------------|-----------|
| Age (y)                         | -0.079                  | .029      |
| Isolated coronary operation     | -0.075                  | .039      |
| Lowest temperature on CPB       | -0.219                  | .001      |
| Lowest hematocrit on CPB        | -0.149                  | .001      |
| CPB duration                    | 0.049                   | .001      |
| Lowest pump flow                | -0.239                  | .001      |
| CPB lowest DO$_2$               | -0.254                  | .001      |
| CPB peak blood glucose          | 0.497                   | .001      |

CPB, Cardiopulmonary bypass; DO$_2$, indexed oxygen delivery.

**TABLE 4. Subgroup analysis for peak blood lactate and lowest 
indexed oxygen delivery (DO$_2$) in relation to indexed oxygen 
extraction ratio (O$_2$ERi) on cardiopulmonary bypass for group A 
(n = 250)**

| Variable                       | No HL or HG | HL alone | HG alone | HL and HG |
|--------------------------------|-------------|----------|----------|-----------|
| No. of patients                | 223         | 4        | 12       | 11        |
| Peak blood lactate (mmol/L)    | 1.28 $\pm$ 0.45 | 3.68 $\pm$ 0.35 | 1.82 $\pm$ 0.65 | 4.91 $\pm$ 3.21 |
| Lowest DO$_2$ (mL/min/m$^2$)   | 304 $\pm$ 21 | 287 $\pm$ 13 | 289 $\pm$ 21 | 195 $\pm$ 40 |
| Highest O$_2$ERi (%)           | 20 $\pm$ 3   | 25 $\pm$ 2 | 25 $\pm$ 3 | 38 $\pm$ 4 |

Values are presented as mean $\pm$ standard deviation. HL, Hyperlactatemia; HG, hyper-
glycemia; DO$_2$, indexed oxygen delivery; O$_2$ERi, indexed oxygen extraction ratio.

**FIGURE 1.** Receiver operating characteristic curves for lactate peak pre-
diction based on target indexed oxygen delivery (DO$_2$), indexed oxygen 
extraction ratio (O$_2$ERi), cardiac index (CI), and mixed venous oxygen 
saturation (SvO$_2$).

**FIGURE 2.** Lactate and glucose trend according to the distribution of 
target indexed oxygen delivery (DO$_2$) level and indexed oxygen extraction 
ratio (O$_2$ERi) during cardiopulmonary bypass.
TABLE 5. Subgroup analysis for peak blood lactate and lowest cardiac index (CI) in relation to mixed venous oxygen saturation (SvO2) on cardiopulmonary bypass for group B (n = 250)

| Variable                  | No HL or HG | HL alone | HG alone | HL and HG |
|---------------------------|-------------|----------|----------|-----------|
| No. of patients           | 187         | 10       | 21       | 32        |
| Peak blood lactate (mmol/L)| 1.39 ± 0.69 | 3.48 ± 0.38 | 1.79 ± 0.55 | 5.31 ± 3.83 |
| Lowest CI (L/min/m²)      | 2.4 ± 0.2   | 2.4 ± 0.1 | 2.4 ± 0.1 | 1.8 ± 0.4 |
| Lowest SvO2 (%)           | 80 ± 3      | 73 ± 1   | 72 ± 1   | 55 ± 12   |

Values are presented as mean ± standard deviation. HL, Hyperlactatemia; HG, hyperglycemia; CI, cardiac index; SvO2, mixed venous oxygen saturation.

Univariate association with peak blood lactate was tested with a correlation matrix. Factors significantly (P < .05) associated with peak blood lactate at this preliminary step were entered into a stepwise forward multivariable linear regression analysis, with adequate corrections to avoid multicollinearity within the model. The multivariable approach was applied to assess the independent association between the variables tested and peak blood lactate. Subsequently, the population was explored in terms of HL (>3 mmol/L) incidence. Normally distributed continuous variables are expressed as means ± standard deviation, and categorical variables as frequencies and percentages. DO2i in relation to target O2ERi vs CI in relation to SvO2 during CPB were tested for association with peak lactate and peak glucose blood. Intraoperative variables were tested for predictive ability of HL by using a receiver operating characteristic analysis. Postoperative outcome was firstly analyzed in the population with or without HL during CPB using a univariate approach (Student’s t test for unpaired data or relative risk analysis) and was subsequently corrected for other covariates.

RESULTS

Demographic, preoperative, and operative details of the patient population are shown in Tables 1 and 2. Eight pre- and intraoperative factors were found to be significantly associated with peak blood lactate level during CPB at univariate analysis (Table 3): age, isolated coronary operation, lowest pump flow, lowest temperature, Hct, and DO2i. Lactate and glucose trend according to the distribution of cardiac index (CI) level and mixed venous oxygen saturation (SvO2) during cardiopulmonary bypass.

FIGURE 3. Lactate and glucose trend according to the distribution of cardiac index (CI) level and mixed venous oxygen saturation (SvO2) during cardiopulmonary bypass.
DISCUSSION

In this analysis we tried to analyze the correlation of lactates and glycemia with the target managed in relation to the oxygen consumption variables, in a different way than in the previous studies, strengthening their conclusions.1-3,9,10 Our analysis demonstrates that the management of DO2i in relation to O2ERi was 16\% more specific in terms of negative predictive value for HL during CPB compared with the use of CI in relation to SvO2. The group managed with DO2 and O2ERi reported a significant reduction in the incidence of intraoperative lactate peak, correlated with postoperative reduction of serum creatinine value, mechanical ventilation time, and ICU stay, compared with group managed with CI and SvO2.

The link between HL and hyperglycemia through the mechanism explained above was confirmed by Revelly and colleagues16 in an elegant study dealing with cardiogenic or septic shock. The role of adrenergic agonists in this setting is well defined: in cardiogenic shock, they are both endogenous or administered for cardiovascular therapy; in our model, they are endogenous in the majority of patients. None received epinephrine during CPB, and few received norepinephrine; however, unlike epinephrine, norepinephrine usually does not increase glucose production or induce an increase in plasma lactate concentration.6,17 The 2 mechanisms leading to HL in various clinical conditions are therefore anaerobic metabolism due to a poor DO2 and excess lactate production due to glucose failing to enter the oxidative pathway and being degraded to lactate by the glycolytic pathway.17 These mechanisms, if independently considered, lead to different acid–base balance conditions, the former being accompanied by metabolic acidosis and the latter not necessarily so. However, in the clinical conditions of this observational study, the acid-base balance is constantly maintained at a normal pH value by bicarbonate corrections applied by the perfusionist whenever the base excess starts decreasing. Therefore, we are unable to identify differences in HL related to different values of peak blood lactate. However, the evidence that only 4 patients demonstrated HL without hyperglycemia and that only patients with an HL-hyperglycemia syndrome had a significantly lower value of DO2 seems to confirm that, in our specific clinical environment, HL and hyperglycemia are linked by the causative

![TABLE 6. Receiver operating characteristic analysis for the 5 intraoperative positive predictive value (PPV) of hyperlactatemia](image)

- **Lowest DO2i on CPB**
  - AUC: 0.71
  - 95\% confidence interval: 0.58-0.81
  - P value: 0.001
  - Cutoff value: 180 mL/min/m\(^2\)
  - Sensitivity: 69\%
  - Specificity: 75\%
  - PPV: 78\%

- **High O2ERi on CPB**
  - AUC: 0.77
  - 95\% confidence interval: 0.73-0.85
  - P value: 0.001
  - Cutoff value: 40\%
  - Sensitivity: 73\%
  - Specificity: 76\%
  - PPV: 78\%

- **Peak blood glucose on CPB**
  - AUC: 0.92
  - 95\% confidence interval: 0.82-0.97
  - P value: 0.001
  - Cutoff value: 160 mg/dL
  - Sensitivity: 81\%
  - Specificity: 80\%
  - PPV: 85\%

- **Low CI on CPB**
  - AUC: 0.67
  - 95\% confidence interval: 0.62-0.80
  - P value: 0.009
  - Cutoff value: 1.8 L/min/m\(^2\)
  - Sensitivity: 65\%
  - Specificity: 69\%
  - PPV: 74\%

- **Low SvO2 on CPB**
  - AUC: 0.65
  - 95\% confidence interval: 0.60-0.78
  - P value: 0.007
  - Cutoff value: 55\%
  - Sensitivity: 68\%
  - Specificity: 67\%
  - PPV: 77\%

**AUC**: Area under the curve; **PPV**: positive predictive value; **DO2i**: indexed oxygen delivery; **CPB**: cardiopulmonary bypass; **O2ERi**: indexed oxygen extraction ratio; **CI**: cardiac index; **SvO2**: mixed venous oxygen saturation.
factor of a poor DO$_2$, leading on 1 hand to lactate production through the anaerobic pathway and on the other hand to a vicious cycle of lactate production due to poor ability to use glucose through the aerobic pathway.$^{2,5,10}$ Reduced oxygen content in cases of acute anemia is usually compensated by reduced blood viscosity with increased blood flow in the microcirculation and by a compensatory increase in cardiac output.$^{12}$ This last mechanism may be impaired during CPB, where pump flow is usually adjusted on the basis of the patient’s body surface area and temperature, not the Hb value. On the basis of our data, the main rationale for explaining HL during CPB is a DO$_2$ inadequate to guarantee the needed oxygen consumption of the patient.

In the present study, we investigated the role of potentially modifiable factors related to CPB surgery in determining postoperative HL and hyperglycemia.$^{11}$ Our results demonstrate, in a relatively large series of patients treated at different sites, that a DO$_{2ij}$ <270 mL/min/m$^2$ with O$_2$ER$_i$ >35% and low CI (<2.4 L/min/m$^2$) with SvO$_2$ <65% during CPB are associated with HL and hyperglycemia and DO$_{2ij}$ >290 mL/min/m$^2$ with O$_2$ER$_i$ <25% and CI >2.4 L/min/m$^2$ with SvO$_2$ >75% during CPB are associated with a low incidence of HL and hyperglycemia. Various preoperative factors or comorbidities may create the right environment for HL during CPB. Age, female sex, congestive heart failure, low left ventricular ejection fraction, hypertension, atherosclerosis, diabetes, preoperative Hb value, redo or complex surgery, and emergency procedures were found to be risk factors for HL by Demers and colleagues,$^,$ who reported an HL incidence of 18%. Some of these factors were confirmed in our study, and other new factors were identified; however, our study population had a significantly shorter CPB duration and a lower degree of hemodilution during CPB. Given that both these factors seem to favor the onset of HL, the lower HL rate in our population is reasonably explained. The role of CPB duration in the determination of HL during CPB has been highlighted by other authors.$^{1}$

Some study limitations should be acknowledged. First, the design of this analysis compares 2 different extracorporeal circulation management methods. In relation to the available literature, the values taken of 75% for SvO$_2$ and 25% for O$_2$ER$_i$ are not directly comparable because the roller pump used in group B does not correlate the calculated heart rate with the measured heart rate. Second, several patients had peripheral cannulation for CPB, which does not allow us to make a comparison between peripheral versus central cannulation. Moreover, during conventional management; we believed it appropriate not to use hypothermia because the calculated data that we were monitoring corresponded to the set objectives of 2.4 L/min flow; this nondifferentiation of management is intrinsically part of the retrospective nature of the study. Finally, the study focused on CPB with the use of a roller pump and does not consider the centrifuge, but it is also necessary to consider that, with its limitations, the roller pump is predominant in the daily use of cardiac surgery centers. The pump flow is delivered with a roller pump, often the flow management is calculated and not measured with an ultrasonic flowmeter,$^{1}$ this often

### TABLE 7. Receiver operating characteristic analysis for the 5 intraoperative negative predictive value (NPV) of hyperlactatemia

| Factor                        | AUC | 95% confidence interval | $P$ value | Cutoff value | Sensitivity, % | Specificity, % | NPV, % |
|-------------------------------|-----|-------------------------|-----------|--------------|----------------|----------------|--------|
| High DO$_2$, on CPB           | 0.75| 0.70-0.83               | .001      | 299 mL/min/m$^2$ | 73             | 74             | 77     |
| Low O$_2$ER$_i$, on CPB       | 0.79| 0.73-0.85               | .001      | 24%          | 73             | 76             | 79     |
| Low blood glucose on CPB      | 0.89| 0.82-0.93               | .001      | 128 mg/dL    | 79             | 80             | 74     |
| High CI on CPB                | 0.68| 0.65-0.79               | .039      | 2.4 L/min/m$^2$ | 64             | 69             | 63     |
| High SvO$_2$ on CPB           | 0.63| 0.60-0.78               | .035      | 85%          | 62             | 67             | 62     |

AUC, Area under the curve; NPV, negative predictive value; DO$_2$, indexed oxygen delivery; CPB, cardiopulmonary bypass; O$_2$ER$_i$, indexed oxygen extraction ratio; CI, cardiac index; SvO$_2$, mixed venous oxygen saturation.

### TABLE 8. Incidence of hyperlactatemia (HL) and hyperglycemia (HG) in the study population

| Variable     | Group A (n = 250) | Group B (n = 250) | $P$ value |
|--------------|-------------------|-------------------|-----------|
| No HL-HG     | 223               | 187               | .035      |
| HL alone     | 4                 | 10                | .041      |
| HG alone     | 12                | 21                | .029      |
| HL-HG        | 11                | 32                | .032      |
| Total HG     | 23                | 53                | .001      |
| Total HL     | 15                | 42                | .001      |

HL, Hyperlactatemia; HG, hyperglycemia.

### TABLE 9. Hyperlactatemia (HL) during cardiopulmonary bypass and postoperative outcome

| Variable             | Group A (n = 250) | Group B (n = 250) | $P$ value |
|----------------------|-------------------|-------------------|-----------|
| No HL                | (n = 235; 94%)    | (n = 15; 6%)      |           |
| HL                   | 1.1 ± 1.0         | 1.9 ± 1.5         |           |
| No HL                | (n = 208; 83.2%)  | (n = 42; 16.8%)   |           |
| HL                   | 1.2 ± 1.1         | 1.9 ± 1.5         |           |
| Peak serum creatinine (mg/dL) | 20.6 ± 45      | 54 ± 49           | 23.6 ± 55 | 54 ± 49 |
| MV time (h)          | 20.6 ± 45         | 54 ± 49           | 23.6 ± 55 | 54 ± 49 |
| ICU stay (d)         | 2.8 ± 2.1         | 5.7 ± 4.9         | 3.1 ± 2.1 | 6.4 ± 3.9 |

Values are presented as mean ± standard deviation. HL, Hyperlactatemia; MV, mechanical ventilation; ICU, intensive care unit.
The Journal policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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FIGURE 5. Data on 500 cardiopulmonary bypass (CPB) procedures were retrospectively collected, the management of indexed oxygen delivery (DO2i) in relation to indexed oxygen extraction ratio (O2ERi) follow the CPB was more specific in terms of negative predictive value for hyperlactatemia compared with the use of cardiac index (CI) in relation to mixed venous oxygen saturation (SvO2). That management can correlate with postoperative better outcome especially in terms of serum creatinine, mechanical ventilation time and intensive care unit stay.

CONCLUSIONS
This retrospective observational study showed that management of DO2i in relation to O2ERi was 16% more specific in terms of negative predictive value for HL during CPB compared with the use of CI in relation to SvO2. Group A patients showed a significant reduction in the incidence of intraoperative lactate peak, correlated with postoperative reduction of serum creatinine value, mechanical ventilation time, and ICU stay, compared with group B patients.

Conflict of Interest Statement
The authors reported no conflicts of interest.