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## CARDIOVASCULAR

# Assessment of changes in lactate concentration with intravascular microdialysis during high-risk cardiac surgery using the trend interchangeability method

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## Abstract

Background. Blood lactate is a strong predictor of mortality, and repeated blood lactate assays are recommended during surgery in high-risk patients. We hypothesized that the use of intravascular microdialysis incorporated in a central venous catheter would be interchangeable with the reference blood gas technique to monitor changes in blood lactate. Methods. Microdialysis and central venous blood lactate measurements were recorded simultaneously in high-risk cardiac surgical patients. The correlation between absolute values was determined by linear regression, and the Bland–Altman test for repeated measurements was used to compare bias, precision, and limits of agreement. Changes in lactate measurements were evaluated with a four-quadrant plot and trend interchangeability method (TIM).

**Results.** In the 23 patients analysed, the central venous catheter was used as part of standard care, with no complications. The correlation coefficient for absolute values (n=104) was 0.96 (P<0.0001). The bias, precision, and limits of agreement were -0.19, 0.51, and -1.20 to 0.82 mmol litre<sup>-1</sup>, respectively. The concordance rate for changes in blood lactate measurements (n=80) was 94% with the four-quadrant plot. In contrast, the TIM showed that 23 (29) changes in lactate measurements were not interpretable, and among the remaining 57 (71) interpretable changes, 18 (32) were interchangeable, 8 (14) were in the grey zone, and 31 (54) were not interchangeable.

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**Conclusions.** Microdialysis with a central venous catheter appears to provide reliable absolute blood lactate values. Although changes in blood lactate measurements showed an excellent concordance rate, changes between the two methods were poorly interchangeable with the TIM.

Clinical trial registration. NCT02296593.

Key words: cardiac surgery; lactic acid; microdialysis

#### Editor's key points

- Blood lactate monitoring is increasingly used, and changes in lactate correlate with outcome in critical illness, sepsis, and after cardiac surgery.
- Devices using intravascular microdialysis to monitor lactate continuously are now available, but their accuracy is not fully established.
- In this study of high-risk cardiac surgical patients, there was good correlation between absolute values and changes in lactate measured using intravascular dialysis and a standard blood gas analyser.
- However, trend interchangeability analysis showed that the majority of the changes in lactate were not interpretable or not interchangeable.
- Further data are needed, but clinicians should be aware of the limitations of intravascular dialysis for monitoring lactate.

The concept of lactate clearance was developed >15 yr ago. Defined as the percentage decrease in blood lactate from emergency department admission to 6 h after admission, it has been described as an independent predictor of mortality.<sup>1</sup> A multicentre randomized controlled study subsequently showed that lactate goal-directed therapy with lactate monitoring decreased hospital mortality in unselected critically ill patients.<sup>2</sup> Recently, two studies have confirmed that bedside lactate monitoring can improve clinical outcomes in septic patients.<sup>3</sup> <sup>4</sup> Similar results have been reported for critically ill surgical patients.<sup>5</sup> <sup>6</sup> In particular, intraoperative changes in blood lactate have been reported to be associated with postoperative outcome in cardiac surgery patients.<sup>7</sup> <sup>8</sup>

Repeated blood lactate assays are therefore recommended to monitor lactate production and clearance over time during surgery in high-risk patients<sup>9</sup> and during initial resuscitation in septic patients.<sup>10</sup>

New technologies that use a central venous catheter combined with a microdialysis method now permit continuous blood lactate monitoring. Two recent studies have reported encouraging results with this device by comparing absolute values (Eirus; Maquet Critical Care, Solna, Sweden), but without the evaluation of trending ability.<sup>11</sup> <sup>12</sup> Before considering the more extensive use of this new device for daily practice, its accuracy must be evaluated further in independent studies.

The objective of the present study, conducted in selected high-risk cardiac surgical patients, was to compare intravascular microdialysis with the measurement of central venous blood gases as the reference method. We tested the hypothesis that blood lactate changes determined by intravascular microdialysis would be interchangeable with those measured via the reference method.

## Methods

### Ethics committee approval

After approval by the local Ethics Committee [Reference A14-D36-VOL.22, CPP Nord Ouest III, Caen University Hospital, France (Chairman: Dr C. Gourio) on October 21, 2014], all consecutive adult patients admitted from January 2015 to July 2015 who were undergoing high-risk cardiac surgery were eligible for inclusion in the study. As data were collected during the administration of routine care according to standard procedures currently used in our institution, the need for written informed consent was waived. However, preoperative verbal consent was obtained from all study participants. The study was registered at ClinicalTrials.gov (NCT02296593), and the study methodology complied with the STROBE Statement<sup>13</sup> and GRRAS guidelines.<sup>14</sup>

#### Study population

High-risk cardiac surgical patients (i.e. those with an elevated risk of elevated blood lactate) were included before surgery if they had a left ventricular ejection fraction of <30% or were undergoing high-risk cardiac surgery (aortic dissection, double valve replacement, left ventricular assist device, left ventriculoplasty, or endocarditis) with cardiopulmonary bypass (CPB), or both. An appointed anaesthetist (C.G.) acquired all data. Patients without high surgical risk, off-pump cardiac surgery (predictable short operating time), or for whom the investigator was not available were not included. Patients with central venous catheter misplacement (not positioned with the tip in the superior vena cava above the right atrium confirmed by echocardiography) were excluded from the study. As recommended by the manufacturer, blood lactate values  $>10\,mmol\ litre^{-1}$  were not analysed, as the Eirus device V2.0 cannot provide accurate values in this range (the monitor simply displays '>10 mmol.l<sup>-1</sup>').

#### Study procedure

All patients underwent general anaesthesia with propofol and remifentanil to maintain a bispectral index between 40 and 60 during surgery. Patients' lungs were ventilated using a volumecontrolled method. After the induction of anaesthesia, a radial arterial catheter and a right jugular central venous catheter (CVC) with an integrated microdialysis function (Eirus; Maquet Critical Care AB, Solna, Sweden) were placed using ultrasound guidance in all patients. The CVC was then connected to a dedicated monitor (Eirus V2.0; Maquet Critical Care AB) via a specific microdialysis sensor, which converts biochemical data into numerical data (lactate<sub>Eirus</sub>). This specific five-lumen central venous catheter used two dedicated lumens for the microdialysis system and three lumens for usual drug administration. After the automatic rinsing of the system with sodium chloride 0.9% solution, venous blood lactate measurements were calibrated with a blood sample obtained from the central venous

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