Heart, Lung and Circulation (2017) xx, 1–5
1443-9506/04/$36.00
http://dx.doi.org/10.1016/j.hlc.2017.02.006

ORIGINAL ARTICLE

Lactate and Echocardiography before Veno-Venous Extracorporeal Membrane Oxygenation Support

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Received 20 August 2016; received in revised form 1 February 2017; accepted 6 February 2017; online published-ahead-of-print xxx

Background Lactate has been recognised as a prognostic factor in several critical conditions. Veno-Venous Extracorporeal Membrane Oxygenation (VV-ECMO) is a well-established therapy in patients with Acute Respiratory Disease Syndrome (ARDS) unresponsive to conventional therapy and echocardiography pre ECMO initiation has been recently reported to help in risk stratifying these patients.

Methods We assessed whether the detection of hyperlactataemia could be associated with the presence of left ventricle (LV) or right ventricle (RV) dysfunction in 121 consecutive patients with refractory ARDS.

Results The mortality rate was 42.9% (52/121). Higher dosages of norepinephrine and dobutamine were administered to non survivors ($p = 0.023$ and $p = 0.047$, respectively) who showed significantly higher levels of lactate ($p = 0.002$). At echocardiography, non survivors showed higher values of systolic pulmonary artery pressure (sPAP) ($p = 0.05$) and a higher incidence of RV dysfunction (as indicated by lower Tricuspid Annular Plane Excursion (TAPSE)) and RV dilatation ($p = 0.001$). At multivariate logistic regression analysis, the following variables were independent predictors of death: body mass index (BMI) (OR: 0.914, 95% CI 0.857–0.975, $p = 0.006$), RV dilatation (OR: 0.239, 95%CI 0.101–0.561, $p = 0.001$) and lactate (OR: 1.292, 95% CI 1.015–1.645, $p = 0.038$). Lactate values were directly correlated with the simplified acute physiology score (SAPS) II ($r = 0.38$, $p < 0.001$), while they showed an indirect correlation with left ventricular ejection fraction (LVEF) ($r = -0.24$, $p = 0.009$) and TAPSE ($r = -0.21$, $p = 0.024$).

Conclusions In refractory ARDS, hyperlactataemia before VVV-ECMO identified a subset of patients at higher risk of death, being an independent predictor of in-Intensive Care Unit (ICU) mortality. Lactate values are mainly related to disease severity (as indicated by SAPS II) and haemodynamic impairment (as inferred by LVEF) and RV failure, as (indicated by TAPSE).

Keywords Lactate • Echocardiography • ARDS • VV-ECMO • Prognosis

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Please cite this article in press as: Lazzeri C, et al. Lactate and Echocardiography before Veno-Venous Extracorporeal Membrane Oxygenation Support. Heart, Lung and Circulation (2017), http://dx.doi.org/10.1016/j.hlc.2017.02.006

Introduction

Lactate has been recognised as a prognostic factor in several critical conditions, ranging from sepsis to acute respiratory failure [1–4]. In patients with Acute Respiratory Distress Syndrome (ARDS) mechanical ventilation decreased lactate values [5] and lactate clearance within the first 72 hours upon Intensive Care Unit (ICU) admission were able to predict early mortality in these patients [6].

Veno-Venous Extracorporeal Membrane Oxygenation (VV-ECMO) is a well-established therapy in patients with ARDS unresponsive to conventional therapy [7–9] and echocardiography pre ECMO initiation has been recently reported to help in risk stratifying these patients since RV dilatation was an independent predictor for ICU mortality in refractory ARDS requiring ECMO support [10]. In 121 consecutive patients with refractory ARDS we tested the hypothesis that the detection of hyperlactataemia could be associated with the presence of left ventricular (LV) or right ventricular (RV) dysfunction and we further assessed their prognostic impact on ICU death.

Methods

In our retrospective observational study, we enrolled 121 patients with refractory ARDS [11] supported with VV-ECMO consecutively admitted to our Intensive Care Unit, which is an ECMO referral centre [12–16] from September 30th 2009 to February 28th 2015. Data were prospectively recorded and retrospectively analysed.

Baseline characteristics were collected for all patients and the simplified acute physiology score (SAPS II) [17] was calculated.

The requirement of ECMO implantation was decided on the basis of the Italian Ministry of Health criteria, as previously described [14,16].

Lactate values, pH, pCO2 pO2 and norepinephrine dosage before ECMO implantation were recorded.

Echocardiographic Assessment

Echocardiography is performed routinely before ECMO implantation at our ICU by the cardiologist (CL and PB) who is part of our ECMO team, which also includes an intensivist, a cardiac surgeon and a perfusionist, all trained in ECMO technique and management. The cardiologist's main task is to evaluate cardiac function in the pre-ECMO phase and guide the correct positioning of ECMO cannulas by transoesophageal/transthoracic ultrasonography [7,12,15].

According to our protocol [10,12,13,15] the echocardiographic examination is transthoracic (TTE), transoesophageal (TEE) or both, according to the best acoustic window (Esaote MyLab^{TM}30Gold Cardiovascular, Esaote S.p.A, Genoa, Italy) [18]. The LV ejection fraction (LVEF) was estimated by eyeball examination on short-axis views [19]. Left ventricular systolic dysfunction was defined as LV ejection fraction less than 45% [20].

The right ventricle size was assessed by the RV end-diastolic area (EDA) (four-chamber view) and the ratio between EDAs of the right and left ventricles was calculated (RVEDA/LVEDA). Right ventricular dilatation was defined as RVEDA/LVEDA > 0.6 [12,21].

Systolic pulmonary artery pressure (sPAP) was obtained using the simplified Bernouilli's equation: 4 • (Vmax tricuspid regurgitation)^2 + central venous pressure (CVP). To reduce the lack of precision of CVP estimation based on the size of the inferior vena cava, CVP was invasively measured through central venous catheters [12,18].

Tricuspid Annular Plane Excursion (TAPSE) was also measured, as the difference of displacement during diastole and systole. A TAPSE < 16 mm is known to indicate RV dysfunction [10,12,18].

Mortality during ICU stay was the outcome.

All participants (or their relatives) signed a written informed consent for storing their clinical data. The study is a retrospective analysis of data and the study design was approved by our Institutional Board.

Statistical Analysis

Data have been stored in a dedicated data-base and analysed with PASW 17.0 for Windows® statistical software (IBM-SPSS Inc., USA). Categorical values have been reported as frequency (percentage); continuous variables have been reported as mean±SD or median (interquartile range, IR) as appropriate. Between-group (survivors vs. non survivors) comparisons were made by means of chi-square and unpaired Student's t-test or Mann-Whitney U test when needed. Multivariate correlation with in-ICU mortality was investigated with logistic regression analysis (backward stepwise selection algorithm): candidate variables were carefully chosen among those known to be clinically related or those with significant differences in baseline characteristics to outcome in order to avoid model overfitting; Hosmer-Lemeshow goodness-of-fit test and Nagelkerke pseudo-R2 are reported.

Correlations with lactate were studied with Pearson's R, both uni- and multivariable. Lactate (dependent) as well as independent variables were tested for normality with Kolmogorov-Smirnov one-sample test, and non parametric variables were transformed in order to meet normality so that a linear regression could be performed. To perform the forward stepwise multivariable linear regression analysis, those which were significantly (or considered clinically) related to lactate, that is, SAPS II, LVEF ($\log_{10}$) and TAPSE ($\log_{10}$) were taken as independent.

Results

Our population comprised 121 patients, mainly males (67.7%) (Table 1). Seventy-two patients (59.5%) came from peripheral centres. All the ECMO transportations were carried out by ambulance and no adverse event was observed. The average distance from the local hospital to our ECMO

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