

CORRESPONDENCE



Prognostic relevance of serum lactate kinetics should be approached with caution

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Dear Editor,

We read with interest the article recently published by Masyuk et al. in *Intensive Care Medicine* [1]. By coincidence, we also recently analyzed blood lactate kinetics in our ICU patients.

The methodology of lactate measurements in our study and the Masyuk et al. study was largely similar. All consecutive patients treated in our general ICU between 2012 and 2016 were included in the analysis ($n=639$). Maximum lactate concentrations on day 1 and day 2 were identified by manual retrieval of medical records (information coming from point of care devices are not entered into our hospital information system). Patients who died or were discharged from the ICU within 24 h following admission, and those with incomplete data on lactate concentrations on day 1, day 2 or both, were excluded ($n=210$). Finally, 429 patients were included in the analysis. Lactate concentrations were linked to the hospital database containing detailed information on each patient, including ICU mortality and all-cause mortality during the follow-up period. Due to the retrospective and anonymous nature of the study, the Ethics Committee at the Medical University of Silesia in Katowice waived the need for consent of patients to be enrolled in the study.

Among the 429 patients analyzed, there were 192 patients (44.8%) with a lactate concentration above 2.0 mmol/L on day 1 (admission day). ICU mortality in this group was 49.5%. 114 patients (59.4%) were assessed

according to the APACHE II on admission with a mean score of 26.5 ± 5.6 points. Cardiovascular system disorder was the principal reason for admission in the majority of patients. Mean lactate concentration on day 1 was 5.3 ± 4.5 mmol/L in survivors and 6.3 ± 7.4 mmol/L in non-survivors ($p=0.295$). On day 2, mean lactate concentrations significantly declined in both groups: to 3.2 ± 2.8 mmol/L ($p<0.001$) and 3.7 ± 3.0 mmol/L ($p<0.001$), respectively. Mean decrease in lactate concentration was $28.5\% \pm 59.3\%$ in survivors vs $20.4\% \pm 54.9\%$ in non-survivors ($p=0.228$).

According to the cutoff proposed by Masyuk et al. 170 of our patients had a $\Delta 24\text{Lac} \leq 19\%$, while the remaining 22 patients had a $\Delta 24\text{Lac} > 19\%$. ICU mortality was significantly lower in patients with lower $\Delta 24\text{Lac}$ (45.9% vs 77.3%, $p=0.005$). Data on long-term mortality were available but were not assessed due to small sample size (only five survivors among patients with $\Delta 24\text{Lac} > 19\%$). The ROC curve was computed, and our optimal cutoff point ($\Delta 24\text{Lac}$ 17.5%) was calculated by means of the Youden's index (Fig. 1).

We would like to comment on these findings. Generally, ICU mortality in our study was higher compared to the study of Masyuk et al. [1]. This was not a surprise since the available data clearly indicate that mortality in Polish intensive care units is high [2], but appropriate for the patient's condition on ICU admission, assessed with the use of the APACHE II and SAPS III scoring systems [3].

Observation of a better outcome associated with decreasing blood lactate concentrations seems to be consistent throughout published clinical studies [4]. Therefore, our results are not in line with these findings. Additionally, a few serious methodological issues should be discussed.

The area under the ROC curve in our study was only 0.55 (95% CI 0.47–0.63) and the cutoff point was 17.5%.

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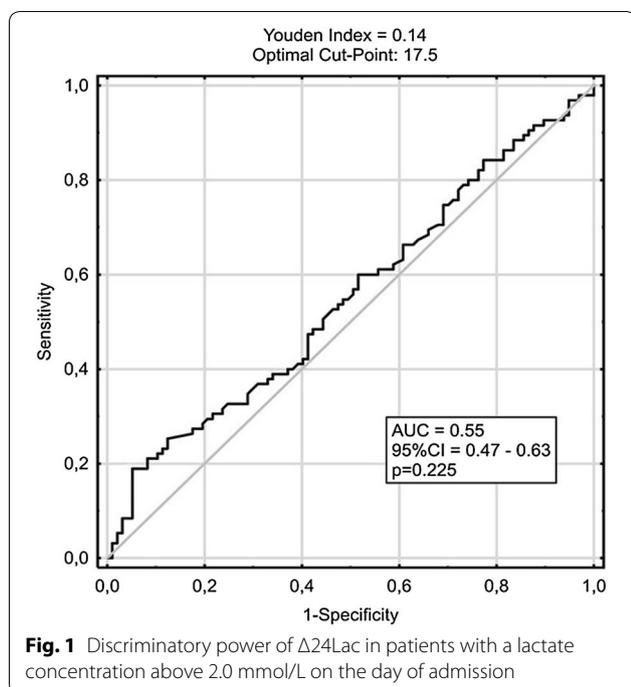


Fig. 1 Discriminatory power of $\Delta 24\text{Lac}$ in patients with a lactate concentration above 2.0 mmol/L on the day of admission

Therefore, the discriminatory power of our cutoff point was comparable to that of chance alone. It would have been instructive if the area under the ROC curve in the study carried out by Masyuk et al. was reported, along with the proportions of patients with $\Delta 24\text{Lac}$ higher and lower than 19% in their study. Unfortunately, these data were not presented [1].

Regrettably, this is not the only problem. The terms used in the study by Masyuk and colleagues are confusing. As a generally accepted term in science, the word “delta” implies difference or change and means an increase in value over time (if not clearly stated otherwise). Masyuk et al. however, compare their results many times to the studies analyzing lactate clearance, which is a completely different term. It is generally considered, that a decrease of lactate concentration is a substitute for lactate clearance. The difference lies in the formula used. In this particular case $\Delta 24\text{Lac} = (\text{day}2\text{Lac} - \text{day}1\text{Lac}) / \text{day}1\text{Lac} \times 100$, and lactate clearance $= (\text{day}1\text{Lac} - \text{day}2\text{Lac}) / \text{day}1\text{Lac} \times 100$. In the study by Masyuk et al. the formula is not presented and, therefore, the meaning of “ $\leq 19\% \Delta 24\text{Lac}$ ” is not clear.

If the authors mean in that $\Delta 24\text{Lac}$ is in fact lactate clearance, then according to their cutoff point, 66 of our patients had a lactate clearance $\leq 19\%$, while the remaining 126 patients had a lactate clearance $> 19\%$. ICU mortality in patients with lower and higher lactate clearance was 53.0% and 47.6%, respectively ($p = 0.544$), so there

was no difference between the groups. The cutoff point in this case is obviously -17.5% and the area under the ROC curve is also 0.55.

Moreover, Masyuk et al. state that they managed to demonstrate, for the first time, the impact of lower $\Delta 24\text{Lac}$ not only on in-hospital, but also long-term mortality, analyzing follow-up data for up to 9 years [1]. We feel that, to draw such a revolutionary conclusion, the survival curves should be analyzed in patients surviving to ICU or hospital discharge only, and therefore, start no sooner than at hospital (or ICU) discharge. Figure 1 in their study clearly shows that the Kaplan–Meier curves become parallel at some point, and therefore, it seems that a higher $\Delta 24\text{Lac}$ was responsible for higher mortality only in a period directly following ICU admission [1].

Therefore, in our opinion, prognostic relevance of serum lactate kinetics should be approached with more caution.

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Compliance with ethical standards

Conflicts of interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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