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Mortality of septic shock patients is associated with impaired mitochondrial oxidative coupling efficiency in lymphocytes: a prospective cohort study

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Background: Septic shock is a life-threatening condition that challenges immune cells to reprogram their mitochondrial metabolism towards to increase ATP synthesis for building an appropriate immunity. This could print metabolic signatures in mitochondria whose association with disease progression and clinical outcomes remain elusive.

Method: This is a single-center prospective cohort study performed in the ICU of one tertiary referral hospital in Brazil. Between November 2017 and July 2018, 90 consecutive patients, aged 18 years or older, admitted to the ICU with septic shock were enrolled. Seventy-five patients had Simplified Acute Physiology Score (SAPS 3) assessed at admission, and Sequential Organ Failure Assessment (SOFA) assessed on the first (D1) and third (D3) days after admission. Mitochondrial respiration linked to complexes I, II, V, and biochemical coupling efficiency (BCE) were assessed at D1 and D3 and Δ (D3-D1) in isolated lymphocytes. Clinical and mitochondrial endpoints were used to dichotomize the survival and death outcomes. Our primary outcome was 6-month mortality, and secondary outcomes were ICU and hospital ward mortality.

Results: The mean SAPS 3 and SOFA scores at septic shock diagnosis were 75.8 (\pm 12.9) and 8 (\pm 3) points, respectively. The cumulative ICU, hospital ward, and 6-month mortality were 32 (45%), 43 (57%), and 50 (66%), respectively. At the ICU, non-surviving patients presented elevated arterial lactate (2.8 mmol/L, IQR, 2-4), C-reactive protein (220 mg/L, IQR, 119-284), and capillary refill time (5.5 s, IQR, 3-8). Respiratory rates linked to CII at D1 and D3, and Δ CII were decreased in non-surviving patients. Also, the BCE at D1 and D3 and the Δ BCE discriminated patients who would evolve to death in the ICU, hospital ward, and 6 months after admission. After adjusting for possible confounders, the Δ BCE value but not SOFA scores was independently associated with 6-month mortality (RR 0.38, CI 95% 0.18-0.78; P = 0.009). At a cut-off of - 0.002, Δ BCE displayed 100% sensitivity and 73% specificity for predicting 6-month mortality

CONCLUSIONS: The Δ BCE signature in lymphocytes provided an earlier recognition of septic shock patients in the ICU at risk of long-term deterioration of health status.

Keywords: Lymphocytes; Mitochondrial signatures; Mortality; Prognostic biomarker; Septic shock.