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Stratifying septic patients using lactate: severe sepsis and cryptic, vasoplegic and dysoxic shock profile

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Background: The current consensus definition of severe sepsis and septic shock includes a heterogeneous profile of patients under the same definition. Although the prognostic value of hyperlactatemia in sepsis is well established, hyperlactatemia can be found both in severe sepsis and septic shock patients. We sought to compare features and outcomes of septic patients stratified by two factors: the presence of hyperlactemia and persistent hypotension.
Materials and methods: This was a secondary analysis of a multicenter observational study from 10 private hospitals in Brazil (Rede Amil-SP) aiming to evaluate the impact of a multifaceted program to implement the Surviving Sepsis Campaign bundles. We retrieved 1,948 septic patients with an initial lactate level collected within the first 6 hours of diagnosis. Based on previous literature, we stratified them into four groups according to the presence of hypoperfusion (lactate >4 mmol/l) and/or persistent hypotension despite adequate fluids: 1, severe sepsis (without both criteria); 2, cryptic shock (hypoperfusion without persistent hypotension) [1]; 3, vasoplegic shock (persistent hypotension without hypoperfusion); and 4, dysoxic shock (with both criteria) [2].
Results: Severe sepsis was found in 1,018 (52%), cryptic shock in 162 (8%), vasoplegic shock in 549 (28%) and dysoxic shock in 219 (12%) patients. Mean age was 60 years, 47% were male and the majority was admitted form the emergency department (47%). The lung was the principal source of infection, followed by the urinary tract and abdominal. Overall, the four groups presented significant differences in APACHE II and SOFA scores ($P < 0.001$ for both), dysoxic shock being the most severe group. In *post-hoc* analysis, patients in the severe sepsis group presented similar SOFA score to patients in the cryptic shock group ($P = 0.20$). Overall, 28-day crude survival was different between groups ($P < 0.001$), being higher for the severe sepsis group (69%, $P < 0.001$ vs. other), similar between cryptic and vasoplegic shock (53%, $P = 0.39$) and lower for dysoxic shock (38%, $P < 0.001$ vs. other). In an adjusted analysis considering age, APACHE II and SOFA, the 28-day survival remained different between groups ($P < 0.001$) and the hazard ratio for the dysoxic shock group was the highest: HR 2.99 (95% CI 2.21 to 4.05).
Conclusions: Current definitions for severe sepsis and septic shock include four different phenotypes, which should be considered for epidemiology purposes, customizing treatment goals and inclusion criteria for future studies. Although previous studies showed similar outcomes between cryptic shock and overt septic shock (vasoplegic and dysoxic profile), we demonstrated that cryptic shock is similar only to vasoplegic shock.
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Antithrombin III concentrate may contribute to sepsis in nonovert disseminated intravascular coagulation

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Background: Antithrombin III (AT III) has been known to contribute to anti-inflammatory response as well as its anticoagulation. Our previous study showed AT III deficiency happened in the early stage of sepsis with no relation to disseminated intravascular coagulation (DIC) status. Whether AT III concentrate is a beneficial therapy or not for septic patients is still a controversial issue. Our hypothesis is that AT III concentrate may have efficacy as an anti-inflammatory for sepsis.
Materials and methods: From January 2009 to June 2013, adult septic patients with nonovert DIC whom were given AT III concentrate in our medico-surgical ICU were included in this study. DIC scoring was used with the definition of the International Society on Thrombosis and Haemostasis (ISTH). AT III concentrate was administered 30 to 60 U/kg intravenously every 24 hours for 3 days in the patients. Between before and after the AT III concentrate therapy, WBC (/mm^3), CRP (mg/dl), platelet (×10^4/μl), PT (seconds), fibrinogen (mg/dl), FDP (μg/ml), SOFA score and DIC score by ISTH were compared. Values are expressed as mean ± SD. Data were analyzed by Wilcoxon signed-rank test. $P < 0.05$ was considered significant.
Results: There were 157 patients (100 men, 57 women; age range 19 to 96 years (mean 70.0 ± 16.0)), and the 28-day mortality rate was 25.5% and APACHE II score was 17.2 ± 8.3. WBC, CRP, PT, and SOFA score were significantly improved after AT III concentrate therapy (13,411 ± 8,794 vs. 11,798 ± 6,562, $P = 0.0007$, 17.1 ± 11.5 vs. 13.9 ± 7.0, $P = 0.0001$, 16.5 ± 10.9 vs. 15.2 ± 5.3, $P = 0.002$, and 8.6 ± 3.6 vs. 7.7 ± 4.5, $P = 0.005$, respectively), although platelet was significantly decreased (15.8 ± 11.3 vs. 13.7 ± 11.3, $P < 0.00013$). There were no significant differences in fibrinogen, FDP and DIC score (464.7 ± 235 vs. 437.6 ± 185.4, $P = 0.10$, 25.1 ± 36.9 vs. 25.6 ± 36.2, $P = 0.85$, 2.0 ± 1.5 versus 2.3 ± 1.7, $P = 0.06$, respectively). One week after the therapy, SOFA score was significantly improved, while the DIC score did not change compared with before the therapy (6.1 ± 4.7, $P < 0.0001$ and 2.3 ± 1.7, $P = 0.98$).
Conclusions: In the patients with septic nonovert DIC, WBC, CRP and SOFA score were immediately improved after the AT III concentrate therapy, while fibrinogen, FDP and DIC score did not change. AT III concentrate may also contribute to anti-inflammatory without DIC status.

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Intravenous immunoglobulin therapy could have efficacy in severe sepsis

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Background: Intravenous immunoglobulin (IVIG) administration has been approved to use for severe sepsis with antibiotics by the Ministry of Health, Labour and Welfare since 1980 in Japan. IVIGs are commonly used for severe sepsis and septic shock in Japan, while the international guidelines for management of severe sepsis and septic shock in 2012 suggest not using IVIG in adult patients. Our hypothesis is that IVIG administration has an efficacy for severe sepsis and septic shock.
Materials and methods: This retrospective observational study included all adult patients in our ICU who were administered IVIG for severe sepsis and septic shock from January 2011 to June 2013. IVIG was used at 5,000 mg/day every 24 hours for 3 days. We compared body temperature (℃), WBC (/mm^3), CRP (mg/dl), procalcitonin (ng/ml) and serum immunoglobulin G (IgG) (mg/dl; normal >870) between before and after IVIG treatment. Values are expressed as the median. The Wilcoxon signed-rank test was used for the statistical analysis. $P < 0.05$ was considered significant.