

Kegagalan Resusitasi, Kadar Protein Carbonyl dan Kadar Receptor-Interacting Protein Kinase 3 sebagai prediktor kematian pasien sepsis = Failed Resuscitation, Protein Carbonyl, and Receptor-Interacting Protein Kinase 3 as sepsis-related mortality predictor

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Abstrak

Latar Belakang: Sepsis merupakan salah satu masalah kesehatan di rumah sakit termasuk di ruang Intensive Care Unit (ICU) dan angka kematiannya masih tetap tinggi meskipun dengan tatalaksana yang maksimal dan biaya yang besar. Kematian merupakan hal yang sulit untuk diprediksi. Pasien yang telah diresusitasi dengan baik masih berpeluang untuk mengalami kematian karena proses disfungsi organ yang terus berlanjut akibat tingginya tingkat inflamasi. Inflamasi yang tidak terkontrol memicu stress oksidasi dan necroptosis. Penelitian terakhir menunjukkan kadar protein carbonyl (PCO) dan receptor-interacting protein kinase 3 (RIPK3) tinggi pada pasien sepsis dan dapat digunakan untuk memprediksi kematian. Penelitian ini bertujuan untuk menilai seberapa besar kegagalan resusitasi, kadar PCO, dan kadar RIPK3 dapat memprediksi kematian pada pasien sepsis.

Metode: Rancangan penelitian ini adalah kohort prospektif di ruang resusitasi dan ICU RSUP. Dr. Moh. Hoesin (RSMH) Palembang. Penelitian dimulai setelah sertifikat etik dan izin lokasi diterbitkan sejak bulan Februari sampai Agustus 2019. Kriteria penerimaan meliputi pasien berusia 18 tahun atau lebih yang didiagnosis sepsis. Kriteria penolakan meliputi keluarga menolak diikutsertakan dalam penelitian, pasien tidak dirawat di ICU, terlambat didiagnosis (lebih dari 24 jam), hamil dan didiagnosis mati batang otak. Kriteria pengeluaran meliputi pasien meninggal kurang dari 4 jam setelah diagnosis ditegakkan dan pasien tidak dapat dilakukan follow up dalam waktu 28 hari. Tim peneliti yang telah dilatih sebelumnya mengidentifikasi semua pasien yang memenuhi kriteria penelitian. Semua subjek penelitian mendapatkan resusitasi standar dan diambil sampel darah untuk diperiksa ke laboratorium. Pasien diamati selama 28 hari: apakah mengalami kematian atau tidak. Kegagalan resusitasi didefinisikan sebagai kadar laktat 2 mmol/l atau reduksi laktat <20%. Data yang didapatkan dianalisis dengan uji statistik yang sesuai menggunakan piranti lunak program STATA.

Hasil: Didapatkan total 72 subjek penelitian, 13 dikeluarkan karena meninggal kurang dari 4 jam setelah diagnosis ditegakkan. Dari hasil analisis bivariat didapatkan hubungan antara kegagalan resusitasi (RR 1,36; IK95% 0,965-1,916; p 0,085), kadar PCO (RR 2,37; IK95% 1,348-4,194; p 0,0001), dan kadar RIPK3 (RR 5,86; IK95% 2,07-16,61; p <0,0001). Dari hasil multivariat hanya didapatkan satu

variabel yang bermakna yaitu kadar RIPK3 (RR 5,39; IK95% 1,490-19,478; p 0,010). Setelah dikontrol dengan variabel perancu usia, komorbiditas dan skor APACHE II didapatkan variabel RIPK3 memiliki RR 4,64 dengan IK95% 1,233-17,479; p 0,023).

Simpulan: Kegagalan resusitasi, kadar PCO dan kadar RIPK3 dapat memprediksi kematian pada pasien sepsis.

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Background: Sepsis remains one of the health problems at the hospital including intensive care unit (ICU) since its mortality is still high despite maximal efforts on therapy. Mortality is an unpredictable event. Patients who were properly resuscitated still have a probability of mortality because of severe inflammatory state which may lead to ongoing organ dysfunctions. Uncontrolled inflammation will trigger oxidative stress and necroptosis. Recent study showed that high level of protein carbonyl (PCO) and receptor-interacting protein kinase 3 (RIPK3) in septic patients could be used to predict mortality. This study wished to analyze the ability resuscitation failure, PCO level and RIPK3 level to predict mortality in septic patients.

Methods: This prospective cohort study was conducted at resuscitation room and ICU of RSUP. dr. Moh. Hoesin (RSMH), a single tertiary teaching hospital in Palembang, South Sumatera. This study was started after ethical and location authorization were unleashed in February to August 2019. Inclusion criteria were 18 years old or above patients that were diagnosed with sepsis. Exclusion criteria were patients whose family did not give any consent to participate the study, patients that were not treated at the ICU, had a late diagnosis (>24 h), pregnant, and diagnosed with brain dead. Drop out criteria including died <4 h after diagnosed and patients that could not be followed in 28 days. Investigators were trained to identified all eligible patients. Subjects had a standard resuscitation and their blood was taken to be examined at the laboratory. Patients were observed in 28 days whether there were any mortality or not. Failed resuscitation defined by examined lactate level 2 mmol/l or lactate reduction <20%. Data was statistically analyzed with STATA™.

Results: Seventy two subjects were included to the study but 13 of them were dropped out because died within 4 h after diagnosed. From bivariate analysis, there was an association between failed resuscitation (RR 1.36; CI95% 0.965-1.916; p 0.085), PCO level (RR 2.37; CI95% 1.348-4.194; p 0.0001), and RIPK3 level (RR 5,86; CI95% 2.07-16.61; p <0.0001). From multivariate analysis using cox regression time constant, the only variable statistically significant was RIPK3 (RR 5.39; CI95% 1.490-19.478; p 0.010). After adjusted by confounding variables, including age, comorbidities, and APACHE II score, RIPK3 had RR 4.64 with CI

95% 1.233-17.479; p 0.023.

Conclusions: Failed resuscitation, PCO level, and RIPK3 level can predict mortality in sepsis patients