Erythropoietin stimulating agents resistance is associated with all-cause mortality in maintenance hemodialysis patients

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Objective: Erythropoietin stimulating agents is widely used for renal anemia in dialysis patients. Our study aims to investigate risk factors associated with high erythropoietin stimulating agents(ESA) dose and ESA resistance in maintenance hemodialysis(MHD) patients, and the correlation between ESA resistance and mortality.

Methods: A single-center cohort study enrolled MHD patients in Ruijin Hospital affiliated to Shanghai Jiaotong University School of Medicine from Jan 1st, 2011 to Dec 31th, 2011. All patients were observed for 1 year and followed up for 3 years. Clinical characteristics and biochemical indexes were collected at baseline. Hemoglobin (Hb) were regularly measured every 2 months, and ESA dose were collected in the 1-year observation period. Erythropoitin resistance index(ERI) was calculated as the weekly weight-adjusted dose of ESA divided by Hb level. All-cause death and cardiovascular disease (CVD) death were the primary endpoints.

Results: 250 MHD patients were involved in this study. 156(62.40%) patients were male, with median age 56.63(45.13,65.06) yrs old, median dialysis duration was 24.00(8.00,57.25) months. Logistic regression analysis showed female, longer dialysis duration, lower Hb level, lower pre-albumin level, lower spKt/V and use of intervenous iron were significantly associated with higher weekly ESA dose. Female, longer dialysis duration, lower BMI, lower Hb level, higher ALP, lower TIBC, higher CRP level and lower spKt/V were significantly associated with higher ERI. After 3-year follow-up, 26.40% (66 of 250) patients died. In the Kaplan-Meier analysis, patients with high weekly dose had the significantly highest all-cause mortality (log rank=6.630, P=0.036). Patients with higher ERI had relatively greater all-cause death (log rank=5.601, P=0.061). After adjustment for age and gender, high weekly ESA dose had a 2.22 times (95%CI, 1.18-4.17) increased all-cause mortality than low ESA dose, and high ERI also had a 3.17 times (95%CI, 1.63-6.14) increased all-cause mortality. The association of ERI and all-cause mortality still remained unchanged in multivariate analyses [HR 2.11 (95%CI, 1.03, 4.30)]. No significant difference was observed in the association of ESA dose, ERI with CVD mortality. In the multivariate Cox analysis, older age, higher pre-HD SBP, lower ALB level, lower URR and lower blood flow were significant risk factors associated with all-cause mortality, while older age, higher pre-HD SBP and lower MCH were significant risk factors related to CVD mortality.

Conclusions: High weekly ESA dose and ESA resistance had significantly increased all-cause mortality and can predicted clinical poor outcome. In clinical practice, we can calculate ERI index to assess clinical status or to evaluate prognosis of MHD patients.

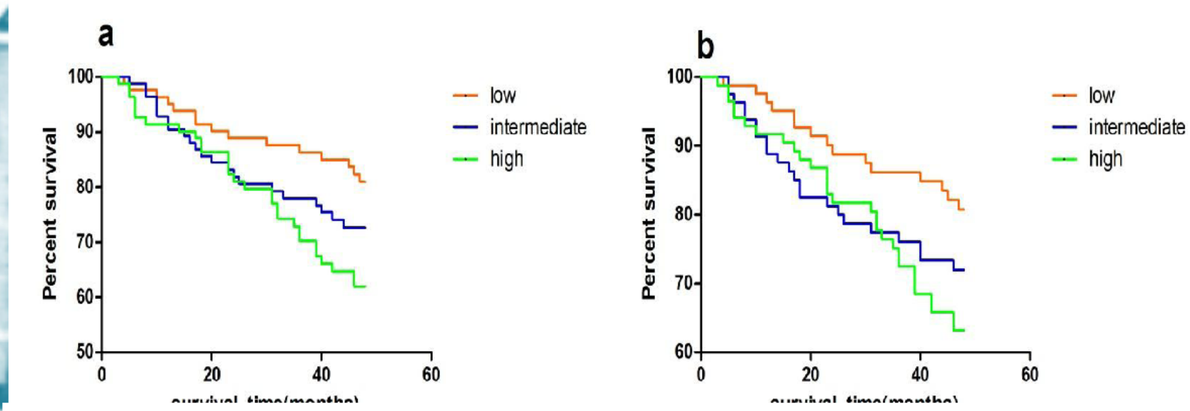

Fig. Survival curves of weekly ESA dose (a) and ERI(b) by tertiles for all-cause mortality

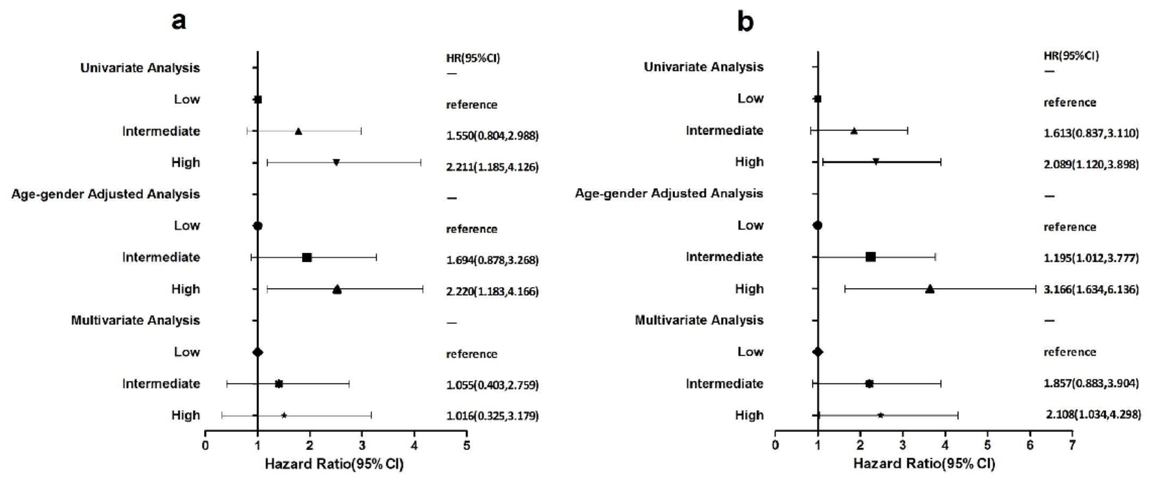

Fig. Effects of weekly ESA dose (a) and) ERI (b) by tertiles for all-cause mortality

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