

The Greatly Misunderstood Erythropoietin Resistance Index

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Objective

Examine whether the erythropoiesis-stimulating agents (ESA) resistance index (ERI) is an adequate measure of ESA resistance.

Background

- The optimal use of erythropoiesis stimulating agents to treat anemia in end-stage renal disease (ESRD) remains controversial due to reported associations with adverse events.
- Association studies often utilize ERI to characterize the patient's response to ESA.
- ESA is confounded by medical indication and time-dependent conditions, resulting in possible biased estimated effect on outcome.

Methods

- Retrospective data from a non-concurrent cohort study of incident hemodialysis patients in the United States (2004-2005, n=9386).
- ERI is defined as average weekly erythropoietin (EPO) dose per kg body weight (wt) per average hemoglobin (Hgb) over a 3-month period, $ERI = (EPO/wt)/Hgb$.
- Linear regression was used to demonstrate a linear relationship between ERI and weight-adjusted EPO.
- The coefficient of variation (CV) was used to compare the variability of Hgb with that of weight-adjusted EPO in order to explain this relationship
- Analysis was done for each quarter during the first year of dialysis.

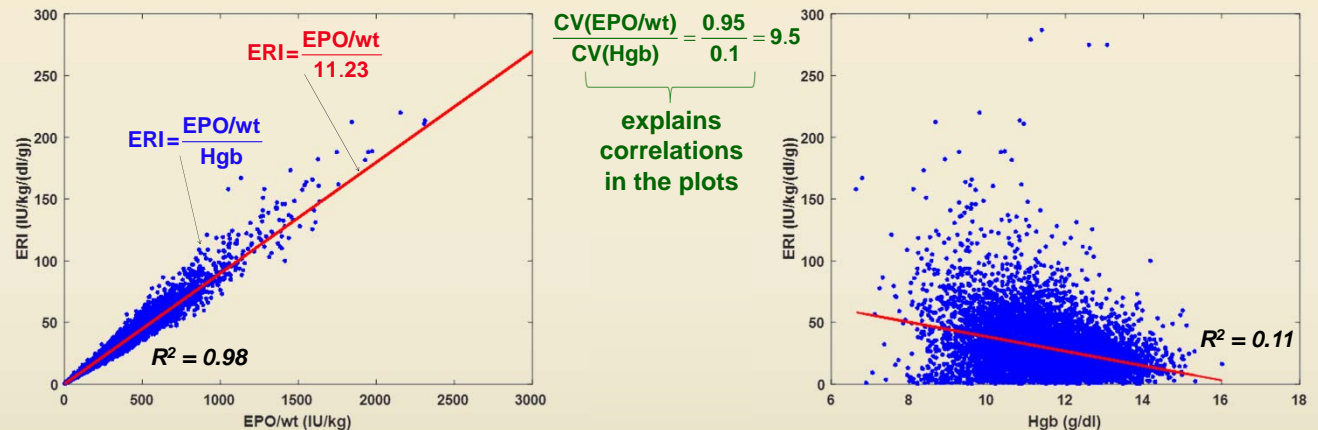
Results

Baseline characteristics for the study population; Categorical data are n (%). Continuous measures are mean ± SD.

Variable	All subjects (n=9386)
Age, yr	62.2 ± 15.5
Women	4268 (45.5)
White race	5663 (60.3)
Comorbidities:	
Coronary artery disease / myocardial infarction	929 (9.9)
Diabetes mellitus	2192 (23.4)
Vascular access: catheter	5564 (26.7)
Weight (kg)	77.2 ± 21.9

Quarterly correlations between ERI and EPO/wt and CV ratios

	Q1	Q2	Q3	Q4
n	9386	7925	6403	4415
R ² : ERI and (EPO/wt)	0.97	0.97	0.98	0.98
CV(EPO/wt)	9.5	10.9	13.6	13.4
CV(Hgb)				



Scatter plots of first-quarter Q1 (weeks 1-13) ERI for all patients (n = 9386) shows strong correlation with EPO dose (left) and weak correlation with Hgb (right).

Conclusions

- ERI is strongly linearly related to weight-adjusted EPO dose by a “universal”, not patient-specific formula, and thus is a surrogate of EPO dose and does not offer additional information regarding responsiveness.
- Associations between ERI and clinical outcomes are only associations between EPO dose and outcomes.
- The estimated effect of EPO on an outcome, and therefore of ERI, may be biased without appropriate adjustment for confounding.