Carbamylation of Serum Albumin and Erythropoietin Resistance in End Stage Kidney Disease

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Supplemental Materials

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Supplemental Table 1. Associations to natural log erythropoietin resistance index using single time point measurements at day 90

Predictor	Univariate Analysis Change in log ERI (95% CI)	P value	Multivariable Model 1 Change in log ERI (95% CI)	P value	Multivariable Model 2 Change in log ERI (95% CI)	P value
Carbamylation						
quartile 4 vs. 1	0.38 (0.02, 0.75)	0.04[a]	0.36 (0.01, 0.71)	0.04[b]	0.45 (0.08, 0.82)	0.02[c]
3 vs. 1	0.17 (-0.19, 0.53)	0.36[a]	0.18 (-0.16, 0.53)	0.30[b]	0.25 (-0.12, 0.63)	0.19[c]
2 vs. 1	-0.19 (-0.55, 0.18)	0.31[a]	0.08 (-0.25, 0.41)	0.63[b]	0.10 (-0.27, 0.47)	0.60[c]
Age	0.01 (-0.01, 0.02)	0.12			-0.01 (-0.01, 0.01)	0.52
Female	-0.03 (-0.29, 0.23)	0.82			0.09 (-0.20, 0.38)	0.56
White Race	0.01 (-0.28, 0.30)	0.94			-0.04 (-0.33, 0.23)	0.73
Urea Reduction Ratio	0.02 (0.01, 0.04)	0.02	0.01 (-0.01, 0.03)	0.17	0.02 (0.00, 0.04)	0.04
Hemoglobin (g/dl)	-0.28 (-0.36, -0.20)	<0.001	-0.26 (-0.35, -0.16)	<0.001	-0.25 (-0.35, -0.16)	<0.001
†Parathyroid Hormone (pg/ml)	-0.09 (-0.25, 0.08)	0.31			-0.03 (-0.20, 0.14)	0.70
Albumin (g/dl)	-0.82 (-1.09, -0.55)	<0.001	-0.64 (-0.91, -0.36)	<0.001	-0.55 (-0.84, -0.25)	<0.001
†Ferritin (ng/ml)	0.13 (-0.02, 0.27)	0.08	-0.01 (-0.15, 0.12)	0.87	0.02 (-0.12, 0.17)	0.74
Transferrin Saturation (%)	-0.01 (-0.03, 0.01)	0.16			-0.01 (-0.02, 0.01)	0.44
Received IV Iron Therapy	-0.30 (-0.62, 0.02)	0.07	0.07 (-0.23, 0.38)	0.64	0.11 (-0.22, 0.44)	0.50
Body Mass Index	-0.05 (-0.07, -0.03)	<0.001	-0.03 (-0.05, -0.01)	0.006	-0.02 (-0.04, -0.01)	0.02
Vascular Access (catheter)	-0.13 (-0.41, 0.14)	0.34			-0.08 (-0.35, 0.19)	0.56
†IL-6 (pg/ml)	0.12 (0.02, 0.22)	0.02	-0.03 (-0.12, 0.06)	0.52	-0.05 (-0.16, 0.05)	0.32
Myeloperoxidase (ng/ml)	0.00 (-0.01, 0.01)	0.89			0.00 (-0.01, 0.01)	0.91

Effect estimates of the association between various predictors and the natural log EPO resistance index (ERI) in univariate and multivariable analysis. Change in log ERI (95% CL) represents the change in the log ERI per unit change in the predictor (95% confidence interval).
Adjusted model 1 includes only variables significant in univariate analysis at P<0.1 level.
Adjusted model 2 includes all variables from the univariate analysis.
[a]P for overall trend across all quartiles = 0.01.
[b]P for overall trend across all quartiles = 0.04.
[c]P for overall trend across all quartiles = 0.01.
† Variable log-transformed.

Supplemental Table 2. Associations to natural log erythropoietin resistance index using the entire cohort (no subjects excluded, n=187)

Predictor	Univariate Analysis Change in log ERI (95% CI)	P value	Multivariable Model 1 Change in log ERI (95% CI)	P value	Multivariable Model 2 Change in log ERI (95% CI)	P value
Carbamylation						
quartile 4 vs. 1	0.70 (0.24, 1.11)	0.002[a]	0.55 (0.18, 0.92)	0.004[b]	0.68 (0.26, 1.11)	0.002[c]
3 vs. 1	0.27 (-0.15, 0.69)	0.21[a]	0.07 (-0.28, 0.43)	0.69[b]	0.23 (-0.20, 0.66)	0.29[c]
2 vs. 1	-0.15 (-0.57, 0.26)	0.47[a]	-0.24 (-0.59, 0.11)	0.17[b]	-0.19 (-0.60, 0.21)	0.34[c]
Age	0.01 (-0.01, 0.02)	0.27			-0.01 (-0.01, 0.01)	0.79
Female	-0.18 (-0.50, 0.13)	0.25			-0.22 (-0.54, 0.09)	0.16
White Race	-0.03 (-0.36, 0.31)	0.88			0.09 (-0.21, 0.38)	0.57
Urea Reduction Ratio	0.01 (-0.01, 0.03)	0.50			0.01 (-0.01, 0.02)	0.71
Hemoglobin (g/dl)	-0.43 (-0.52, -0.34)	<0.001	-0.29 (-0.38, -0.20)	<0.001	-0.28 (-0.39, -0.18)	<0.001
†Parathyroid Hormone (pg/ml)	-0.15 (-0.34, 0.04)	0.12			-0.06 (-0.23, 0.12)	0.53
Albumin (g/dl)	-1.0 (-1.31, -0.68)	<0.001	-0.46 (-0.79, -0.13)	0.01	-0.44 (-0.82, -0.07)	0.02
†Ferritin (ng/ml)	-0.20 (-0.36, -0.04)	0.01	-0.11 (-0.25, 0.03)	0.11	-0.10 (-0.26, 0.07)	0.24
Transferrin Saturation (%)	-0.04 (-0.06, -0.03)	<0.001	-0.03 (-0.04, -0.01)	<0.001	-0.03 (-0.04, -0.01)	<0.001
Received IV Iron Therapy	-0.57 (-0.97, 0.18)	0.005	-0.24 (-0.56, 0.08)	0.13	-0.26 (-0.64, 0.12)	0.18
Body Mass Index	-0.05 (-0.07, -0.03)	<0.001	-0.03 (-0.04, -0.01)	0.01	-0.02 (-0.04, 0.01)	0.04
Vascular Access (catheter)	-0.26 (-0.59, 0.64)	0.11			-0.06 (-0.37, 0.25)	0.72
†IL-6 (pg/ml)	0.16 (0.05, 0.28)	0.01	-0.05 (-0.14, 0.05)	0.35	-0.09 (-0.21, 0.03)	0.15
Myeloperoxidase (ng/ml)	0.01 (-0.01, 0.01)	0.47			0.01 (-0.01, 0.01)	0.72

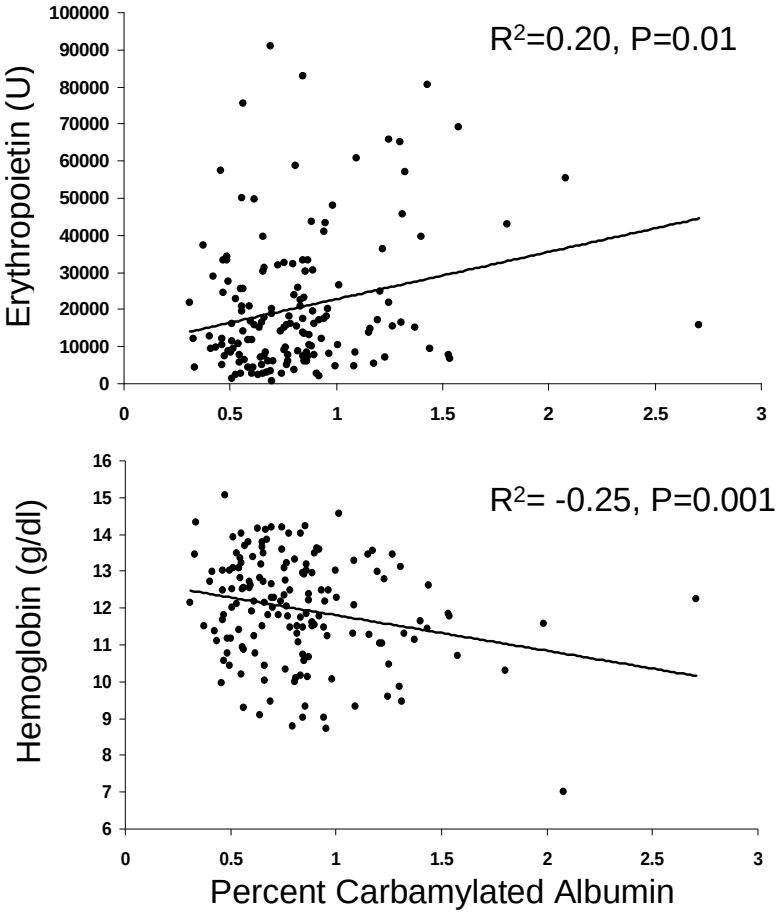
Effect estimates of the association between various predictors and the natural log EPO resistance index (ERI) in univariate and multivariable analysis. Change in log ERI (95% CL) represents the change in the log ERI per unit change in the predictor (95% confidence interval).
Adjusted model 1 includes only variables significant in univariate analysis at P<0.1 level.
Adjusted model 2 includes all variables from the univariate analysis.
[a]P for overall trend across all quartiles = <0.001.
[b]P for overall trend across all quartiles = 0.002.
[c]P for overall trend across all quartiles = <0.001.
† Variable log-transformed.

Supplemental Table 3. Baseline characteristics by 1-year mortality status in the entire cohort (no subjects excluded, n=187)

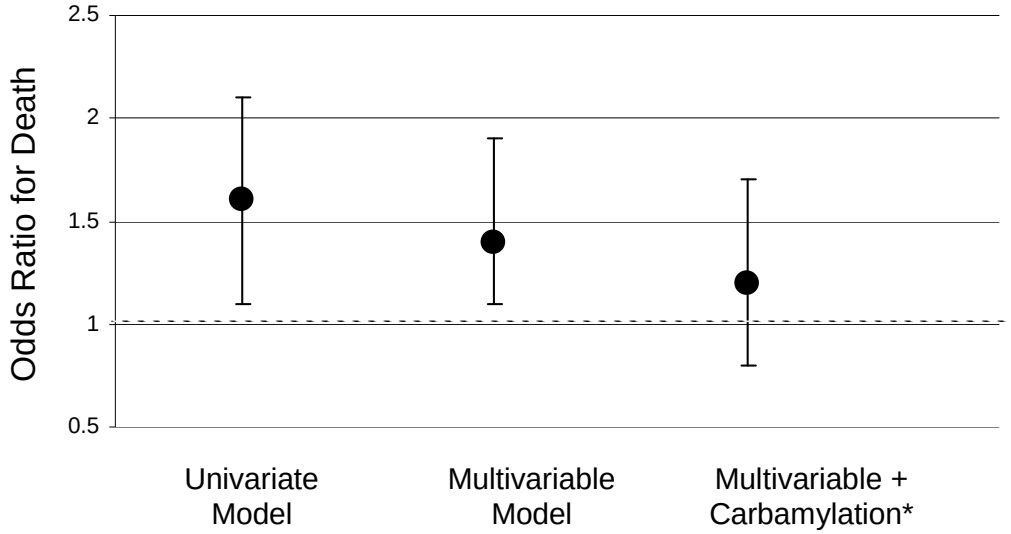
	Subjects alive at 1 year (n=106)	Subjects dead at 1 year (n=81)	P value*
Age, years	69.5 ± 12.7	70.1 ± 12.7	0.76
Female	51 (48.1)	40 (49.4)	0.86
White Race	73 (68.9)	57 (70.4)	0.83
Co-morbidities			
Diabetes mellitus	31 (29.3)	17 (21.0)	0.20
Coronary artery disease	13 (12.3)	9 (11.1)	0.81
Congestive heart failure	20 (18.9)	20 (25.0)	0.34
Vascular access: Catheter	58 (56.9)	55 (71.4)	0.05
Body Mass Index (kg/m^2)	26.5 ± 7.2	26.5 ± 7.0	0.95
Systolic blood pressure (mmHg)	147.8 ± 22.5	137.5 ± 25.2	0.004
Diastolic blood pressure (mmHg)	73.7 ± 11.6	69.0 ± 13.6	0.01
Urea reduction ratio	68.3 ± 10.6	68.6 ± 8.7	0.88
Laboratory data			
Hemoglobin (g/dl)	10.5 (9.7-11.3)	10.6 (9.5-11.2)	0.70
Albumin (g/dl)	3.5 (3.3-3.9)	3.5 (3.2-3.8)	0.10
Ferritin (ng/ml)	183 (100-324)	200 (88-437)	0.76
Transferrin saturation (%)	19 (15-25)	18 (13-24)	0.21
Phosphorus (mg/dl)	4.6 (3.8-5.7)	4.0 (3.2-5.0)	0.01
Parathyroid hormone (pg/ml)	221 (115-318)	190 (98-439)	0.92
IL-6 (pg/ml)	11.9 (6.0-31.0)	25.9 (11.8-59.2)	0.002
Myeloperoxidase (ng/ml)	35.4 (19.6-69.6)	38.2 (19.3.-60.1)	0.89

Categorical data are n (percentages). Continuous measures are means ± standard deviations. Laboratory values are median (quartile 1 – quartile 3). Values reflect baseline measurements taken during the first 90 days of initiating dialysis.

*P values represent alive vs. dead chi square, Wilcoxon rank sum, or t-tests as appropriate.



Supplemental Figure 1. Pearson correlations of percent carbamylated albumin level with erythropoietin dose and hemoglobin.



Supplemental Figure 2. Odds ratio for death by erythropoietin resistance index (no subjects excluded, n= 187)
Odds ratios represent odds per unit change in natural log ERI. Bars are 95% confidence interval. Multivariable model includes systolic blood pressure, diastolic blood pressure, vascular access (catheter vs. no catheter), phosphorous, and IL6. *In the final model, percent carbamylated albumin, highest vs. lowest quartile had an odds ratio for death of 4.3 (1.4-12.9), P 0.003.