

Association Between Adiponectin and Mortality in Hemodialysis Patients from the MADRAD Study

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BACKGROUND

- **Adipose tissue** has gained recognition as an **endocrine organ** and a source of biologically active **adipokine** hormones (e.g., adiponectin, leptin).
- In the general population, circulating adiponectin has **anti-atherogenic, anti-inflammatory, and insulin-sensitizing properties** and is associated with **decreased cardiovascular morbidity and mortality**.
- **Maintenance hemodialysis (MHD)** patients have comparatively **higher adiponectin** concentrations.
- Prior studies examining the relationship between **adiponectin** concentration and **mortality in MHD patients** have been **inconsistent**.

OBJECTIVE

- To examine the association between **adiponectin** level and **all-cause mortality** in a prospective cohort of MHD patients.

RESULTS

Table 1. Baseline Characteristics by Adiponectin Tertile. Among 501 patients who underwent adiponectin measurement (mean ± SD 26.9 ± 17.6 mcg/ml; range 5.3-100.0 mcg/ml), the mean ± SD age was 55.2 ± 14.9 years, and 44% were female, 40% were African-American, and 47% had diabetes.

	Tertile 1 % (n)	Tertile 2 % (n)	Tertile 3 % (n)	p-value*
No. of patients	32.9% (165)	33.1% (166)	33.9% (170)	N/A
Adiponectin range (mcg/ml)	0-16.1	>16.1-<30.1	>30.1	N/A
Age (years)	52.8 ± 14.5	56.6 ± 15.6	56.0 ± 14.6	0.6
Vintage (years)	2.9 (1.2, 5.3)	3.6 (1.5, 7.3)	3.9 (1.9, 7.1)	0.007
Female	34.6% (57)	48.2% (80)	47.7% (81)	0.02
Black race	45.5% (75)	36.1% (60)	38.2% (65)	0.2
Hispanic ethnicity	38.2% (63)	48.8% (81)	48.8% (83)	0.08
Diabetes	46.1% (76)	48.8% (81)	46.5% (79)	0.9
LABORATORY TESTS				
Median (IQR)				
Serum albumin (g/dl)	4.1 (3.9, 4.3)	4.0 (3.7, 4.2)	4.0 (3.7, 4.2)	0.06
Creatinine (mg/dl)	9.9 (8.0, 12.3)	8.9 (7.2, 11.5)	9.3 (7.6, 11.0)	0.05
Phosphorus (mg/dl)	4.8 (4.2, 6.1)	4.9 (4.0, 5.7)	4.9 (4.1, 6.1)	0.7
Hemoglobin (g/dl)	10.0 (10.6, 11.2)	10.8 (10.2, 11.3)	10.7 (10.1, 11.3)	0.4
WBC	7.0 (5.8, 8.4)	6.6 (5.5, 8.3)	5.9 (4.5, 7.2)	<0.001
TIBC	224 (207, 251)	221 (188, 253)	213 (193, 242)	0.08
nPCR	1.0 (0.8, 1.2)	1.0 (0.9, 1.2)	1.0 (0.8, 1.2)	0.4

*P-value calculated by ANOVA, chi-square, or Kruskal Wallis tests.

Abbreviations: WBC, white blood cell count; TIBC, total iron binding capacity; nPCR, normal protein catabolic rate

Table 2. Association of Adiponectin Level in Tertiles and in Continuous Increments with All-Cause Mortality. Compared with the lowest adiponectin tertile, the highest adiponectin tertile was associated with increased all-cause mortality risk in unadjusted, case-mix, and case-mix + laboratory adjusted models. When examined in continuous increments, higher adiponectin level was associated with increased all-cause mortality in all models.

	Unadjusted		Case-mix adjusted		Case-mix + Laboratory adjusted	
	HR (95% CI)	p-value*	HR (95% CI)	p-value**	HR (95% CI)	p-value***
Adiponectin Tertile 2 (>16.1-<30.1 mcg/ml)	1.81 (0.79- 4.15)	0.2	1.71 (0.74-3.95)	0.2	1.71 (0.73-4.01)	0.2
Adiponectin Tertile 3 (>30.1 mcg/ml)	3.13 (1.46- 6.72)	0.003	3.09 (1.42-6.75)	0.005	3.35 (1.50-7.47)	0.003
Continuous Increments						
	Unadjusted		Case-mix adjusted		Case-mix + Laboratory adjusted	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Δ Adiponectin by 10.0 mcg/ml	1.27 (1.13-1.42)	<0.001	1.26 (1.12- 1.41)	<0.001	1.25 (1.10-1.41)	0.001
Δ Adiponectin by 1 standard deviation†	1.52 (1.24-1.86)	<0.001	1.50 (1.22-1.83)	<0.001	1.47 (1.18-1.84)	0.001

*p for trend=0.002; **p for trend=0.001; ***p for trend=0.002

†Standard deviation=17.6 mcg/ml

METHODS

- Study Design:
 - Prospective observational cohort study.
- Study Population:
 - 501 prevalent MHD patients from the prospective "**Malnutrition, Diet, and Racial Disparities in Kidney Disease**" (**MADRAD**) cohort.
 - Recruited from 13 DaVita Healthcare Partners Inc. dialysis clinics from October 2011 to February 2013.
- Exposure:
 - Baseline serum **adiponectin** level.
- Outcome:
 - **All-cause mortality**.
- Statistical Analyses:
 - Cox proportional hazards regression using 3 levels of multivariable adjustment for potential confounders:
 - ❖ Unadjusted.
 - ❖ Case-mix adjusted: age, sex, African-American race, Hispanic ethnicity, diabetes, vintage.
 - ❖ Case-mix + laboratory test adjusted: case-mix model covariates + serum albumin, serum creatinine, phosphorus, normalized protein catabolic rate, hemoglobin, total iron binding capacity, white blood cell count.

Figure 1. Kaplan Meier Survival Curves for Adiponectin Tertiles. In unadjusted analyses, the lowest and second adiponectin tertiles were associated with greater survival compared to the highest adiponectin tertile.

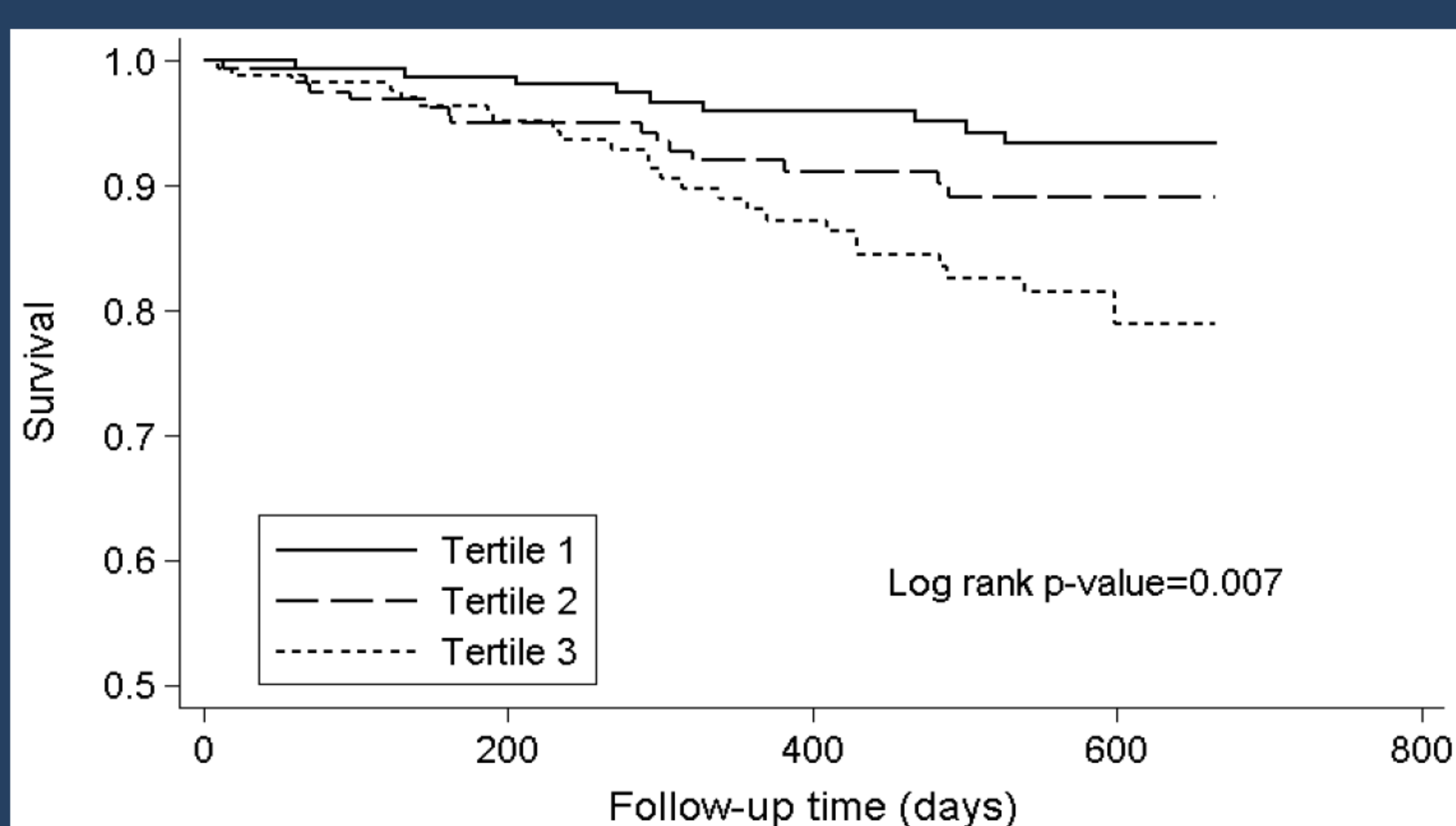
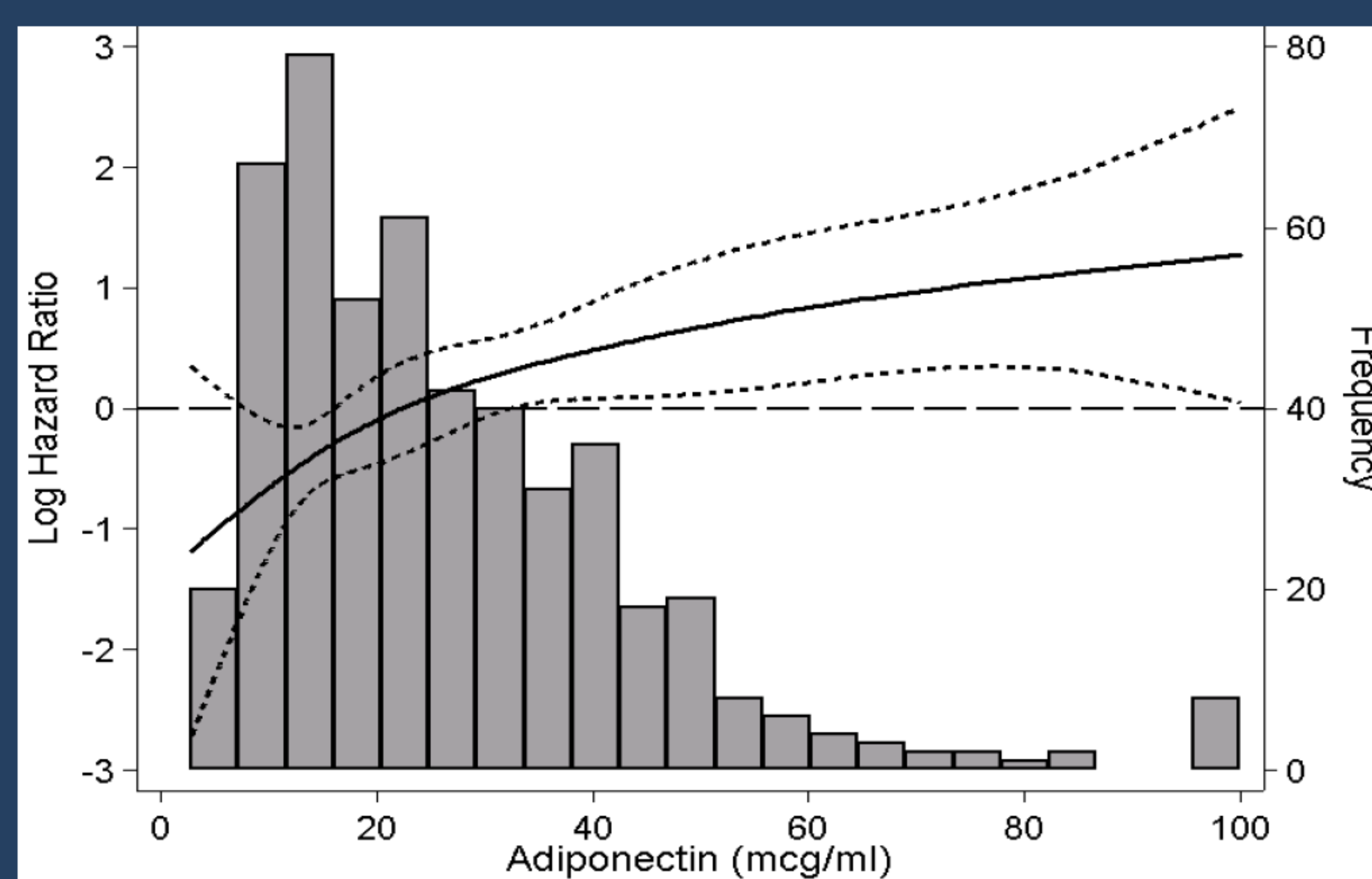


Figure 2. Adiponectin as a Continuous Predictor of Mortality Using a Spline Model Adjusted for Case-Mix + Laboratory Covariates. In sensitivity analyses that examined adiponectin as a continuous variable, incrementally higher adiponectin level was associated with increased death risk.



CONCLUSION

- Higher circulating adiponectin levels in MHD patients are paradoxically associated with higher all-cause mortality.
- Future studies are needed to confirm findings and to elucidate mechanistic pathways.