



Anemia, irrespective of Iron Deficiency, is associated with Graft Failure in Renal Transplant Recipients

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Introduction

Post-transplant anemia and iron deficiency (ID) are highly prevalent in renal transplant patients (RTRs). Recently, it was shown that ID, irrespective of anemia, is associated with all-cause mortality in RTRs. In this study, we aimed to assess the effect of anemia, iron deficiency anemia (IDA), and ID on renal outcome in RTRs. Since ID may have a differential effect on the heart and the kidney, we further studied whether ID contributes to a putative association of anemia with death-censored graft failure (DCGF).

Methods

The study was performed in an extensively phenotyped RTRs cohort. ID was defined as absolute ID with a ferritin <100 ng/ml due to the availability of only ferritin levels. Anemia was defined as Hb<13 g/dL (M) or <12 g/dL (F). Cox regression analyses were used to investigate prospective associations with DCGF.

Results

We included 604 RTRs (age 51±12 years; 55% males at median (IQR) 6.0 (2.6-11.5) years after transplantation). Mean Hb was 13.7±1.6 g/dL, ferritin was 155 (75-283) µg/L. Prevalences of anemia, ID, and IDA were 18%, 31%, and 8%, resp. During follow-up for 6.2±1.9 yr, 54 (9%) RTRs developed DCGF. In univariable analysis, anemia was strongly associated with DCGF (HR 6.99 [95%CI 4.09-11.97], *P*<0.001). In contrast, ID (0.84 [0.46-1.53], *P*=0.56) and IDA (1.83 [0.83-4.06], *P*=0.14) were not associated with DCGF. The association of anemia with DCGF was independent of adjustment for age, gender, and BMI (6.55 [3.79-11.30], *P*=0.001). The association remained after further adjustment for eGFR (2.18 [1.20-3.95], *P*=0.01) and after adjustment for ID and erythropoietin levels (2.42 [1.31-4.47], *P*=0.005). The association also remained independent of further adjustment for hs-CRP and FGF23 (HR 2.09 [1.12-3.87], *P*=0.02).

Table 1. Baseline characteristics

Variables	Anemia (n=108)	No anemia (n=496)	P-value
Age (years)	48.5±11.6	52.1±12.1	0.005
Sex (male, %)	63	53	0.06
BMI (kg/m ²)	25.8±4.7	26.0±4.2	0.62
eGFR (ml/min/1.73m ²)	36.0±16.6	49.4±14.6	<0.001
Hb (g/dL)	11.5±1.0	14.2±1.2	<0.001
Ferritin (ug/L)	187 (102-337)	150 (73-271)	0.03
EPO (IU/L)	20.3 (12.0-27.2)	17.0 (11.9-23.6)	0.03
hs-CRP (mg/L)	2.6 (1.0-7.8)	2.0 (0.8-4.6)	0.16
cFGF23 (RU/mL)	248 (142-493)	129 (88-195)	<0.001

Table 2. Cox regression analysis between anemia and graft failure

Model	HR (95% CI)	P-value
Univariate	6.99 (4.09-11.97)	<0.001
Model 1	6.55 (3.79-11.30)	0.001
Model 2	2.18 (1.20-3.95)	0.01
Model 3	2.42 (1.31-4.47)	0.005
Model 4	2.09 (1.12-3.87)	0.02

Model 1: Adjustment for age, sex, and BMI;

Model 2: Model 1 + adjustment for eGFR

Model 3: Model 2 + adjustment for absolute ID and EPO levels;

Model 4: Model 2 + adjustment for hs-CRP and FGF23

Figure 1. Kaplan-Meier curves for risk of anemia on graft failure

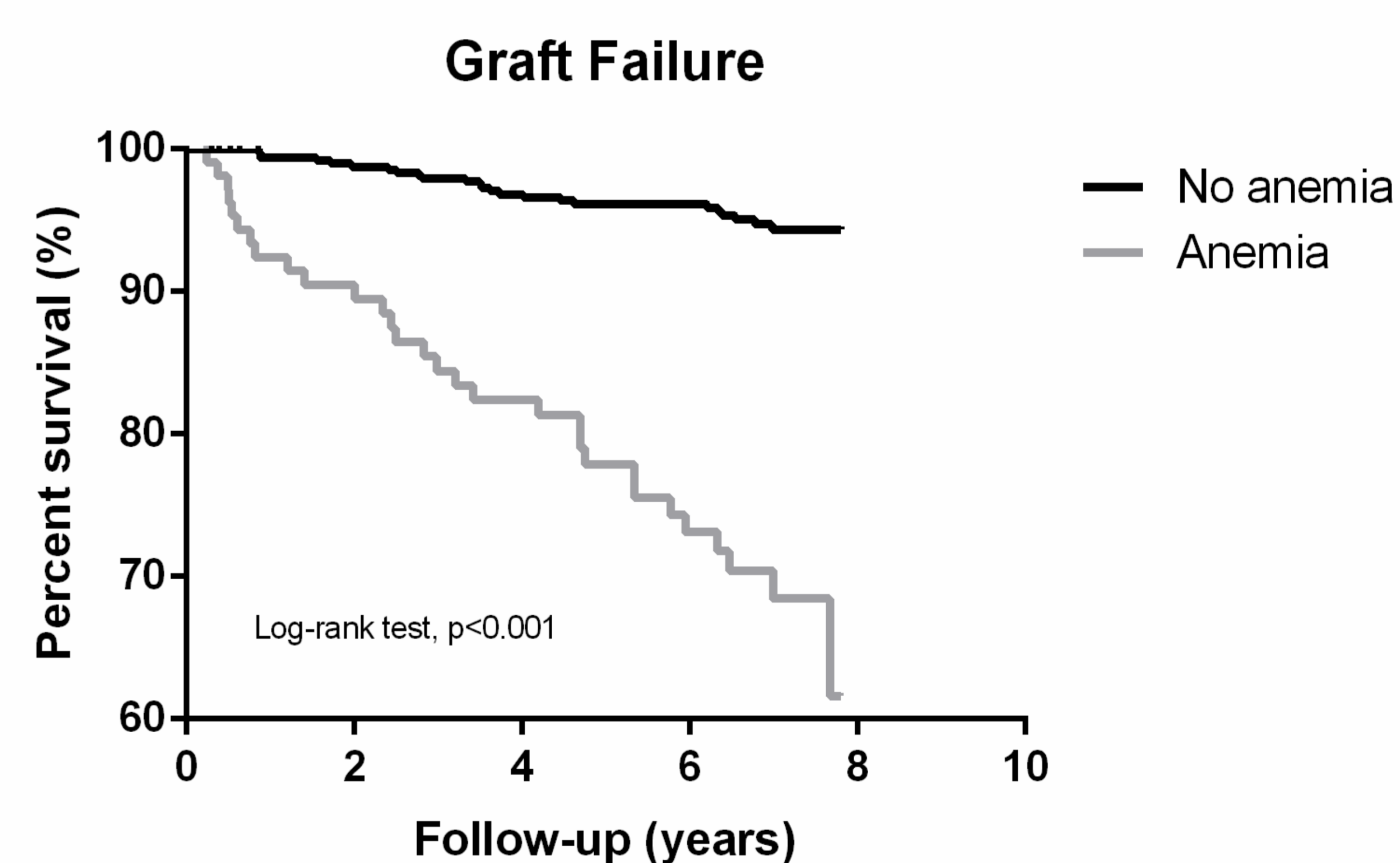


Figure 1: Kaplan-Meier curves for graft survival based on presence of anemia

Conclusion

Anemia, irrespective of ID, is associated with a markedly increased risk of DCGF, whereas both IDA and ID were not associated with DCGF. Interestingly, the association of anemia with DCGF remained after adjustment for eGFR and erythropoietin levels, suggesting that the association is not explained by renal function or erythropoietin resistance. Further research is needed to elucidate the mechanism linking anemia to renal outcome.