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Hyporesponsiveness to erythropoiesis-stimulating agents in kidney transplant recipients with late posttransplant anemia

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Background

Posttransplant anemia (PTA)

Posttransplant anemia (PTA) is a common complication of kidney transplant recipients. Previous reports demonstrated that PTA could be associated with increased mortality, reduced graft survival, and decline in glomerular filtration rate. Erythropoiesis-stimulating agents (ESAs) are used for the treatment of late PTA to achieve better graft survival.

Hyporesponsiveness to ESAs

Hyporesponsiveness to ESAs in patients with chronic kidney disease (CKD) is a predictor for poor renal and cardiovascular outcome. Previously, up to 10% of patients with CKD showed poor hyporesponsiveness to ESAs. However, a method to measure ESA hyporesponsiveness has not yet been established. Moreover, there are few reports regarding hyporesponsiveness to ESAs in kidney transplant recipients with PTA

Purpose

In this present study, we analyzed the prevalence of ESA hyporesponsiveness in kidney transplant recipients with late PTA.

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I have no financial conflicts of interest to disclose.

Patients and Methods

A cross-sectional observational study was conducted to investigate the prevalence of ESAs hyporesponsiveness in kidney transplant recipients with late PTA at Osaka Metropolitan University Hospital. A total of 249 patients who were followed at least a year after living or dceased kidney transplantation between April 2020 to July 2020 were enrolled in this study.

Definition

PTA

PTA is defined as hemoglobin level<11 g/dl or receiving an ESA.

Hyporesponsiveness to ESAs

Hyporesponsiveness to ESAs is defined as kidney transplant recipients requiring >6,000 units/week of rHuEPO or requiring 0.75μg/kg/2 weeks of darbepoetin alfa(DA) to maintain the target hemoglobin level (hemoglobin >11 g/dl).

ESA doses of epoetin beta pegol (CERA) and DA were multiplied by 200 to be converted to rHuEPO doses, and ESA doses, and ESA dosage f CERA and DA are considered equal.

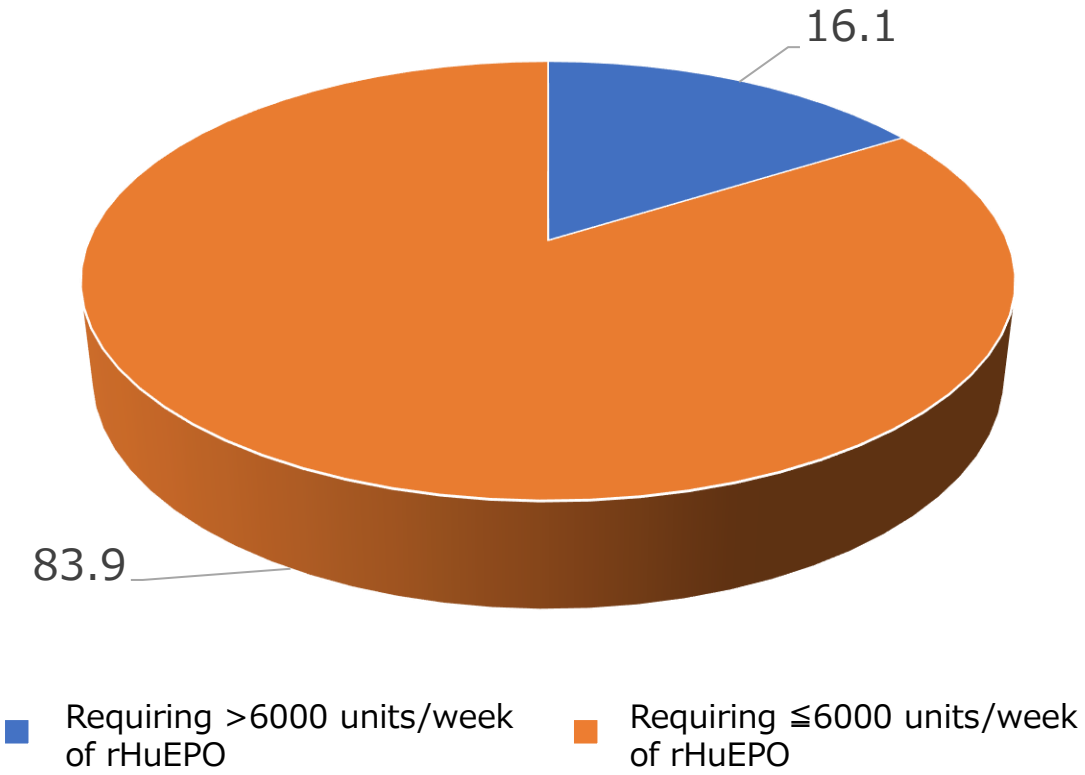
Patients' characteristics

	Posttransplant anemia (-) n=189	Posttransplant anemia (+) n=60	
ESA		n=56	
ESA (unit/week)		4166 (2500.0-5000.0)	
DA(CERA) (μg/kg/2 weeks)		0.71 (0.45-1.06)	
age (year)	56.0 (47.0-60.0)	48.0 (42.5-61.8)	p=0.0303
male/femal	119/70	28/32	p=0.034
Dialysis duration (months)	17.0 (6.0-57.0)	17.0 (9.5-39.0)	P=0.833
Posttransplant duration (months)	128.5 (69.3-183.8)	108.0 (48.3-160.3)	P=0.147
Red blood cell ($10^6/\mu$ L)	376 (341-403)	447.0 (414.0-479.0)	p<0.001
Hemoglobin (g/dl)	10.8 (10.1-11.6)	13.3 (12.3-14.2)	p<0.001
Serum creatinine (mg/dl)	1.23 (1.00-1.50)	1.57 (1.19-2.01)	p<0.001
eGFR (ml/min/1.73m$^{2)}$	44.4 (35.7-53.9)	34.9 (27.3-42.6)	p<0.001
C-reactive protein (mg/dl)	0.05 (0.02-0.12)	0.04 (0.01-0.08)	p=0.334
Albumin (g/dl)	4.0 (3.8-4.1)	4.0 (3.8-4.1)	P=0.0603
Urinary albumin creatinine ratio (mg/g Cr)	21.5 (7.0-106.3)	37.5 (15.5-103.5)	P=0.134
Low density lipoprotein cholesterol (mg/dl)	101.0 (85.0-124.0)	102.5 (79.5-124.5)	P=0.681
Body mass index (kg/m$^{2)}$	22.3 (20.1-25.4)	21.4 (19.6-23.6)	p=0.058
Hypertension (+/-)	149/39	Apr-56	p=0.0108
Antimetabolite/mTORi	138/50	38/22	P=0.144

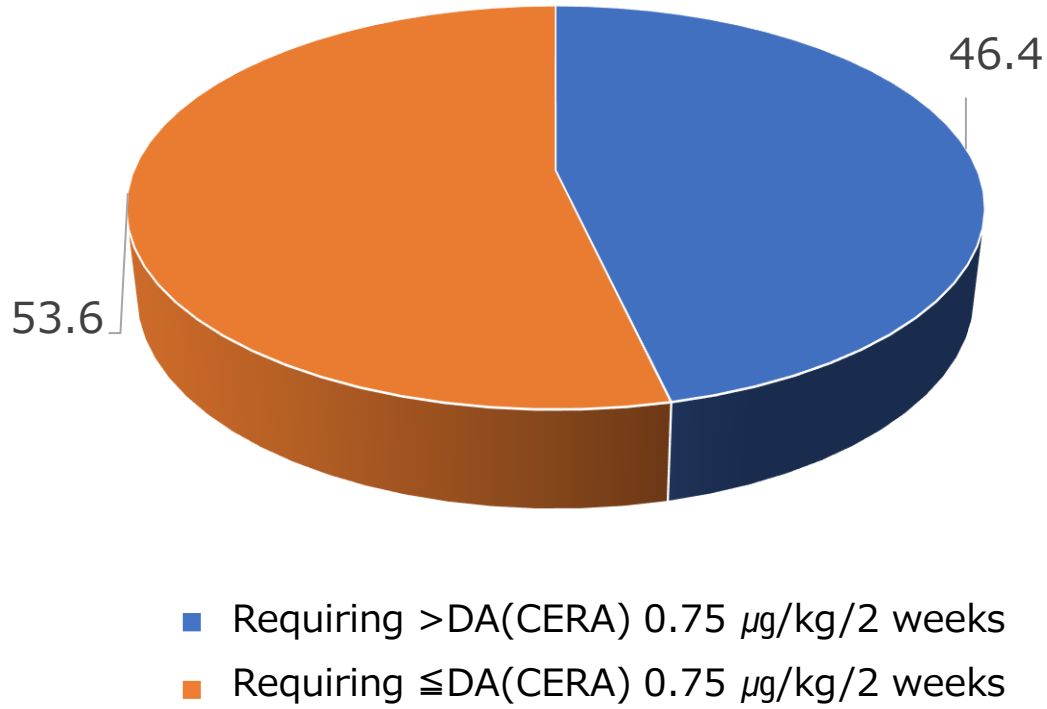
ESA; Erythropoiesis-stimulating agent, DA; darbepoetin-alfa, CERA; Epoetin Beta Pegol, eGFR; estimated glomerular filtration rate, mTORi; mammalian target of rapamycin inhibitor

The prevalence of ESA hyporesponsiveness in kidney transplant recipients with late PTA

Criteria of ESA hyporesponsiveness, which is recipients requiring >6000 units/week of rHuEPO



Criteria of ESA hyporesponsiveness, which is recipients requiring >DA (CERA)0.75 μg/kg/week



Discussion

- Although the prevalence of ESA hyporesponsiveness in kidney transplantation differed according to the criteria used to this present study, the prevalence of ESA hyporesponsiveness may be higher in kidney transplantation than in non-dialysis CKD patients. Previously, up to 10% of patients with CKD showed ESA hyporesponsiveness.
- ESA hyporesponsiveness may be involved in the pathophysiology of PTA, possibly relating to risk factors such as iron deficiency, infections, and myelotoxic drugs.