

Hypo-responsiveness to ESAs is associated with lipid metabolism in patients with chronic kidney disease at the time of dialysis initiation.

Authors

Daijo Inaguma, Yuki Kato, Kazunori Goto, Minako Murata, Hibiki Shinjo, Yasuhiro Otsuka, Keiji Horike, Asami Takeda, Kunio Morozumi, AICOPP study group
Japanese Red Cross Nagoya Daini Hospital, Kidney Disease Center

Background:

Hypo-responsiveness to erythropoiesis-stimulating agents (ESA) develops under variable conditions such as iron deficiency, inflammation, and malignancy. Hypo-responsiveness to ESAs is crucial for the association with high mortality. Several studies have indicated a relationship between hypo-responsiveness to ESAs and hypoalbuminemia caused by inflammation, but data regarding the relation to lipid metabolism are lacking. Therefore, we examined whether hypo-responsiveness to ESAs influenced lipid metabolism in patients with chronic kidney disease during the period of dialysis initiation.

Objects & Methods:

We performed a multicenter retrospective observational study of 542 patients newly starting on dialysis therapy under the auspices of the AICOPP study group. All patients were followed by nephrologists and administered only darbepoetin for 3 months before the initiation of dialysis or did not receive ESAs. The ESA responsiveness index (ERI) was defined as the average weekly darbepoetin dose divided by the hemoglobin level and body weight at the time of the first dialysis session. The average weekly darbepoetin dose was calculated by dividing the total 3-month dose by 12.

Results:

Patients Profiles

Age (y.o)	66.7±13.0	Hemoglobin	9.58±1.31
Male : Female	365 : 177	Hematocrit	29.3±4.1
Diabetes (51.3%)	278	ERI	10.0±7.0
History of CAD 78 (14.4%)	Albumin	3.28±0.59	
PCI 49 (9.0%)	BUN	88.5±26.5	
CABG 18 (3.3%)	Creatinine	9.02±2.96	
History of CHF (19.2%)	eGFR	5.3±1.9	
History of Stroke 72 (13.3%)	TSAT	25.9±6.5	
CCS 4.6±1.7	Ferritin	144±126	
BMI 23.6±4.0	CRP	1.13±3.49	
BI 91.8±18.5	iPTH	364±259	

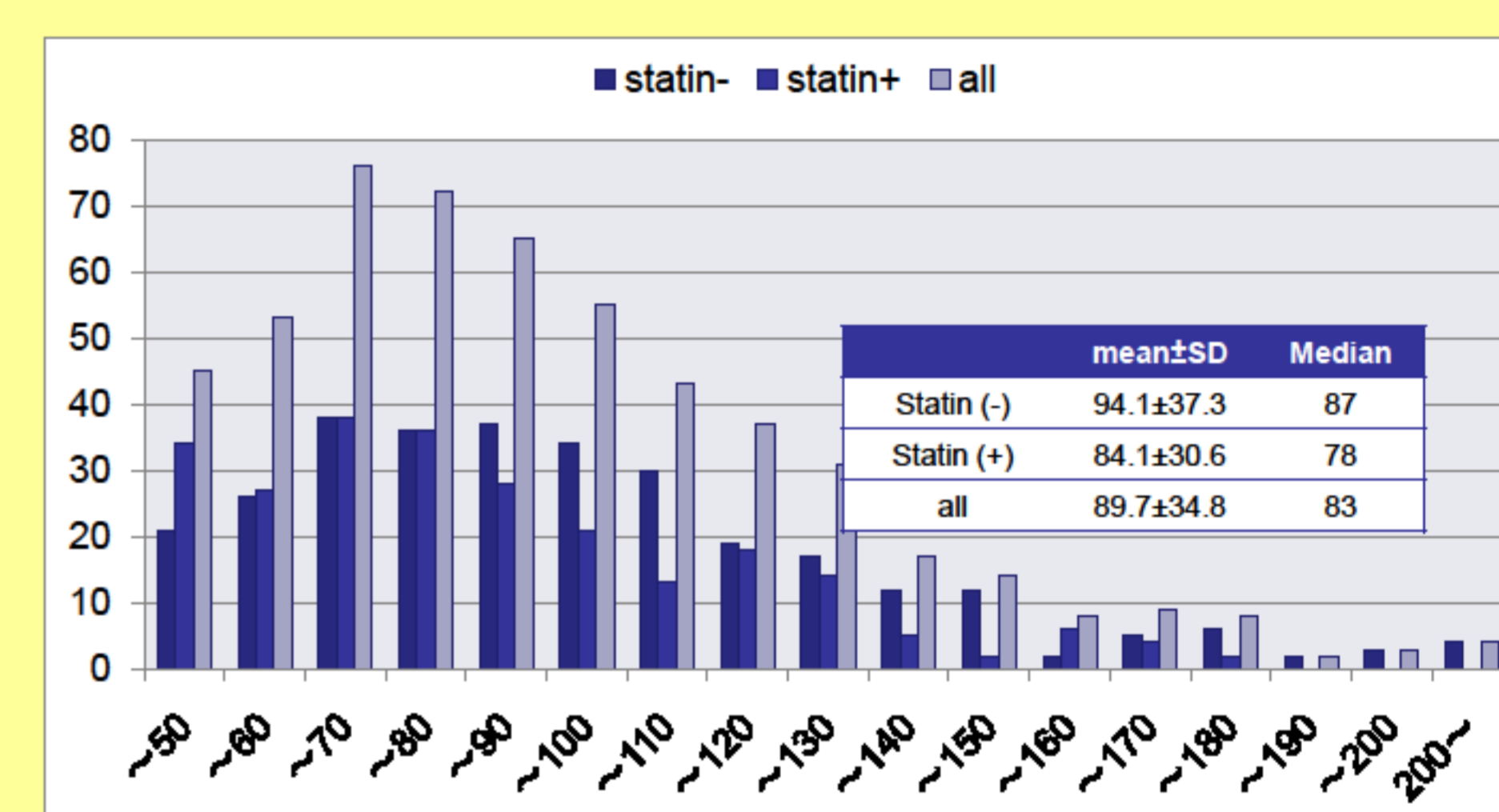
Correlation between ERI and lipids

(Univariate regression analysis)

Variables	Correlation coefficient	Regression coefficient	p value	95%CI (lower)	95%CI (upper)
T-Chol	-0.056	-0.009	0.1938	-0.023	0.005
nonHDL	-0.123	-0.021	0.0046	-0.036	-0.007
LDL	-0.097	-0.02	0.0235	-0.037	-0.003
HDL	0.147	0.06	0.0006	0.026	0.095
LDL/HDL	-0.193	-1.178	<0.0001	-1.685	-0.671
TG	-0.175	-0.018	<0.0001	-0.026	-0.009

The distribution of serum LDL-C

(Use of statin 238patients · Unuse 304patients)



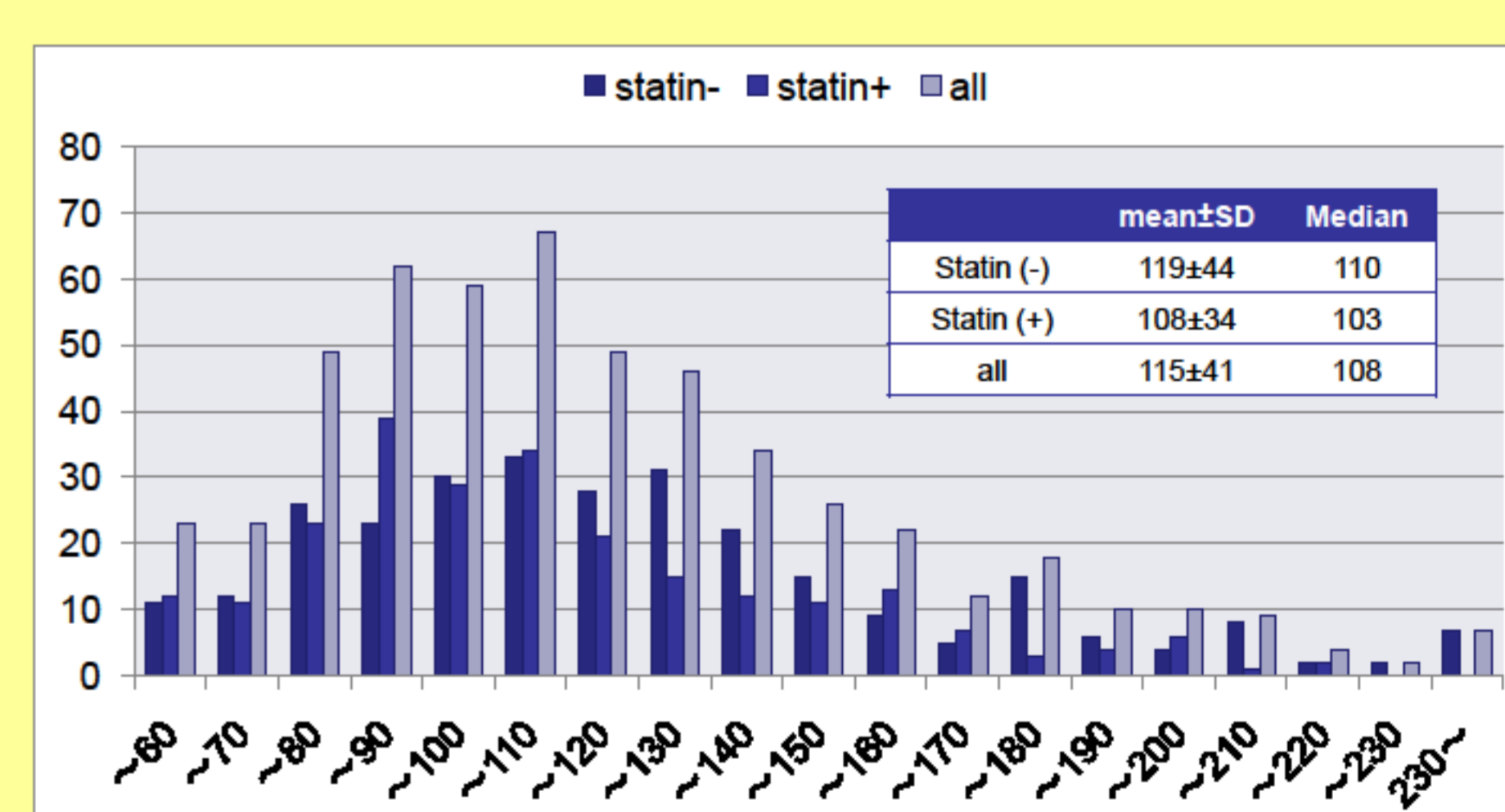
Correlation between ERI and lipids

(Multivariate regression analysis)

Variables	Regression coefficient	p value	95%CI (lower)	95%CI (upper)
Adjusted for age and gender				
nonHDL	-0.024	0.0009	-0.038	-0.01
LDL	-0.022	0.0074	-0.022	-0.006
HDL	0.049	0.0043	0.015	0.082
LDL/HDL	-1.073	<0.0001	-1.558	-0.588
TG	-0.019	<0.0001	-0.027	-0.01
Adjusted for age, gender, diabetes, malignancy, BI, BMI, use of statin, albumin, BUN, TSAT, ferritin, CRP, Urinary protein				
nonHDL	-0.018	0.0306	-0.033	-0.002
LDL	-0.015	0.1092	-0.034	0.003
HDL	0.05	0.0129	0.011	0.089
LDL/HDL	-0.878	0.0034	-1.463	-0.293
TG	-0.012	0.0064	-0.021	-0.003

The distribution of serum non HDL-C

(Use of statin 238patients · Unuse 304patients)



Correlation between ERI and parameters

(Univariate regression analysis)

Variables	Correlation coefficient	Regression coefficient	p value	95%CI (lower)	95%CI (upper)
Age	0.221	0.121	<0.0001	0.076	0.166
Female gender	0.23	3.442	<0.0001	2.209	4.675
Diabetes	-0.102	-1.433	0.0176	-2.616	-0.251
CAD	0.041	0.815	0.3448	-0.878	2.507
Malignancy	0.094	2.126	0.0283	0.227	4.026
CCS	0.007	0.028	0.8749	-0.317	0.372
BI	-0.104	-0.04	0.0164	-0.072	-0.007
BMI	-0.196	-0.341	<0.0001	-0.486	-0.196
RAS inhibitors	0.018	0.263	0.6765	-0.976	1.503
Loopdiuretics	0.059	0.893	0.1733	-0.394	2.18
Statin	0.042	0.588	0.3348	-0.608	1.784
VDR	0.016	0.248	0.7132	-1.075	1.57
AST120	0.064	0.977	0.137	-0.312	2.265
Bicarbonate	0.048	0.68	0.2608	-0.507	1.868
Alb	-0.042	-0.499	0.3326	-1.509	0.511
BUN	0.122	0.032	0.0046	0.01	0.055
Cr	-0.066	-0.158	0.1227	-0.358	0.043
eGFR	-0.054	-0.204	0.2107	-0.525	0.116
β2MG	0.113	0.142	0.0334	0.011	0.272
adjusted Ca	-0.031	-0.215	0.4695	-0.797	0.368
P	0.039	0.167	0.3609	-0.192	0.525
TSAT	-0.093	-0.101	0.0454	-0.2	-0.002
ferritin	-0.18	-0.01	<0.0001	-0.015	-0.005
BNP	0.055	0.001	0.3075	-4.73E-04	0.001
CRP	0.038	0.078	0.3884	-0.099	0.255
iPTH	0.099	0.003	0.0238	3.64E-04	0.005
calcitriol	0.033	0.034	0.5985	-0.094	0.162
HCO ₃ ⁻	-0.001	-0.002	0.9807	-0.143	0.139

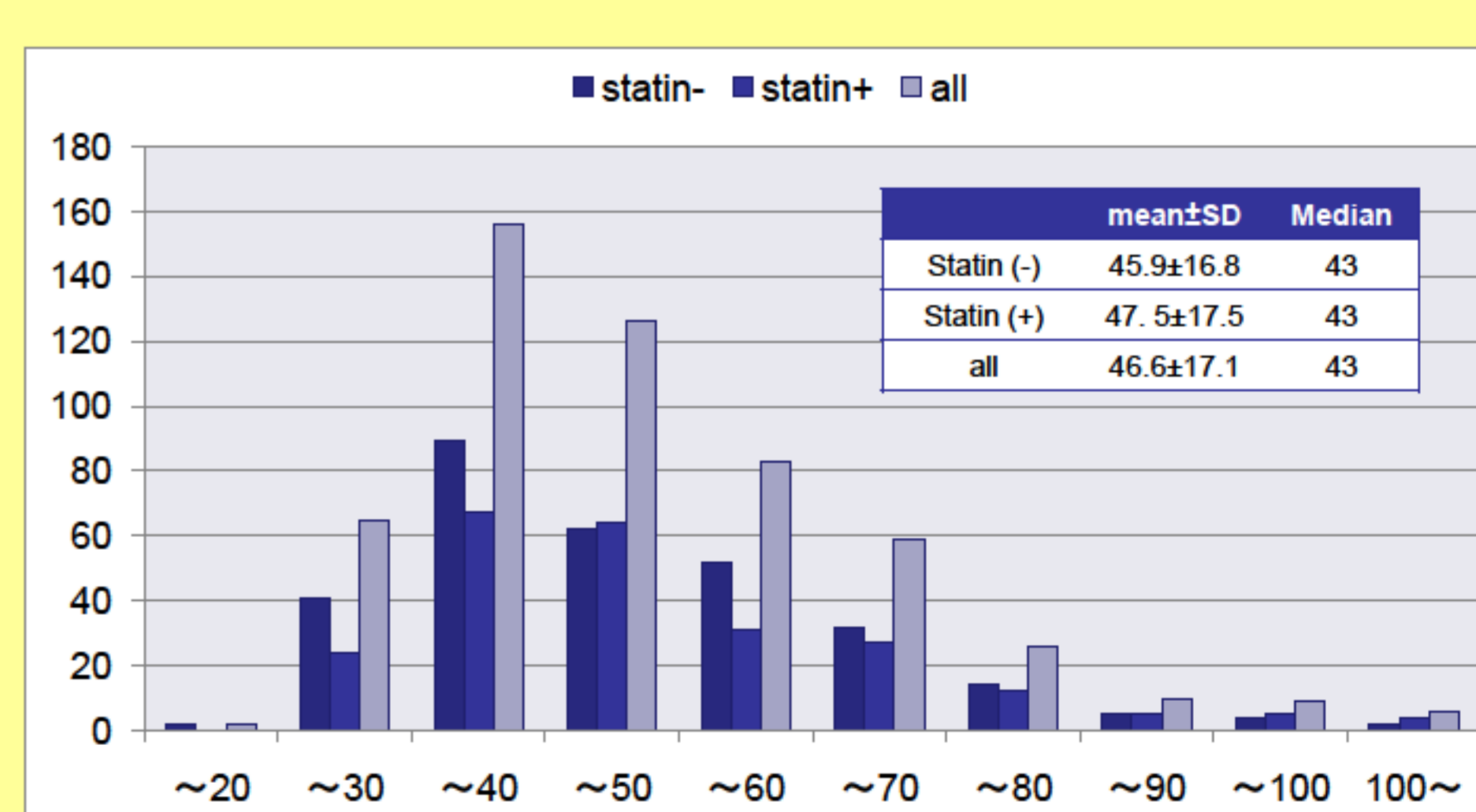
Correlation between ERI and lipids

(Classified according to urine Protein)

Variables	Regression coefficient	p value	95%CI (lower)	95%CI (upper)	Variables	Regression coefficient	p value	95%CI (lower)	95%CI (upper)
UP(-~+) (N=59)					UP(2+) (N=172)				
nonHDL	-0.174	0.1887	-0.102	0.021	nonHDL	-0.158	0.0409	-0.056	-0.001
LDL	-0.173	0.1900	-0.123	0.025	LDL	-0.077	0.3124	-0.049	0.016
HDL	0.069	0.6054	-0.130	0.221	HDL	0.118	0.1245	-0.013	0.109
LDL/HDL	-0.221	0.0921	-3.689	0.287	LDL/HDL	-0.114	0.1368	-1.794	0.248
TG	-0.228	0.0830	-0.056	0.004	TG	-0.118	0.1256	-0.024	0.003
UP(3+) (N=234)					UP(4+) (N=71)				
nonHDL	-0.059	0.3701	-0.030	0.011	nonHDL	-0.177	0.1423	-0.069	0.010
LDL	-0.062	0.3478	-0.035	0.012	LDL	-0.161	0.1788	-0.076	0.015
HDL	0.177	0.0067	0.018	0.109	HDL	0.308	0.0090	0.037	0.251
LDL/HDL	-0.215	0.0009	-1.878	-0.489	LDL/HDL	-0.289	0.0144	-2.969	-0.340
TG	-0.220	0.0007	-0.040	-0.011	TG	-0.164	0.1729	-0.038	0.007

The distribution of serum HDL-C

(Use of statin 238patients · Unuse 304patients)



Conclusions:

Hypo-responsiveness to ESAs influenced lipid metabolism in patients with chronic kidney disease during the period of dialysis initiation.

