ANEMIA MANAGEMENT AND CARDIOVASCULAR RISK IN NEWLY VISITED CKD PATIENTS IN JAPAN

Hidenori Nishida[1)], Soichiro Iimori[2)], Tomokazu Okado[2)], Tatemitsu Rai[2)], Shinichi Uchida[2)] and Sei Sasaki[2)]
[1)] Department of Nephrology, Hiratsuka kyosai hospital
[2)] Department of Nephrology, Tokyo Medical and Dental University

BACKGROUND

Treatment with erythropoietin stimulating agents (ESA) is an effective but costly therapy for CKD patients with renal anemia. On the other hand, correction of iron deficiency (ID) with iron supplementation can reduce the severity of renal anemia efficiently and inexpensively.

PURPOSE

1. To investigate the association between renal anemia with ID and cardiovascular (CV) risk.
2. To assess the changes of anemia and iron status, management for renal anemia.

In a cohort of non-dialysis CKD patients put in specialized nephrologist care.

METHODS

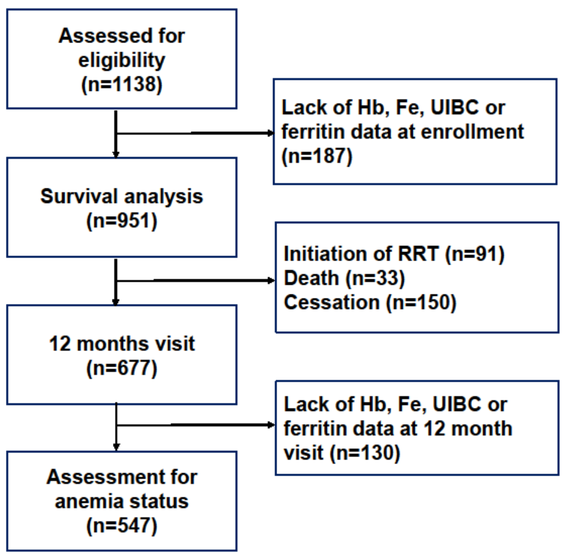
1. We prospectively evaluated the risk of CV events in 951 newly non-dialysis CKD G2-G5 patients followed in 16 nephrology centers (Figure 1). Anemia was defined as Hb <10 g/dl, ID was defined as TSAT ≤20 % and ferritin ≤100 ng/ml. Patients were stratified into 4 groups to analyze cardiovascular risk (Table 1).
2. 547 patients were assessed for management of renal anemia during 12 months (Figure 1). Patients were stratified into 3 groups according to the target level of renal anemia therapy in Japanese guideline (Hb 10-12 g/dl).

CKD-ROUTE study
CKD Research of OUtcomes in Treatment and Epidemiology

Table 1. Four groups stratified by anemia and iron deficiency

	Anemia	Iron deficiency
Group 1	No	No
Group 2	Yes	No
Group 3	No	Yes
Group 4	Yes	Yes

Figure 1. Flow chart for the study



RESULTS

Result 1: Risk factors for cardiovascular events

- During the 12-month follow up, CV events occurred in 59 patients; congestive heart failure n=35, ischemic heart failure n=9, stroke n=9, peripheral arterial disease n=6.
- Multivariate Cox hazard analysis showed that the CV risks of Group 2 and Group 4 were significantly higher than Group 1 : adjusted hazard ratios were 1.99, 95% CI (confidential interval) 1.06-3.70, and 2.70, 95%CI 1.12-6.51, respectively (Table 3, Figure 2).
- Higher serum ferritin level (>250 ng/ml) was associated with higher CV morbidity. CV risk of patients with higher serum ferritin was significantly higher than patients with lower serum ferritin: adjusted hazard ratio was 2.19, 95%CI 1.26-3.79(Table 4).

Table 2. Baseline characteristics for 951 patients stratified by anemia and iron deficiency

	All n=951	Group 1 n=641	Group 2 n=167	Group 3 n=96	Group 4 n=47	*P* -value
Age (yr)	68	67	72	64	73	<0.001
Male (%)	69.2%	75.2%	59.9%	54.2%	51.1%	<0.001
History of CVD (%)	27.8%	23.7%	31.7%	35.4%	53.2%	<0.001
eGFR (ml/min per 1.73m^2)	32	36.5	18.3	31.9	19.2	<0.001
Hb (g/dl)	11.8	12.7	8.9	12.2	8.6	<0.001
TSAT (%)	28.2	31.4	27.8	15.5	11.9	<0.001
ferritin (ng/ml)	174	190.1	224.4	45.7	37.2	<0.001
ESA use (%)	11.8%	5.0%	32.9%	5.2%	42.6%	<0.001
iron use (%)	5.3%	3.0%	9.0%	6.3%	21.3%	<0.001

Figure 2. Cox proportional hazard analysis on risk factor for cardiovascular events (n=951)

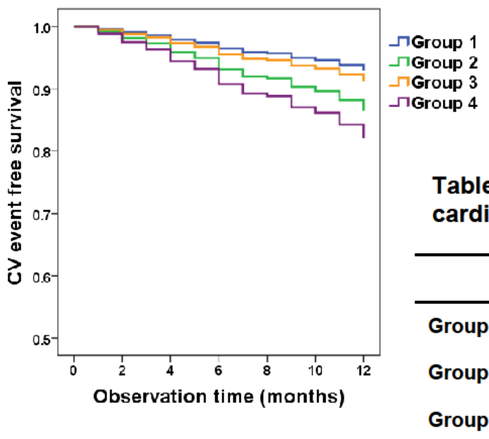


Table 3. Cox proportional hazard analysis on risk factor for cardiovascular disease (n=951)

	HR	95.0% CI	*P* -value	aHR	95.0% CI	*P* -value
Group 1	1 (reference)			1 (reference)		
Group 2	2.13	[1.16-3.92]	0.015	1.98	[1.06-3.71]	0.033
Group 3	1.08	[0.42-2.77]	0.871	1.26	[0.49-3.26]	0.631
Group 4	2.93	[1.23-6.99]	0.016	2.70	[1.12-6.51]	0.027

aHR: adjusted for age and gender

Table 4. Adjusted hazard ratio for cardiovascular risk stratified by serum ferritin level at baseline (n=951)

ferritin	aHR	95% CI	*P* -value
≤250 ng/ml	1 (reference)		
>250 ng/ml	2.19	[1.26-3.79]	0.009

Result 2: Changes in iron and anemia status, and management for anemia

- Prescription of ESA and iron supplementation significantly increased during 12 months. (Table 5).
- Among the patients with low hemoglobin at enrollment, the prevalence of patients with ID (22.6%) decreased at 12 months visit (12.9%) (Figure 3).
- Among the patients with low hemoglobin at enrollment, the percentage of patients prescribed with ESA was 33.4% and increased to 75.3% at 12 months visit (Figure 4); however the low prevalence of patients prescribed with iron supplementation (15.1%) only slightly increased during follow up (28.0%) (Figure 5).

Table 5. Changes in the anemia status and treatment (n=547)

	baseline	12 month	*P* -value
Hb (g/dl)	12.1	12.0	0.814
Hb <10 g/dl (%)	16.7%	16.5%	0.842
TSAT ≤20 % (%)	23.5%	17.9%	0.004
ferritin ≤100 ng/ml (%)	44.5%	44.8%	0.920
Iron deficiency (%)	14.6%	11.3%	0.059
ESA use (%)	7.7%	24.5%	<0.001
Iron use (%)	4.8%	11.0%	<0.001
Treatment for anemia (%)	10.6%	28.9%	<0.001

Figure 3. Change of percentage of patients with iron deficiency between 12 months classified by hemoglobin groups at enrollment (n=547)

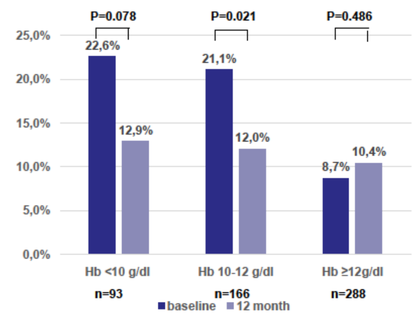


Figure 4. Change of percentage of patients prescribed with ESA classified by Hb groups at enrollment (n=547)

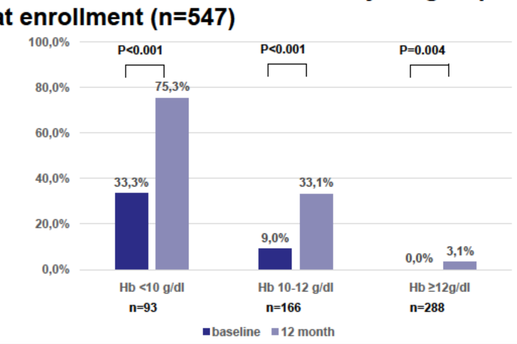
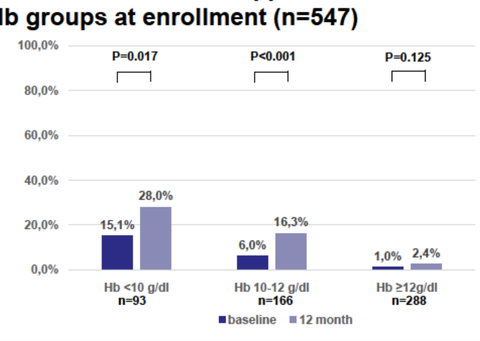


Figure 5. Change of percentage of patients prescribed with iron supplementation classified by Hb groups at enrollment (n=547)



SUMMARY

- Anemia with ID and higher serum ferritin level was associated with a higher risk of CV events than without ID.
- Compared to increasing prescription of ESA, prescription of iron did not increase sufficiently.

CONCLUSION

These results suggest that it is necessary to assess ID and to use iron supplementation appropriately. Iron deficiency anemia is associated with increased CV risk in non-dialysis CKD patients in short term follow up. Clinical trials are needed to examine if correction of iron level can reduce CV risk in CKD patients.

51ERA-EDTA
226--SP
H) Clinical Nephrology, CKD. H3) Anaemia in CKD 1-5.
Hidenori Nishida
DOI: 10.3252/pso.eu.51era.2014
Poster presented at: 51 ERA-EDTA CONGRESS AMSTERDAM 2014
PosterSessionOnline.com