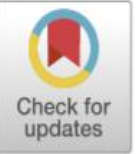


Relation of Preprocedural Hemoglobin Level to Outcomes After Percutaneous Coronary Intervention



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Background

low baseline hemoglobin (Hb) level is related to a greater risk of adverse clinical outcomes after percutaneous coronary intervention (PCI).

high Hb level impact on post-PCI outcomes is unclear

high hematocrit is related to increased blood viscosity leading to endothelial injury and rupture of vulnerable plaques through the increase of shear forces

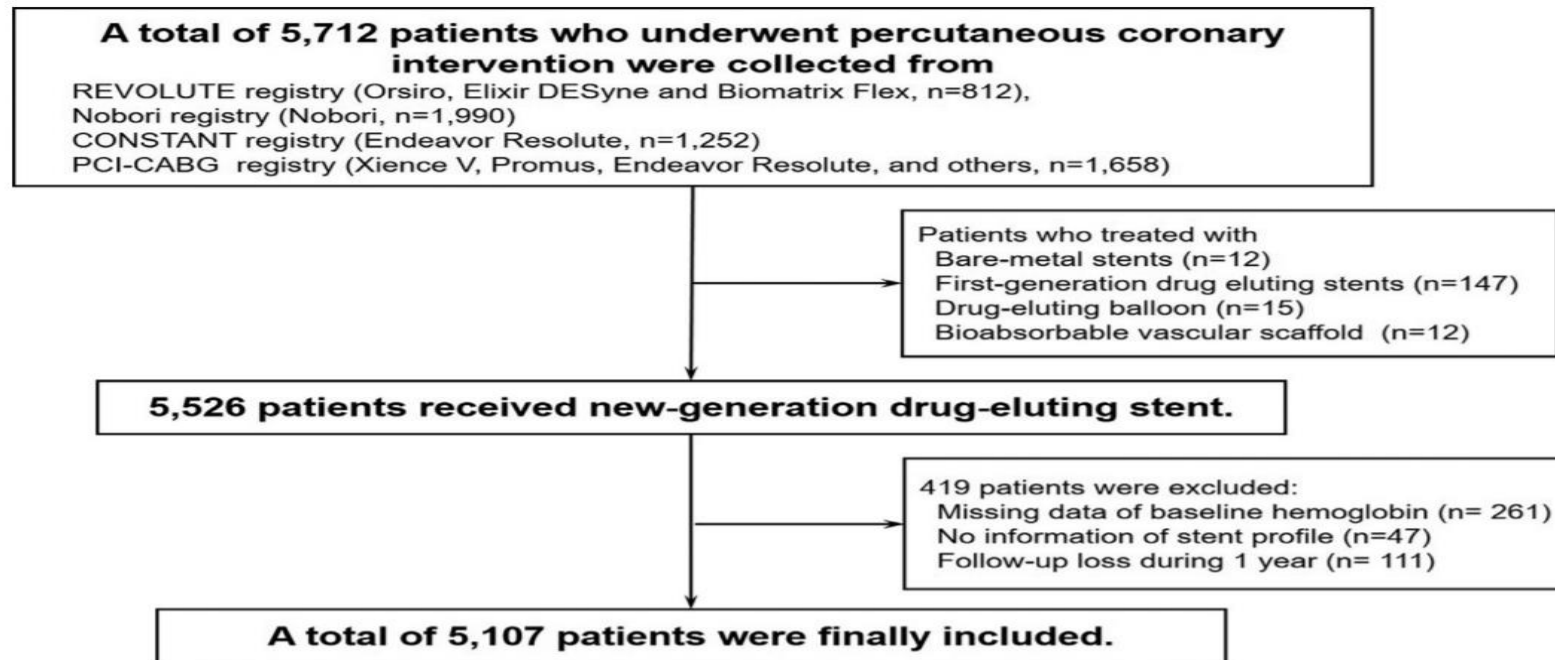
Aim of study

assess whether patients with poorly controlled polycythemia are at a greater risk of adverse outcomes after PCI.

Materials

derived from 4 different Korean multicenter drug-eluting stent (DES) registries.

included patients who needed DES implantation without specific inclusion or exclusion criteria,



Materials

The enrolled patients were categorized into 5 groups according to the baseline Hb level

<10

10-12,9

13-14,9

15-16,9

≥17 g/dl

Primary end point :

the occurrence of major adverse cardiac and cerebrovascular events (MACCE) at 12 months
a composite of all-cause mortality, nonfatal myocardial infarction (MI), and ischemic stroke.

Secondary end point:

all-cause mortality at 12 months.

Clinical outcomes were assessed 1-year post-PCI, either through a visit to the clinic or a telephone interview.

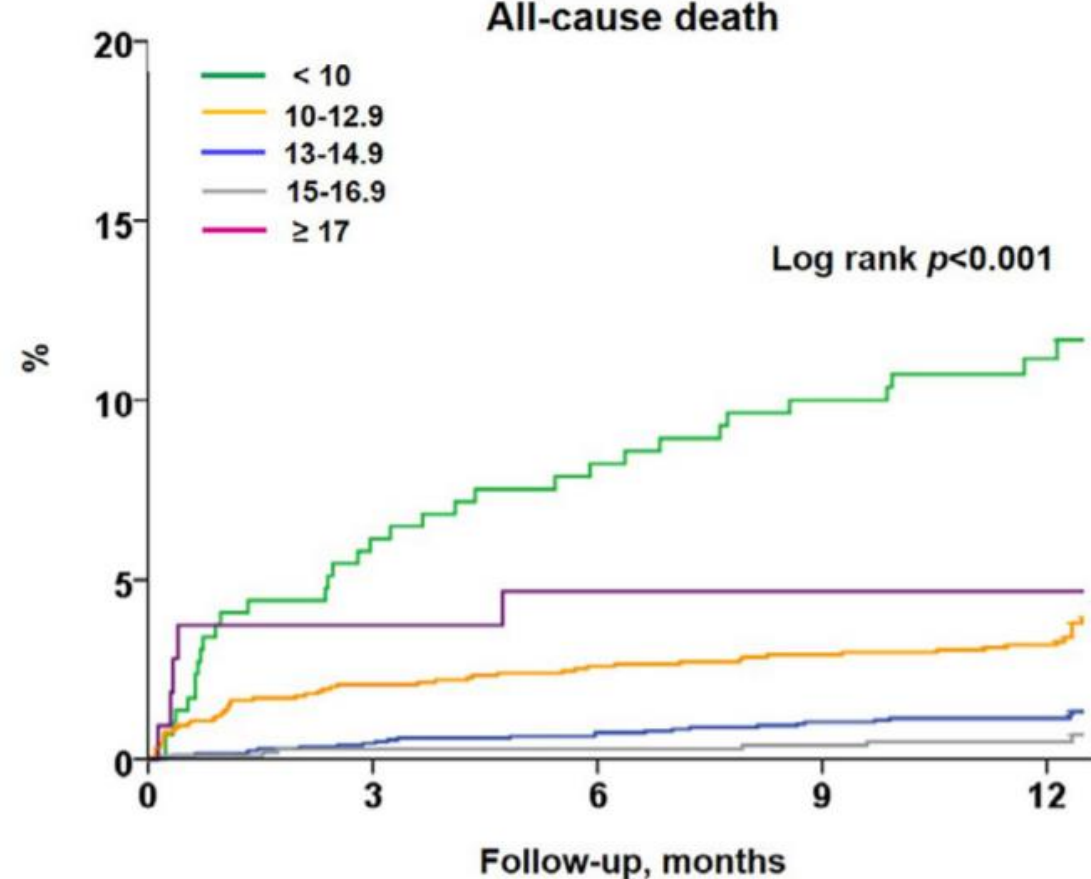
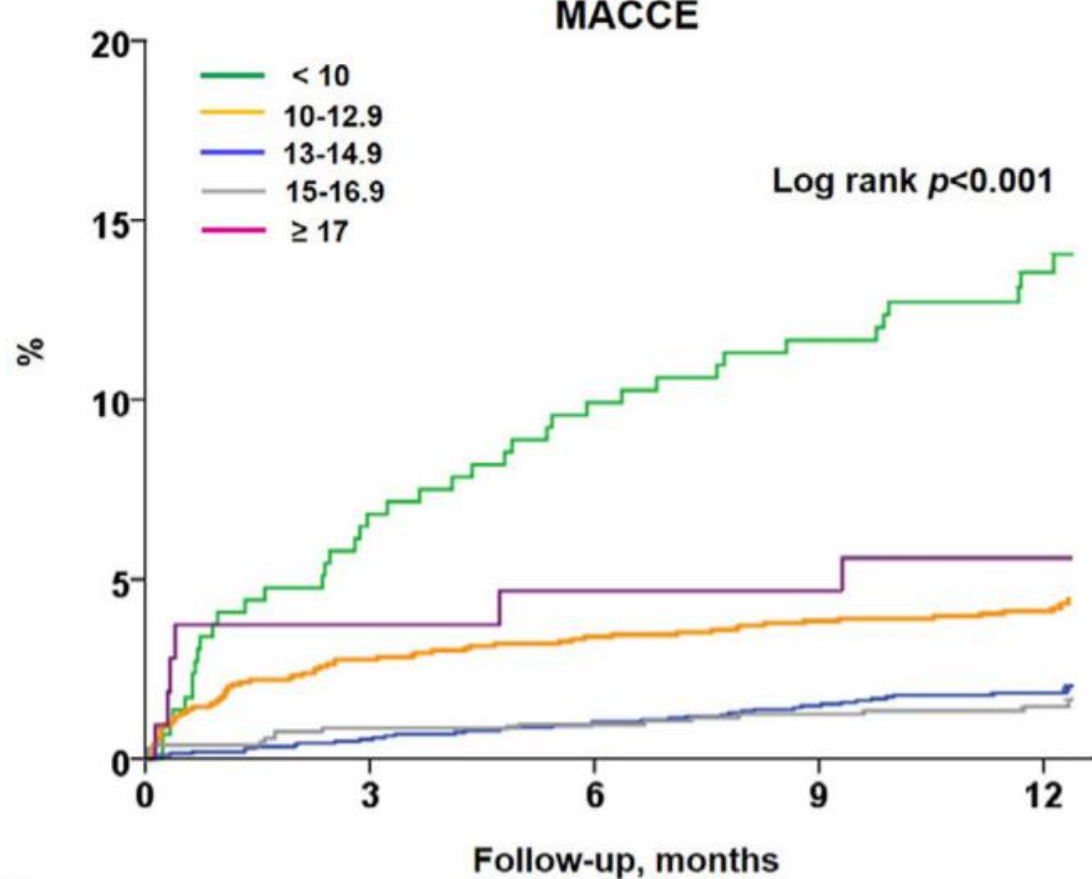
Results

Baseline characteristics according to baseline hemoglobin level

Variables	Hemoglobin (g/dl) at baseline					p Value
	<10 (n = 295)	10 to 12.9 (n = 1,599)	13 to 14.9 (n = 2,051)	15 to 16.9 (n = 1,055)	≥17 (n = 107)	
Age (years)	69.1 ± 10.1	69.7 ± 9.6	64.5 ± 10.6	58.7 ± 10.8	54.3 ± 11.4	<0.001
Men	162 (54.9%)	777 (48.6%)	1,570 (76.5%)	1,008 (95.5%)	107 (100%)	<0.001
Body mass index (kg/m ²)	23.6 ± 3.6	24.0 ± 3.5	24.6 ± 3.0	25.2 ± 3.0	25.9 ± 3.3	<0.001
Hypertension	228 (77.8%)	1,136 (71.4%)	1,293 (63.4%)	581 (55.5%)	56 (52.3%)	<0.001
Diabetes mellitus	186 (63.3%)	710 (44.6%)	720 (35.2%)	301 (28.8%)	26 (24.3%)	<0.001
Dyslipidemia	186 (63.3%)	1,098 (68.8%)	1,427 (70.0%)	766 (73.2%)	76 (71.0%)	0.020
Current smoker	41 (13.9%)	210 (13.4%)	549 (27.4%)	410 (39.5%)	59 (56.7%)	<0.001
Previous smoker	58 (19.7%)	282 (18.0%)	468 (23.4%)	267 (25.7%)	21 (20.2%)	<0.001
Smoking status (pack-years)	37.7 ± 25.0	35.7 ± 23.3	34.6 ± 21.3	32.9 ± 21.8	28.3 ± 13.7	0.109
Chronic kidney disease	128 (43.5%)	179 (11.3%)	52 (2.6%)	9 (0.9%)	3 (2.8%)	<0.001
Chronic obstructive lung disease	13 (4.4%)	42 (2.6%)	46 (2.3%)	16 (1.5%)	2 (1.9%)	0.052
Previous PCI	56 (19.0%)	337 (21.1%)	418 (20.4%)	221 (21.0%)	15 (14.0%)	0.447
Previous MI	26 (8.8%)	118 (7.4%)	147 (7.2%)	84 (8.0%)	5 (4.7%)	0.630
Previous bypass surgery	10 (3.4%)	43 (2.7%)	35 (1.7%)	16 (1.5%)	2 (1.9%)	0.076
Previous CVA	46 (15.6%)	205 (12.9%)	209 (10.3%)	59 (5.7%)	7 (6.5%)	<0.001
Clinical presentation						
Stable coronary artery disease	131 (44.4%)	856 (53.8%)	1,041 (51.0%)	435 (41.4%)	33 (31.1%)	<0.001
Acute coronary syndrome	164 (55.6%)	735 (46.2%)	1,002 (49.0%)	615 (58.6%)	73 (68.9%)	<0.001
Unstable angina pectoris	70 (23.7%)	422 (26.5%)	572 (28.0%)	283 (27.0%)	17 (16.0%)	0.055
NSTEMI	80 (27.1%)	200 (12.6%)	230 (11.3%)	129 (12.3%)	21 (19.8%)	<0.001
STEMI	14 (4.7%)	113 (7.1%)	200 (9.8%)	203 (19.8%)	35 (33.0%)	<0.001
Cardiogenic shock	3 (1.0%)	13 (0.8%)	8 (0.4%)	4 (0.4%)	1 (0.9%)	0.301
Laboratory data						
White blood cell count (K/mm ³)	7.97 ± 3.70	7.57 ± 3.08	7.88 ± 2.89	8.74 ± 3.27	9.81 ± 3.29	<0.001
Platelet count (K/mm ³)	229.9 ± 108.5	240.5 ± 82.1	237.2 ± 68.3	233.3 ± 66.0	223.7 ± 51.1	0.017
Low-density lipoprotein cholesterol (mg/dl)	81.7 ± 36.0	90.4 ± 33.9	98.7 ± 35.3	106.8 ± 35.9	113.4 ± 43.4	<0.001
High-density lipoprotein cholesterol (mg/dl)	36.4 ± 11.0	41.1 ± 10.9	42.3 ± 11.1	41.9 ± 10.0	40.5 ± 9.1	<0.001
Serum Creatinine (mg/dl)	3.6 ± 3.3	1.6 ± 3.0	1.1 ± 2.1	1.1 ± 3.3	1.0 ± 0.3	<0.001
C-reactive protein (mg/l)	18.5 ± 40.5	10.1 ± 29.2	4.6 ± 12.0	4.6 ± 18.7	10.4 ± 29.5	<0.001
Ejection fraction (%)	49.1 ± 16.2	55.4 ± 18.3	55.9 ± 17.8	55.0 ± 17.1	53.0 ± 15.6	<0.001
Ejection fraction <40%	62 (23.8%)	177 (12.9%)	156 (9.0%)	77 (8.5%)	14 (14.4%)	<0.001
Medication at discharge						
Statins	240 (81.9%)	1,370 (86.2%)	1,846 (90.2%)	970 (92.1%)	99 (93.4%)	<0.001
Beta blockers	170 (67.7%)	803 (65.0%)	1,021 (65.0%)	574 (65.5%)	68 (71.6%)	0.667
Angiotensin converting enzyme or angiotensin receptor blockers	152 (65.5%)	730 (61.6%)	945 (62.9%)	539 (65.3%)	76 (83.5%)	0.001
Clopidogrel	287 (97.2%)	1,570 (98.2%)	2,016 (98.3%)	1,034 (98.0%)	104 (97.2%)	0.963
Ticagrelor	4 (1.4%)	27 (1.7%)	35 (1.7%)	21 (2.0%)	2 (1.9%)	0.868
Antiplatelet agents at 12 months						
Dual antiplatelet therapy	111 (58.7%)	554 (56.4%)	720 (56.7%)	401 (56.5%)	40 (52.6%)	0.930
Aspirin	244 (82.7%)	1,332 (83.3%)	1,719 (83.8%)	894 (84.7%)	88 (82.2%)	0.867
Clopidogrel	185 (62.7%)	352 (63.5%)	1,302 (63.5%)	666 (63.1%)	64 (59.7%)	0.889
Ticagrelor	2 (0.7%)	11 (0.7%)	14 (0.7%)	11 (1.0%)	2 (0.2%)	0.868

At 12 months, unadjusted risks of the primary and secondary outcomes were significantly different in Hb groups.

The incidence of MACCE and all cause mortality gradually decreased with increasing Hb level (from 10 to 16,9 g/dl) but increased at a level of ≥ 17.0 g/dl



Baseline Hemoglobin	0	3	6	9	12
< 10	295	272	259	252	187
10-13	1599	1541	1520	1502	1183
13-15	2051	2022	2006	1987	1565
15-17	1055	1038	1032	1016	797
≥ 17	107	102	100	96	73

Number at risk	0	3	6	9	12
< 10	295	272	259	252	188
10-13	1599	1542	1520	1502	1184
13-15	2051	2023	2007	1987	1565
15-17	1055	1038	1032	1016	797
≥ 17	107	102	100	98	75

Figure 2. Kaplan-Meier curves of 12-month MACCE and mortality according to baseline hemoglobin groups. MACCE = major adverse cardiac and cerebro-

Adjusted HRs for MACCE and its individual components according to baseline Hb level

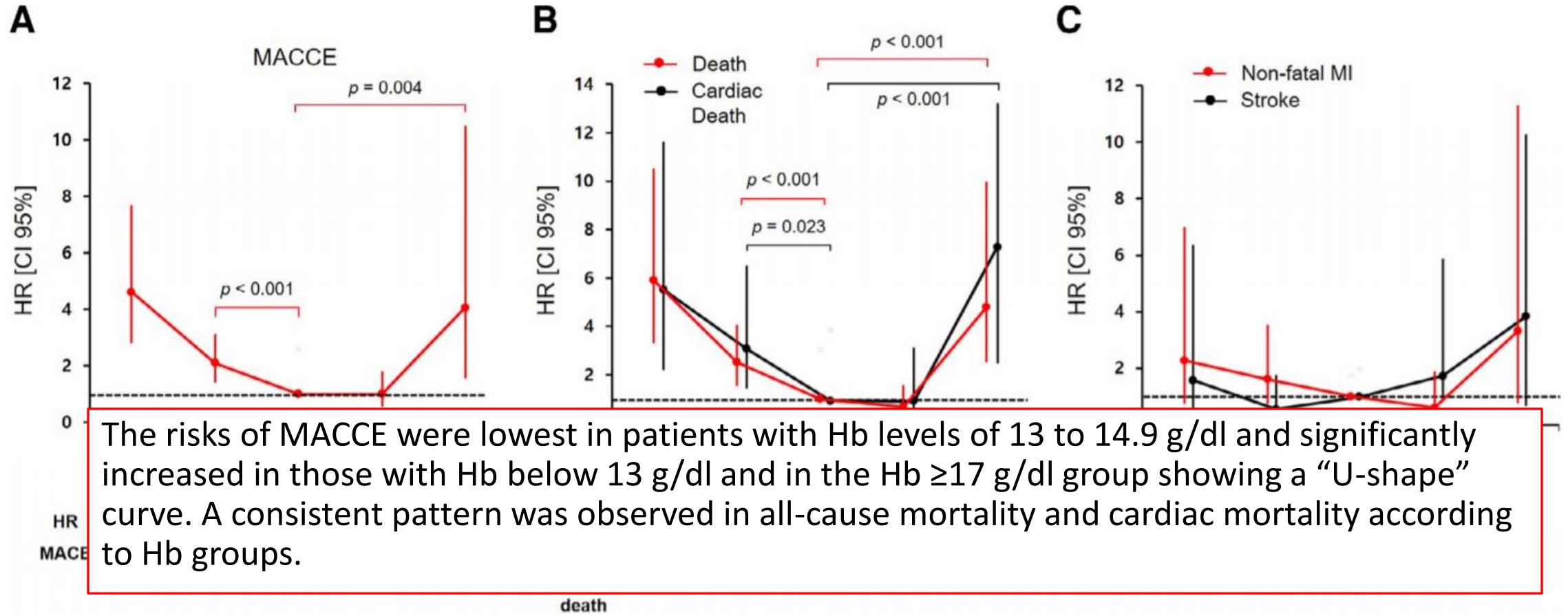


Figure 3. Multivariable adjusted risk of (A) MACCE, (B) all-cause mortality and cardiac mortality, and (C) nonfatal MI and ischemic stroke. Hemoglobin level of 13 to 14.9 g/dl is used as a reference. Model adjusted for age, sex, body mass index, hypertension, diabetes, dyslipidemia, chronic kidney disease, current smoking status, previous cerebrovascular accident, acute coronary syndrome, and multivessel disease. CI = confidence interval; HR = hazard ratio;

Additionally, we assessed the effect of high Hb level on clinical outcomes in patients without anemia (Hb of ≥ 13 g/dl), and the results are reported

Clinical outcomes for 12 months after PCI according to baseline hemoglobin in patients without anemia (hemoglobin of ≥ 13 g/dl)

	No. of events	Event rate (%)	Age- and sex-adjusted		Multivariable-adjusted*	
			HR (95% CI)	p Value	HR (95% CI)	p Value
<i>MACCE</i>						
13-14.9	42	2.0	Reference		Reference	
15-16.9	18	1.7	1.11 (0.61-2.02)	0.728	1.25 (0.65-2.40)	0.496
≥ 17	8	7.5	4.88 (1.87-12.77)	0.001	4.36 (1.26-15.10)	0.020
<i>All-cause mortality</i>						
13-14.9	27	1.3	Reference		Reference	
15-16.9	7	0.7	0.65 (0.27-1.57)	0.335	0.86 (0.34-2.18)	0.745
≥ 17	5	4.7	7.73 (2.85-20.99)	<0.001	7.56 (2.04-27.98)	0.002
<i>Cardiac mortality</i>						
13-14.9	10	0.5	Reference		Reference	
15-16.9	4	0.4	0.84 (0.23-2.99)	0.782	1.14 (0.29-4.48)	0.854
≥ 17	4	3.7	15.15 (4.45-51.58)	<0.001	17.54 (3.97-57.55)	<0.001
<i>Nonfatal MI</i>						
13-14.9	14	0.7	Reference		Reference	
15-16.9	5	0.5	0.65 (0.19-2.28)	0.504	0.33 (0.04-2.16)	0.216
≥ 17	2	1.9	5.56 (1.16-26.54)	0.031	3.18 (0.37-27.21)	0.291
<i>Stent thrombosis</i>						
13-14.9	1	0	Reference		Reference	
15-16.9	3	0.3	5.85 (0.61-56.25)	0.126	4.78 (0.39-58.48)	0.221
≥ 17	3	2.8	57.75 (6.01-555.20)	<0.001	33.27 (2.34-472.96)	0.010
<i>Ischemic stroke</i>						
13-14.9	8	0.4	Reference		Reference	
15-16.9	7	0.7	2.79 (0.95-8.23)	0.063	4.23 (1.29-13.91)	0.018
≥ 17	1	0.9	5.83 (0.67-50.26)	0.109	13.08 (1.27-77.74)	0.031

Event rates were calculated by Kaplan-Meier analysis.

CI = confidence interval; HR = hazard ratio; MACCE = major adverse cardiac and cerebrovascular event; MI = myocardial infarction; PCI = percutaneous

When patients with a baseline Hb of 13 to 14.9 g/dl were considered as the reference group, HRs of MACCE, cardiac mortality, stent thrombosis and ischemic stroke tended to gradually increase with increasing Hb level, and patients with Hb ≥ 17 g/dl had significantly higher rates of MACCE, ischemic stroke, all-cause mortality, and cardiac mortality.

Regarding nonfatal MI, a trend toward an increasing HR in the Hb ≥ 17 g/dl group was observed but without statistical significance. The observed relation trend between Hb level and clinical outcomes was unchanged in subgroup analyses of both patients with MI and those with non-MI

Multivariable Cox regression analysis after adjustment for confounding factors showed that Hb ≥ 17 g/dl was significantly associated with a higher incidence of MACCE in the cohort .

Other important predictors for MACCE included age, low body mass index, FE $<40\%$, HTA, CKD, Hb <10 g/dl.

Table 4

Predictors for 12-month MACCE and all-cause mortality after PCI

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p Value	HR (95% CI)	p Value
<i>MACCE predictors</i>				
Age per 1 year	1.06 (1.04-1.08)	<0.001	1.05 (1.03-1.07)	<0.001
Male	1.20 (0.86-1.67)	0.281	1.34 (0.86-2.07)	0.195
Body mass index per 1 kg/m ²	0.90 (0.86-0.94)	<0.001	0.95 (0.90-1.01)	0.121
Hemoglobin <10 g/dl	4.96 (3.497-04)	<0.001	3.00 (1.78-5.06)	<0.001
Hemoglobin ≥17 g/dl	1.78 (0.95-3.35)	0.079	2.98 (1.02-9.72)	0.041
Hypertension	1.62 (1.16-2.26)	0.005	1.85 (1.12-3.05)	0.016
Diabetes	1.92 (1.44-2.56)	<0.001	1.06 (0.70-1.60)	0.601
Dyslipidemia	0.76 (0.56-1.02)	0.068	1.06 (0.70-1.60)	0.774
Chronic kidney disease	4.14 (2.94-5.82)	<0.001	1.72 (1.02-2.89)	0.041
Previous CVA	2.27 (1.59-3.24)	0.001	1.37 (0.84-2.22)	0.208
Current smoking	1.19 (0.93-1.57)	0.096	1.11 (0.75-1.63)	0.609
LVEF <40%	3.74 (2.68-5.20)	<0.001	3.27 (2.15-4.96)	<0.001
Acute coronary syndrome	1.71 (1.27-2.31)	<0.001	1.30 (0.88-1.92)	0.192
Multivessel disease	1.55 (1.10-2.18)	0.012	1.28 (0.81-2.03)	0.292
LDL level (mg/dl)	1.00 (1.00-1.01)	0.001	1.00 (0.99-1.00)	0.172
<i>Mortality predictors</i>				
Age per 1 year	1.08 (1.06-1.10)	<0.001	1.06 (1.03-1.08)	<0.001
Male	1.20 (0.82-1.78)	0.352	1.38 (0.83-2.30)	0.217
Body mass index per 1 kg/m ²	0.87 (0.82-0.92)	<0.001	0.92 (0.86-0.99)	0.030
Hemoglobin <10 g/dl	5.83 (3.94-8.65)	<0.001	3.35 (1.86-6.04)	<0.001
Hemoglobin ≥17 g/dl	1.92 (0.96-4.69)	0.053	4.59 (1.37-15.37)	0.014
Hypertension	1.45 (0.99-2.12)	0.059	1.76 (1.00-3.10)	0.049
Diabetes	2.03 (1.45-2.87)	<0.001	1.13 (0.71-1.78)	0.607
Dyslipidemia	0.64 (0.45-0.90)	0.011	0.90 (0.57-1.44)	0.670
Chronic kidney disease	4.17 (2.79-6.24)	<0.001	1.90 (1.06-3.42)	0.032
Previous CVA	2.01 (1.30-3.10)	0.002	1.30 (0.74-2.30)	0.365
LVEF <40%	4.26 (2.91-6.23)	<0.001	3.69 (2.30-5.90)	<0.001
Acute coronary syndrome	1.95 (1.37-2.79)	<0.001	1.40 (0.88-2.22)	0.156
Multivessel disease	1.42 (0.96-2.11)	0.081	1.11 (0.66-1.86)	0.687

Conclusion

not only low Hb but also elevated Hb of ≥ 17 g/dl was significantly associated with higher MACCE rates and all-cause mortality after PCI. An appropriate treatment strategy for patients with high Hb level should be identified through future studies.