Serum Albumin and Bleeding Events After Percutaneous Coronary Intervention in Patients With Acute Myocardial Infarction (from the HAGAKURE-ACS Registry)

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Low serum albumin (SA) on admission in patients with acute myocardial infarction (AMI) has been reported to be associated with adverse cardiovascular events. The relation between low SA and post-AMI bleeding events is presently unknown. We analyzed 1,724 patients with AMI enrolled in the HAGAKURE-ACS registry who underwent primary percutaneous coronary intervention from January 2014 to December 2018. To assess the influence of low SA at admission, patients were divided into 3 groups according to the albumin tertiles: the low SA group (<3.8 g/100 ml), the middle SA (MSA) group (3.8 to 4.1 g/100 ml), and the normal SA (NSA) group (≥4.2 g/100 ml). The primary end point was the incidence of Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries moderate/severe bleeding. The cumulative 3-year incidence of the primary end point was significantly higher in the low SA group than in the MSA and NSA groups (30.8% and 11.9% vs 7.7%; p <0.001). In the landmark analysis at 30 days, the cumulative incidences of the primary end point were also significantly higher in the low SA group than in the MSA and NSA groups, both within and beyond 30 days (20.1% and 6.1% vs 3.5%; p <0.001, and 12.4% and 6.2% vs 4.5%; p <0.001, respectively). After adjusting for confounders, the low SA group showed excess risk of bleeding events relative to NSA (hazard ratio 1.56; 95% confidence interval 1.06 to 2.30; p = 0.026), whereas risk of bleeding was neutral in MSA relative to NSA (hazard ratio 0.94; 95% confidence interval 0.63 to 1.34; p = 0.752). In conclusion, low SA at admission was independently associated with higher risk for bleeding events in patients with AMI undergoing percutaneous coronary intervention. **(Am J Cardiol 2022;165:19−26)**

Short- and long-term prognoses in patients with acute myocardial infarction (AMI) have improved in the primary reperfusion therapy era.[1,2] The development of coronary stents, optimal medical therapy, and cardiac rehabilitation have all contributed to the reduction of cardiovascular events after AMI.[3,4] Risk reduction for bleeding events is also important to achieve further improvement of prognoses of patients with AMI because bleeding events have been reported to be associated with higher mortality after percutaneous coronary intervention (PCI). Although several risk models were established to stratify the patients with high bleeding risk after PCI,[5−8] there is a need for further risk stratification in patients with AMI as those risk scores were not dedicated to the AMI population. Because serum albumin (SA) is a well-known biomarker of nutrition, frailty, and inflammation,[9] low SA could be a predictor for bleeding events in patients with AMI undergoing PCI.[10] However, there are limited data evaluating the association between low SA and bleeding events after PCI in patients with AMI.

Methods

The HAGAKURE (Heart And vascular disease outcome study in saGA and KyUshu Region) - acute coronary syndrome (ACS) registry is a multicenter, nonrandomized, retrospective study performed in 3 cardiovascular centers in

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See page 25 for disclosure information.

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0002-9149/
https://doi.org/10.1016/j.amjcard.2021.10.043

Japan. Among the total of 2,156 consecutive patients with ACS enrolled from January 2014 to December 2018, 1,787 patients with AMI had primary PCI after excluding 369 patients with recurrent ACS, unstable angina pectoris, and those without primary PCI. After excluding 63 patients who were lacking data on albumin, the present study population consisted of 1,724 patients with AMI who had either ST-segment elevation myocardial infarction (STEMI) or non −ST-segment elevation myocardial infarction (NSTEMI) (Figure 1). The patients were stratified into 3 groups according to the tertiles of SA levels at admission: low SA group (<3.8 g/100 ml), middle SA (MSA) group (3.8 to 4.1 g/100 ml), and normal SA (NSA) group (≥4.2 g/100 ml) (Figure 1). All procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Declaration of Helsinki 1964 and later revisions. Written informed consents were waived because of the retrospective nature of the study. Ethics approval was obtained from the Institutional Review Board of Saga University, Miyazaki Medical Association Hospital, and Ureshino Medical Center.

Diagnoses of STEMI and NSTEMI, based on the 2007 universal definitions,[11] were made by each cardiologist. Details of STEMI and NSTEMI definitions are shown in Supplementary Methods. The therapeutic strategies for AMI treatment depended on the practice of each cardiologist, but all patients' treatments followed the guidelines set forth by the Japanese Circulation Society and the American College of Cardiology/American Heart Association for the diagnosis and treatment of AMI.

The following data were collected: baseline demographics and clinical characteristics of the study patients, including medical history, presenting signs and symptoms, results of blood tests, transthoracic echocardiography, electrocardiography, cardiac procedures, and clinical end points. In addition, blood biomarkers were measured within 24 hours after admission as acute phase data. Clinical follow-up data were obtained from clinic visits, telephone calls, and records from hospital admissions. According to clinical data including follow-up, over 90% of these data were obtained by a single physician in each facility.

The primary end point was major bleeding, defined as Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries moderate/severe bleeding events.[12] Traumatic brain bleeding was included in intracranial bleeding. Secondary end points were all-cause death, cardiovascular death, and hospitalization for heart failure.

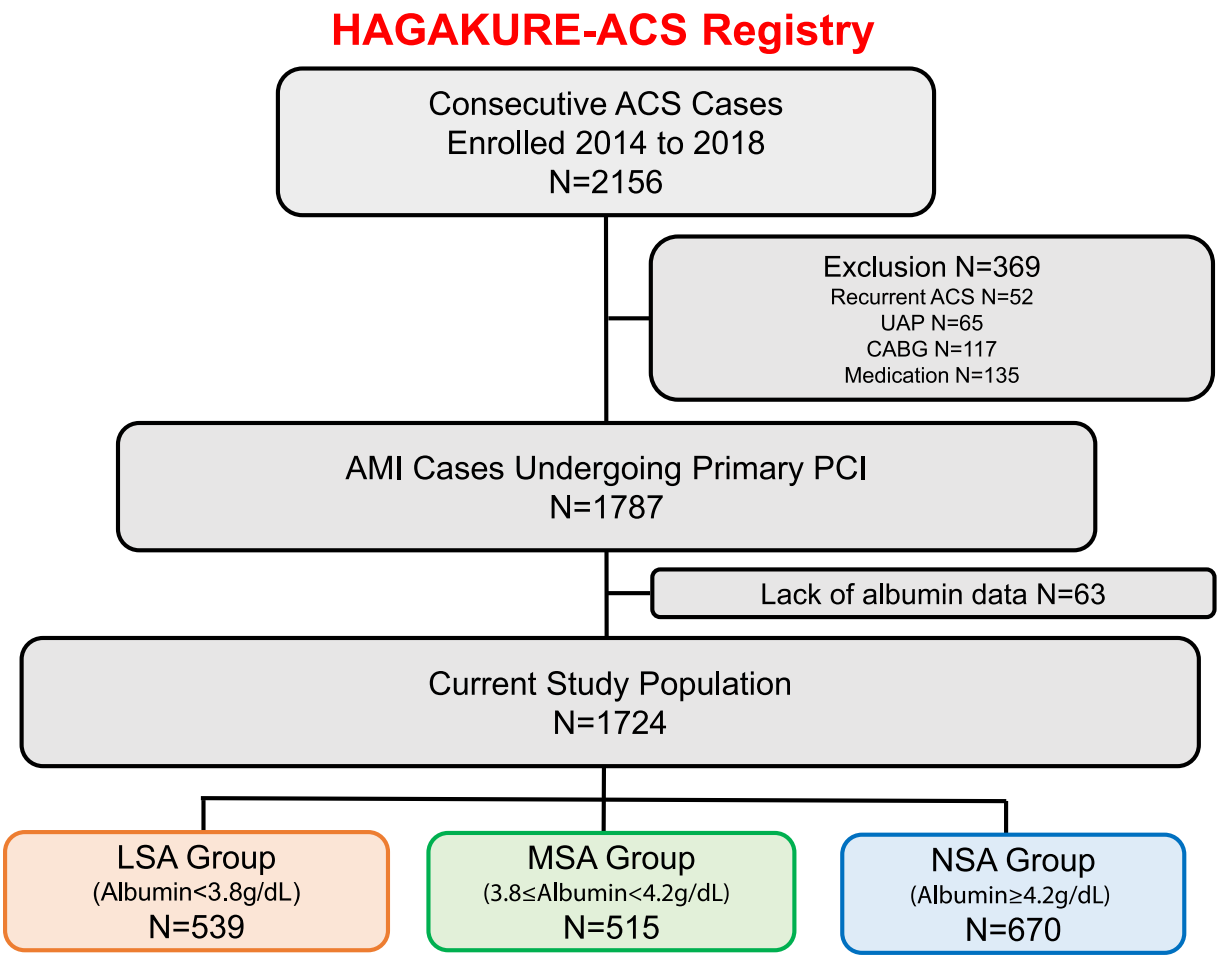

Figure 1. Study flow chart. CABG = coronary artery bypass grafting; UAP = unstable angina pectoris.

In order to evaluate the clinical impact of low SA on bleeding events, we carried out subgroup analysis of patients with or without Academic Research Consortium for High Bleeding Risk (ARC-HBR) criteria.[7] Details of the classification of ARC-HBR in the present analysis are shown in Supplementary Methods.

For continuous variables, normally distributed data are reported as mean ± SD; nonparametric data are reported as median and interquartile range. For categoric variables, data are presented as count and percentage. Comparisons of continuous variables between groups were performed with the analysis of variance or Kruskal-Wallis tests, as appropriate. Comparisons of categoric variables were assessed with the chi-square test. The cumulative incidence of an end point was calculated according to the Kaplan−Meier method. The effect of SA level on the primary end point was determined with a multivariate Cox proportional hazards regression model adjusting for confounding baseline factors selected by stepwise model. As a sensitivity analysis, we also used Cox proportional hazards model to estimate the risk of low SA group relative to other groups adjusting for all variables (Model 1) and variables related to bleeding events as well as those chosen by stepwise model (Model 2). A 2-sided p value <0.05 was considered statistically significant. All statistical analyses were performed with JMP 14 (SAS Institute Inc., Cary, North Carolina).

Results

Patient clinical characteristics and treatments during the acute phase are summarized in Table 1. The low SA group more often had diabetes mellitus, smoking habits, atrial fibrillation, malignancy, anemia, chronic kidney disease, and histories of myocardial infarction than the other 2 groups.

The median follow-up duration was 2.1 (interquartile range: 1.0 to 3.6) years. The cumulative 3-year incidence of the primary end point was significantly higher in the low SA group than in the MSA and NSA groups. In the landmark analysis at 30 days, the cumulative incidence of primary end point was also significantly higher in the low SA group within 30 days, and beyond 30 days (Figures 2 and 3, Table 2). Multivariate analysis showed that the low SA group had an excess risk of bleeding events relative to the NSA group (Table 3). In the sensitivity analysis, the risks for the primary end point were also significantly higher in patients with low SA in both Models 1 and 2 (Supplementary Table 1).

Regarding secondary end points, the cumulative incidences of all-cause death, cardiovascular death, and hospitalization for heart failure were also significantly higher in the low SA group than in the MSA and NSA groups (Table 2). Among 1,724 patients, 698 patients (40.5%) met ARC-HBR criteria (Table 1). The baseline clinical characteristics of those with and without ARC-HBR are shown in Supplementary Table 2. The cumulative incidence of the primary end point was significantly higher in patients with ARC-HBR than in those without (Supplementary Table 3). Cumulative incidences of all-cause death, cardiovascular death, and hospitalization for heart failure were also significantly higher in those with ARC-HBR than in those without (Supplementary Table 3). In the ARC-HBR group, the cumulative 3-year incidence of the primary end point was markedly higher in the low SA group than in the MSA and NSA groups. In the no ARC-HBR group, the cumulative 3-year incidence of primary end point was also significantly higher in the low SA group than in the MSA and NSA groups (Figure 4). Multivariable analysis showed that the low SA group had an excess risk of bleeding events relative to the NSA group in both ARC-HBR and no ARC-HBR group (Supplementary Table 4).

To our knowledge, this is the first multicenter study examining the low SA and bleeding events after PCI in patients with AMI. The major findings of this study were (1) low SA at admission was 1 of the independent predictors for major bleeding after PCI, (2) low SA in patients with AMI was associated with a higher incidence of bleeding events in those with and without ARC-HBR, and (3) low SA at admission was also associated with a higher incidence of all-cause death, cardiovascular death, and hospitalization for heart failure.

The impact of bleeding on clinical prognosis after PCI was well established in previous studies.[13,14] In order to prevent bleeding events after PCI, risk stratification for bleeding events is recommended using several risk scores such as PRECISE-DAPT (Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy) score or ARC-HBR criteria.[5,7,8,15] Patients with AMI undergoing PCI are at high risk for bleeding events from the use of more potent P2Y12 inhibitors, loading of antiplatelet agents, and more frequent use of transfemoral intervention.[14,16] Therefore, evaluation of HBR and prevention of bleeding events are crucially important in patients with AMI. In addition to conventional risk factors of bleeding, the usefulness of low SA was recently reported in risk stratification for bleeding events in coronary artery disease patients after PCI from a single-center registry.[10] In line with the previous report, low SA at admission was an independent predictor for major bleeding after PCI in patients with AMI in this multicenter registry. Furthermore, a higher incidence of major bleeding in the low SA group was found both within and beyond 30 days after PCI. The following pathophysiologic hypotheses are offered for the relation between low serum albumin (LSA) and high bleeding risk. First, the vulnerability of the capillary in systemic organs may be due to low SA.[9,17] Indeed, low SA levels were associated with an increased risk of intracerebral hemorrhage in the general population who were initially free from stroke. Regarding gastrointestinal bleeding, low SA was a predictor of mortality and rebleeding in peptic ulcer bleeding.[18] Moreover, low SA was independently associated with higher upper gastrointestinal bleeding risk in patients with chronic kidney disease.[19] The albumin concentration was also reported to be the predictor of acute variceal bleeding in those with cirrhosis.[20] Second, low SA reflects the malnutrition associated with vitamin C and K deficiencies, resulting in coagulopathy. Indeed, a recent study reported that low SA increases both the likelihood of coagulation instability and the risk of bleeding events in warfarin users.[21] From these

Table 1
Baseline demographics and clinical characteristics

Variables	Total (n = 1724)	Serum albumin (g/dL) <3.8 (n = 539)	3.8-4.1 (n = 515)	≥4.2 (n = 670)
Man	1252 (72.6%)	328 (60.9%)	389 (75.5%)	535 (79.9%)
Age (years)	69.9 ± 12.5	76.1 ± 10.8	70.7 ± 11.6	64.2 ± 12.0
Body mass index (kg/m^2)	23.8 ± 4.0	22.6 ± 3.7	24.0 ± 4.2	24.8 ± 3.7
Heart rate (/min)	77.0 ± 20.4	76.9 ± 24.1	76.5 ± 20.4	77.8 ± 16.8
Systolic blood pressure (mm Hg)	139 ± 31	129 ± 33	137 ± 30	149 ± 27
Medical history				
Hypertension	1216 (70.5%)	381 (70.7%)	364 (70.7%)	471 (70.3%)
Dyslipidemia	919 (53.3%)	231 (42.9%)	278 (54.0%)	410 (61.2%)
Diabetes mellitus	500 (29.0%)	193 (35.8%)	140 (27.2%)	167 (24.9%)
Smoker	807 (46.8%)	212 (39.3%)	256 (49.7%)	339 (50.6%)
Family history of cardiovascular disease	195 (11.3%)	47 (8.7%)	70 (13.6%)	78 (11.6%)
Healed myocardial infarction	89 (5.2%)	38 (7.1%)	31 (6.0%)	20 (3.0%)
Atrial fibrillation	83 (4.8%)	43 (8.0%)	22 (4.3%)	18 (2.7%)
Warfarin use at admission	20 (1.2%)	6 (1.1%)	9 (1.8%)	5 (0.8%)
Direct oral anticoagulant at admission	52 (3.0%)	28 (5.2%)	11 (2.1%)	13 (1.9%)
Malignancy	94 (5.5%)	44 (8.2%)	24 (4.7%)	26 (3.9%)
ARC-HBR	698 (40.5%)	373 (69.2%)	192 (37.3%)	133 (19.9%)
Serum albumin at admission (g/dL)	4.0 ± 0.5	3.3 ± 0.4	4.0 ± 0.1	4.5 ± 0.2
WBC (× 10^3/mL)	90 (71-116)	91 (69-117)	89 (71-113)	91 (71-118)
Hemoglobin (g/dL)	13.7 ± 2.1	12.2 ± 2.1	13.8 ± 1.8	14.9 ± 1.6
Platelet (× 10^4/μL)	22.1 ± 9.9	21.0 ± 7.8	22.2 ± 12.7	23.1 ± 8.9
eGFR (mL/min/1.73m^2)	64.7 ± 24.0	53.9 ± 24.4	64.6 ± 23.3	73.4 ± 20.6
Triglyceride, mg/dL	107 (74-160)	86 (62-117)	107 (76-154)	132 (85-200)
Total-cholesterol (mg/dL)	193.1 ± 44.6	171.8 ± 38.6	190.1 ± 37.8	211.7 ± 45.9
LDL-cholesterol (mg/dL)	120.2 ± 36.1	104.6 ± 32.2	118.9 ± 34.6	133.4 ± 35.2
HDL-cholesterol (mg/dL)	48.2 ± 13.1	46.3 ± 14.3	48.6 ± 12.7	49.5 ± 12.3
High-sensitivity troponin T (ng/mL) (Upper limit of normal: 0.032)	0.27 (0.05-2.61)	0.71 (0.09-5.87)	0.23 (0.05-1.97)	0.19 (0.04-1.12)
Brain natriuretic peptide (pg/mL) (Upper limit of normal: 18.4)	67.8 (24.1-211.6)	226.8 (73.3-674.8)	69.7 (28.2-191.1)	34.3 (15.4-87.0)
NT-pro brain natriuretic peptide (pg/mL) (Upper limit of normal: 125)	319.9 (106.2-1792.5)	1193.0 (287.1-3760.0)	235.5 (96.0-785.8)	153.0 (45.1-383.4)
STEMI	1173 (68.0%)	366 (67.9%)	347 (67.4%)	460 (68.7%)
NSTEMI	551 (32.0%)	173 (32.1%)	168 (32.6%)	210 (31.3%)
Killip class ≥3	172 (10.0%)	119 (22.1%)	40 (7.8%)	13 (1.9%)
LVEF (%)	54.0 ± 13.5	51.4 ± 15.4	54.3 ± 13.8	55.9 ± 11.2
Peak creatine kinase (IU/L)	1380 (396-3051)	1044 (316-2615)	1378 (402-3051)	1607 (458-3365)
Culprit coronary artery				
Right	545 (31.9%)	202 (37.8%)	158 (31.0%)	185 (27.7%)
Left main	45 (2.6%)	26 (4.9%)	12 (2.4%)	7 (1.1%)
Left anterior descending	783 (45.7%)	213 (39.8%)	248 (48.6%)	322 (48.2%)
Left circumflex	267(15.6%)	78 (14.6%)	74 (14.5%)	115 (17.2%)
Other and MVD	84 (4.9%)	20 (3.7%)	23 (4.5%)	41 (6.1%)
Femoral approach	310 (30.4%)	164 (30.4%)	86 (16.7%)	60 (9.0%)
IABP	233 (13.5%)	116 (21.5%)	66 (12.8%)	51 (7.6%)
ECMO	48 (2.8%)	29 (5.4%)	12 (2.3%)	7 (1.0%)
In-hospital mortality	80 (4.6%)	57 (10.6%)	16 (3.1%)	7 (1.0%)
Medication at discharge	n = 1644	n = 482	n = 499	n = 663
Aspirin	1582 (96.2%)	455 (94.4%)	481 (96.4%)	646 (97.4%)
P2Y12 inhibitor	1538 (93.6%)	438 (90.9%)	465 (93.2%)	635 (95.8%)
Prasugrel	584 (35.5%)	145 (30.1%)	186 (37.3%)	253 (38.2%)
Clopidogrel	967 (58.8%)	301 (62.5%)	281 (56.3%)	385 (58.1%)
Warfarin	40 (2.4%)	22 (4.6%)	9 (1.8%)	9 (1.4%)
Direct oral anticoagulant	153 (9.3%)	64 (13.3%)	49 (9.8%)	40 (6.0%)
Statin	1529 (93.0%)	421 (87.3%)	470 (94.2%)	638 (96.2%)
β-blocker	870 (52.9%)	248 (51.5%)	263 (52.7%)	359 (54.2%)
ACE-I	736 (44.8%)	173 (35.9%)	247 (49.5%)	316 (47.7%)
ARB	455 (28.0%)	135 (28.0%)	143 (28.7%)	177 (26.7%)
Proton pump inhibitor	1173 (71.4%)	330 (68.5%)	359 (71.9%)	484 (73.0%)
Histamine Ⅱ blocker	166 (10.1%)	61 (12.7%)	56 (11.2%)	49 (7.4%)

Data for categorical variables given as number (%); data for continuous variables given as mean ± SD for normal distribution or median (interquartile range) for skewed distribution.

ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; ARC-HBR = Academic Research Consortium-High Bleeding Risk; CABG = coronary artery bypass grafting; CPK = creatine phosphokinase; CRP = C reactive protein; ECMO = extracorporeal membrane oxygenation; eGFR = estimated glomerular filtration rate; HDL = high-density lipoprotein; IABP = intra-aortic balloon pumping; LDL = low-density lipoprotein; LSA = low serum albumin; LVEF = left ventricular ejection fraction; MSA = middle serum albumin; MVD = multi-vessel disease; NSA = normal serum albumin; NSTEMI = non-ST elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST elevation myocardial infarction; TIMI = thrombolysis in myocardial infarction; WBC = white blood cell.

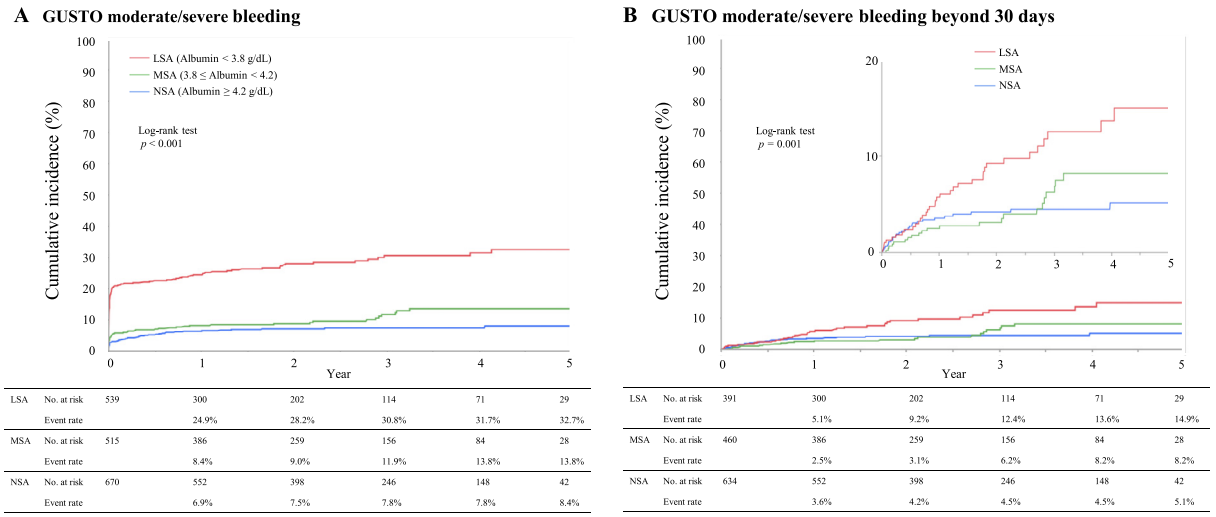

Figure 2. Primary end point stratified by serum albumin level at admission. Kaplan−Meier curves show the 3-year cumulative incidence and log-rank test (*A*) and landmark analysis at 30 days (*B*). Primary end point indicates GUSTO moderate/severe bleeding.

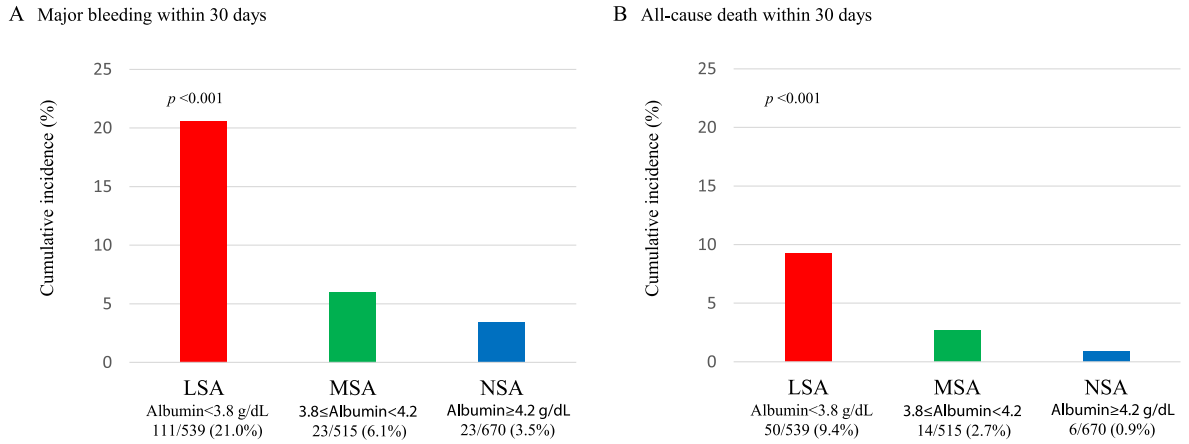

Figure 3. Primary end point (*A*) and all-cause mortality (*B*) within 30 days stratified by serum albumin level at admission. Primary end point indicates GUSTO moderate/severe bleeding.

Table 2
Primary and secondary end points

End points	Total (n = 1724) (Cumulative 3-year incidence)	Serum albumin (g/dL) <3.8 (n = 539) (Cumulative 3-year incidence)	3.8-4.1 (n = 515) (Cumulative 3-year incidence)	≥4.2 (n = 670) (Cumulative 3-year incidence)	*p*
GUSTO moderate/severe bleeding	251 (15.9%)	147 (30.8%)	54 (11.9%)	50 (7.7%)	<0.001
Intracranial hemorrhage	19 (1.7%)	7 (2.0%)	4 (1.6%)	8 (1.5%)	0.470
Gastrointestinal bleeding	25 (1.8%)	16 (5.0%)	6 (1.1%)	3 (0.5%)	<0.001
Access site bleeding	18 (1.2%)	8 (1.8%)	3 (0.7%)	7 (1.1%)	0.250
Others	192 (12.1%)	117 (24.5%)	43 (9.3%)	32 (4.9%)	<0.001
All-cause death	186 (11.8%)	133 (27.2%)	39 (8.1%)	14 (2.6%)	<0.001
Cardiovascular death	98 (6.0%)	72 (15.0%)	21 (3.8%)	5 (0.9%)	<0.001
Hospitalization for heart failure	63 (4.1%)	32 (7.8%)	23 (5.1%)	8 (1.1%)	<0.001
Within 30 days					
GUSTO severe/moderate bleeding	165 (9.6%)	111 (21.0%)	23 (6.1%)	23 (3.5%)	<0.001
All-cause death	70 (4.0%)	50 (9.4%)	14 (2.7%)	6 (0.9%)	<0.001

Number of patients with events was counted until the end of follow-up. Cumulative 3-year incidence was estimated by the Kaplan−Meier method.
LSA = low serum albumin; MSA = middle serum albumin; NSA = normal serum albumin.

Table 3
Univariable and multivariable analysis for the primary end point

	Univariable analysis			Multivariable analysis		
	Hazard ratio	95 % CI	*p*	Hazard ratio	95 % CI	*p*
Age	1.03	1.02-1.05	<0.001			
Female	1.59	1.22-2.06	<0.001			
Body mass index	0.93	0.89-0.96	<0.001	0.95	0.91-0.98	0.006
Hypertension	1.35	1.01-1.81	0.042			
Dyslipidemia	0.71	0.55-0.91	0.007	0.97	0.75-1.25	0.806
Diabetes mellitus	1.50	1.16-1.94	0.002	1.37	1.05-1.78	0.020
Smoking	0.74	0.57-0.95	0.019	1.13	0.86-1.48	0.376
Family history of cardiovascular disease	0.43	0.25-0.74	0.002			
History of malignant tumor	1.53	0.97-2.42	0.068			
Hemodialysis	2.19	1.20-4.01	0.011			
Atrial fibrillation	1.04	0.58-1.86	0.894			
Systolic blood pressure (mmHg)	0.99	0.98-0.99	<0.001			
Heart rate (/min)	1.00	1.00-1.02	0.003			
Cardiogenic shock	4.96	3.73-6.61	<0.001			
Hemoglobin (g/dL)	0.72	0.68-0.76	<0.001	0.80	0.75-0.85	<0.001
Platelet ($\times 10^4/\mu$L)	0.98	0.95-0.99	0.031	1.00	0.98-1.01	0.886
Serum albumin (g/dL)						
≥ 4.2	1.00 (reference)					
< 3.8	4.51	3.26-6.24	<0.001	1.56	1.06-2.30	0.026
3.8 - 4.2	1.50	1.02-2.21	0.04	0.94	0.63-1.34	0.752
Femoral approach	2.82	2.17-3.67	<0.001			
IABP	5.23	4.04-6.76	<0.001	2.66	1.94-3.64	<0.001
ECMO	27.9	19.29-40.29	<0001	8.66	5.37-14.0	<0.001
NT-pro brain natriuretic peptide	1.00	0.99-1.00	0.227			
Warfarin at discharge	1.22	0.58-2.60	0.597			
Direct oral anticoagulant at discharge	1.06	0.77-1.60	0.781			
P2Y12 inhibitor at discharge	0.22	0.17-0.30	<0.001	0.63	0.43-0.90	0.013

Cox regression analysis for the primary end point. Primary end point indicates GUSTO moderate/severe bleeding.

Alb = albumin; CI = confidence interval; ECMO = extracorporeal membrane oxygenation; IABP = intra-aortic balloon pumping; LSA = low serum albumin; MSA = middle serum albumin; NSA = normal serum albumin.

points of view, low SA could be a novel predictor for bleeding in patients with AMI undergoing PCI.

Approximately 40% of patients had ARC-HBR in this study, similar to previous reports,[22,23] and those with ARC-HBR had a higher incidence of bleeding events than those without. This study also demonstrated that low SA was associated with a higher incidence of bleeding events irrespective of the presence of the ARC-HBR. ARC-HBR includes important variables associated with HBR.[7] However, potential bleeding risk factors such as malnutrition or frailty are not included in the ARC-HBR criteria. Therefore, low SA per se could be a predictor for major bleeding in patients with PCI on top of the ARC-HBR criteria.

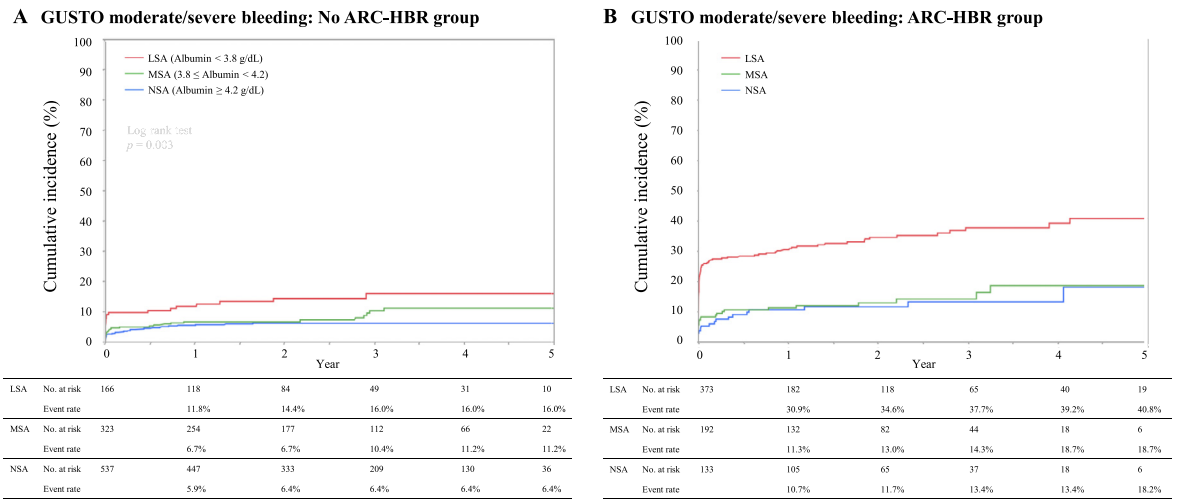

Figure 4. Subgroup analysis for primary end point stratified by ARC-HBR criteria. Kaplan−Meier curves show the 3-year cumulative incidence and log-rank test of no ARC-HBR group (*A*) and ARC-HBR group (*B*).Primary end point indicates GUSTO moderate/severe bleeding.

Recent studies have reported that low LSA is associated with prognosis in patients with cardiovascular disease, including heart failure.[24−26] In patients with STEMI, low LSA at admission predicted in-hospital adverse events, including all-cause death, stroke, and myocardial infarction.[27] The relation between low LSA and prognosis after discharge of AMI was also recently reported.[28,29] In line with previous reports, low LSA at admission was associated with a higher incidence of all-cause death, cardiovascular death, and hospitalization for heart failure in this study. Malnutrition, decreased hepatic synthesis, increased vascular permeability, and frailty were suggested as negative impacts of low LSA on cardiovascular events.[24−26,30,31]

Low SA in patients with AMI was associated with a higher risk for both ischemic and bleeding events in this study. It is possible that low SA is simply a surrogate marker of HBR. However, higher dietary protein intake was associated with a reduced risk of hemorrhagic stroke in the general Japanese population.[32] Moreover, albumin infusion was reported to be associated with reduced risk for rebleeding and in-hospital mortality in patients with cirrhosis admitted for acute gastrointestinal bleeding.[33] A dedicated randomized controlled trial would be necessary to evaluate the direct correlation between an increase of albumin level and risk reduction for bleeding events in patients with AMI.

Some limitations must be taken into account to interpret the present results. First, this was a retrospective, observational study carried out in Japanese centers only. Second, the durations of antiplatelet and anticoagulant therapies after discharge were not evaluated in the present study cohort. Third, the present registry was not designed to investigate the performance of ARC-HBC criteria, and therefore, data were not available for some ARC-HBR criteria. Finally, we defined major bleeding as Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries moderate/severe bleeding, whereas major bleeding was defined as Bleeding Academic Research Consortium 3 or 5 in the ARC-HBR initiative. However, the rates of major bleeding were similar, regardless of the definitions in several previous studies.[34,35]

In conclusion, low SA at admission was independently associated with a higher risk for bleeding events in patients with AMI undergoing PCI.

Disclosures

The authors have no conflicts of interest to declare.

Acknowledgment

The authors thank Aya Yamada (Saga University) for her excellent support.

Funding

None.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2021.10.043.

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