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ORIGINAL ARTICLE

Prediction of need for bowel resection in acute superior mesenteric artery occlusion: A retrospective study of 48 Japanese patients

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Abstract

Aim: This study aimed to predict cases of acute superior mesenteric artery (SMA) occlusion requiring bowel resection using occlusion site and time from symptom onset to diagnosis at five Japanese institutions. Advances in imaging, endovascular treatment, and perioperative management have improved the clinical outcomes of patients with acute SMA occlusion; however, in clinical practice it remains difficult to effectively determine patients requiring bowel resection.

Methods: We retrospectively analyzed the data of 48 patients (mean age: 82.5 y; male: 37.5%) diagnosed with acute SMA occlusion between June 2009 and August 2018. Background data of patients who required and did not require bowel resection were compared. A multivariable predictive model was developed using the time from symptom onset to diagnosis and whether SMA occlusion was proximal, including the origin of the middle colic artery.

Results: Fifteen patients (31.3%) died during the hospital stay. Atrial fibrillation (83.3%) was the most common comorbidity. The median time from symptom onset to diagnosis was 13.0 (interquartile range, 4.75–24.0) h. Laparotomy, bowel resection, and thrombus embolectomy were performed in 41 (85.4%), 26 (54.2%), and 21 (43.8%) patients, respectively. A logistic regression model achieved 78.6% sensitivity in predicting cases not requiring bowel resection. Proximal occlusion was significantly associated with the requirement for bowel resection ($P = .039$).

Conclusion: The time from symptom onset to diagnosis and occlusion site contributed to high sensitivity in determining the need for bowel resection in patients with acute SMA occlusion. Further prospective studies are warranted to investigate the clinical impact of this model.

KEYWORDS
laparotomy, necrosis, prognosis, retrospective study, superior mesenteric artery

1 | INTRODUCTION

Acute superior mesenteric artery (SMA) occlusion is a rare disease with a poor prognosis. Approximately 100 cases of acute mesenteric ischemia are reported in Japan annually, and embolic occlusion occurs twice as often as thrombotic occlusion.[1] The proportion of cases with embolic occlusion in Japan is higher than the proportion (40%–50%) reported in Europe and the United States.[2]

Some retrospective studies reported that endovascular therapy (EVT) provides better outcomes than open surgery,[3–7] and EVT is currently recommended as the first-line therapy for acute thrombotic SMA occlusion according to the guideline of the European Society of Vascular Surgery.[8] In addition, EVT for acute embolic SMA occlusion such as aspiration embolectomy,[9,10] thrombolysis,[11,12] and mechanical thrombectomy[13,14] is progressing, and a previous study revealed similar mortality rates in patients undergoing laparotomy and EVT.[4] However, in Japan laparotomy is often performed even in cases that may not require bowel resection because the rate of embolism is high and stent insertion, thrombolytic therapy, and debulking devices for SMA are not covered by Japanese health insurance. It is presumed that EVT will advance in the future and will become the initial treatment to be recommended. However, in clinical practice it is sometimes difficult to determine whether bowel resection is required at the time of diagnosis. There is a direct relationship between prolonged times to intervention and bowel viability, with 100% of patients with symptoms lasting less than 6 h having viable intestine at exploration. Beyond 6 h, the number of patients with intestinal necrosis increases over time.[15,16] However, the disease progression over time differs whether the occlusion site is proximal or distal.

Therefore, this study aimed to examine the current treatment methods and their outcomes in Japan, where embolic occlusion is common, and to predict the patients requiring bowel resection using the occlusion site and time from symptom onset to diagnosis using data from five centers across Japan.

2 | METHODS

2.1 | Study design and participants

This retrospective study examined the data of 48 patients diagnosed with acute SMA occlusion in the respective departments of surgery at five general hospitals in Japan between June 2009 and August 2018. Diagnosis and management, including operative methods, were performed at the discretion of the vascular surgeon in consultation with a radiologist at each hospital. The principal investigator at each institution obtained Institutional Review Board (IRB) approval, and all IRBs waived the requirement for patient consent because of the retrospective study design. The study protocol was registered in the University Hospital Medical Information Network Clinical Trials Registry (UMIN 000047179), which is one of the network members of the Japan Primary Registries Network and fulfills the WHO registry criteria. The study was conducted in accordance with the ethical standards of the Helsinki Declaration of 1975 and its subsequent revisions. Demographic and clinical data of participants were retrieved from their medical records. Clinical data included risk factors, comorbidities, type of SMA occlusion, as well as intraoperative, perioperative, and long-term outcomes. All data were deidentified at each institution, examined for accuracy and completeness, and collated into a password-encrypted database managed by the Department of Surgery, Kawasaki Municipal Hospital.

2.2 | Diagnosis of acute SMA occlusion

Acute SMA occlusion was diagnosed for each patient based on clinical presentation and physical examination findings, as well as computed tomography angiography findings. Patients with traumatic or iatrogenic aortic dissection were excluded from this study. The occlusion site of the SMA was divided into two regions: proximal occlusion, involving the main trunk including the origin of the middle colic artery (MCA), and distal occlusion, involving the more peripheral portion of the MCA.

2.3 | Management

The physician-partners at each of the five institutions were certified surgeons with expertise in both cardiovascular and endovascular surgery. The management plan for each patient, which comprised conservative treatment, EVT, or surgery, was at the discretion of each physician. Clinical symptoms, laboratory data, and vascular imaging findings were used to determine whether the occlusion was embolic or thrombotic and whether the patient was a candidate for surgery and/or EVT. Patients with bowel resection and/or necrosis in the initial surgery were classified as the bowel resection needed (BRN) group, and the others as the non-BRN group.

2.4 | Statistical analysis

Univariate analysis was performed to examine underlying differences between the BRN and non-BRN groups. Continuous variables are presented as means and standard deviations and were analyzed using the *t*-test. Categorical variables are presented as frequencies and proportions and were analyzed using Fisher's exact test. The time from symptom onset to diagnosis, duration of operation, and blood loss are expressed as medians and interquartile ranges and were analyzed using the Mann–Whitney *U* test. Moreover, we compared the frequency of major adverse events between the groups described above excluding patients who underwent conservative treatments. Additionally, we compared the underlying differences between the in-hospital death and surviving groups.

A multivariable logistic regression model was developed with "time from symptom onset to diagnosis" and "the occlusion site of

the SMA (proximal or distal occlusion from the MCA)" as explanatory variables to examine whether these two variables could be useful as a tool for predicting cases requiring bowel resection. Diagnostic accuracy was determined by the area under the curve (AUC) of the receiver operating characteristic plot. DeLong's method[17] was performed to calculate AUC and its 95% confidence interval (CI). Additionally, the AUC of the predictive model was validated internally using 10-fold crossvalidation and the bootstrap method for 10 000 repetitions. The cutoff point was determined using the Youden index.[18] Finally, for sensitivity analysis we developed another version of the multivariable logistic regression model using the time from onset to diagnosis as a categorical variable (ie, 24 h or less, or longer than 24 h). All *P*-values were two-tailed, with a *P*-value of <.05 considered statistically significant. The R statistical software v. 4.1.2 (The R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analyses, and the R package "rms" was used for the internal validation.

3 | RESULTS

Baseline demographic and clinical data are summarized in Table 1. Fifteen (31.2%) patients died during hospital admission. The mean age of our study population was 82.5 y, and 18 patients (37.5%) were men. Forty-one patients (85.4%) presented with abdominal pain. The median time from symptom onset to diagnosis was 13.0 (interquartile range [IQR], 4.75–24.0) h. The cause of occlusion was embolism in 37 patients (77.1%) and thrombus in seven patients (14.6%). Regarding the occlusion site, 33 patients (68.8%) had proximal occlusion and 15 (31.2%) had distal occlusion. The management approaches are summarized in Table 2. Laparotomy was performed in 41 (85.4%) patients, including one case of laparoscopic surgery. There were 28 patients in the BRN group and 20 in the non-BRN group. No additional bowel resection was performed the non-BRN group. However, there were two patients who experienced postoperative bowel necrosis as a result of reocclusion. Both patients were included in the non-BRN group, as the absence of intestinal necrosis was confirmed during the initial revascularization. In addition, major adverse events within 30 d of intervention and the comparative data of the surviving and in-hospital death groups are summarized in Tables S1 and S2, respectively.

Comparisons between the BRN and non-BRN groups revealed no significant differences in patient demographics, such as age, sex, and comorbidities (Table 1). Regarding preoperative data, only C-reactive protein levels were significantly different between the groups. We developed a multivariable logistic regression model using the time from symptom onset to diagnosis and the occlusion site of the SMA as explanatory variables (Table 3). As shown, proximal occlusion was significantly associated with the BRN group. The AUC of the model was 0.704 (95% CI: 0.551–0.857) (Figure 1). The AUC of the 10-fold crossvalidation was 0.672 and that of the bootstrap validation was 0.675. The cutoff point was determined using the Youden index. The threshold of the linear predictor was 0.315, with a sensitivity of 78.6% and specificity of 55.0%. Therefore, using this model it was determined with 78.6% probability that bowel resection is not required for cases with proximal occlusion within 3.5 h and for those with distal occlusion within 43.6 h. Finally, we created a web application to apply our model in clinical practice (https://okui.shinyapps.io/sma_bowelresection_predictor/). Additionally, we developed another version of the multivariable logistic regression model using the time from onset to diagnosis as a categorical variable with a 24-h cutoff. As a result, the AUC was 0.680 (95% CI: 0.541–0.820), which is lower than the primary model (Table S3).

4 | DISCUSSION

In clinical practice, it is difficult to identify the patients who require bowel resection. We conducted a retrospective study of 48 patients diagnosed with acute SMA occlusion at five hospitals in Japan. In this study there were many patients with atrial fibrillation and embolism that are characteristic features commonly found in Japan, and laparotomy was often performed. We developed a model that may predict the patients who require bowel resection by focusing on the time from symptom onset to diagnosis and the SMA occlusion site.

Multivariable analysis revealed that bowel resection was not necessary within 3.5 h after the onset of proximal occlusion and within 43.6 h after the onset of distal occlusion, with a high sensitivity of 78.6%. As the aim of the model was to rule out patients not requiring bowel resection, the sensitivity is the main parameter used in this study. This model may guide decision-making to perform laparotomy in the clinical setting. Furthermore, proximal occlusion was significantly associated with the need for bowel resection. Although important, it is difficult to determine whether intestinal ischemia is irreversible, because the time taken to reach the irreversible stage varies depending on the degree of ischemia. There are some studies in which the authors created algorithms and actively performed EVT to achieve favorable results.[19,20] However, the time factor considered was only categorical, that is, early or late,[19] and the occlusion site was not mentioned. There is a direct relationship between prolonged time to intervention and bowel viability, with 100% of patients with symptoms lasting less than 6 h having viable intestine at exploration. Beyond 6 h, the number of patients with intestinal necrosis increases over time.[15,16] However, the timing of disease progression differs based on the location of the occlusion site (proximal or distal). Nearly all patients with proximal occlusion underwent laparotomy in this study, and the MCA and inferior pancreaticoduodenal arteries, which originate close to the MCA, connect and communicate with the inferior mesenteric and celiac arteries.[21] Therefore, we analyzed the data based on the occlusion site and the time from symptom onset to diagnosis. This is a retrospective study involving a small number of patients; furthermore, the specificity was low, which does not establish a clear therapeutic index. However, it may be important to investigate the SMA occlusion site in addition to the time from symptom onset in future studies.

TABLE 1 Demographics, clinical presentation, etiology, and preoperative laboratory results of 48 patients with superior mesenteric artery occlusion

	Overall	BRN group	Non-BRN group	*P*-value
N	48	28	20	
Age (y)	82.50 (10.22)	82.75 (10.09)	82.15 (10.65)	.844
Male sex	18 (37.5%)	9 (32.1%)	9 (45.0%)	.385
Atrial fibrillation	40 (83.3%)	21 (75.0%)	19 (95.0%)	.116
Peripheral arterial disease	10 (20.8%)	5 (17.9%)	5 (25.0%)	.721
Hypertension	39 (81.2%)	23 (82.1%)	16 (80.0%)	1
Diabetes mellitus	12 (25.0%)	7 (25.0%)	5 (25.0%)	1
Hyperlipidemia	13 (27.1%)	6 (21.4%)	7 (35.0%)	.339
Coronary artery disease	12 (25.0%)	9 (32.1%)	3 (15.0%)	.311
Cerebrovascular disease	15 (31.2%)	8 (28.6%)	7 (35.0%)	.755
History of smoking	26 (54.2%)	16 (57.1%)	10 (50.0%)	.77
Antiplatelet therapy	16 (33.3%)	10 (35.7%)	6 (30.0%)	.763
Anticoagulant therapy	14 (29.2%)	7 (25.0%)	7 (35.0%)	.528
Statin therapy	12 (25.0%)	5 (17.9%)	7 (35.0%)	.198
Abdominal pain	41 (85.4%)	23 (82.1%)	18 (90.0%)	.683
Vomiting	8 (16.7%)	7 (25.0%)	1 (5.0%)	.116
Diarrhea	7 (14.6%)	2 (7.1%)	5 (25.0%)	.111
Cause of occlusion = Embolism/Thrombus	37/7 (84.1%/15.9%)	19/6 (76.0%/24.0%)	18/1 (94.7%/5.3%)	.119
Site of occlusion = Proximal occlusion[a]	33 (68.8%)	22 (78.6%)	11 (55.0%)	.117
WBC (/μL)	13 629 (5150)	14 139 (4841)	12 914 (5601)	.422
CPK (g/dL)	235.6 (465.4)	280.6 (561.9)	172.6 (282.9)	.434
CRP (mg/dL)	6.54 (10.06)	9.50 (11.69)	2.55 (5.35)	.017
Lactate (mg/dL)	4.35 (2.53)	4.81 (2.78)	3.48 (1.73)	.126
pH	7.40 (0.09)	7.38 (0.06)	7.42 (0.12)	.119
D-dimer (μg/mL)	10.41 (10.65)	12.79 (11.07)	7.52 (9.61)	.111
Time from onset to diagnosis, hours (median [IQR])	13.00 [4.75-24.00]	16.50 [5.75-24.00]	12.50 [3.75-20.25]	.231
Time from diagnosis to intervention, hours (median [IQR])[b]	3.50 [2.75, 4.00]	3.50 [3.00, 4.50]	3.50 [2.50, 4.00]	.417
Operation time, min (median [IQR])	130.50 [92.25-156.75]	139.50 [108.50-184.25]	113.00 [90.50-131.00]	.045
Estimated blood loss (g) (median [IQR])	100.00 [50.00-287.50]	149.00 [63.50-325.75]	73.00 [50.00-100.00]	.142
$CHAD_2$ score	3.04 (1.54)	3.04 (1.40)	3.05 (1.76)	.975
$CHAD_2DS_2$-VASc score	5.15 (1.94)	5.25 (1.71)	5.00 (2.25)	.664
In-hospital death	15 (31.2%)	11 (39.3%)	4 (20.0%)[c]	.212

Note: Patients who had bowel resection and/or necrosis in the initial surgery were classified as the "BRN group" and the others as the "non-BRN group."

Continuous variables are presented as means and standard deviations and were analyzed using the *t*-test. Categorical variables are presented as frequencies and proportions and were analyzed using Fisher's exact test.

Time from symptom onset to diagnosis, time from diagnosis to intervention, duration of operation, and blood loss are expressed as median and interquartile range and were analyzed using the Mann–Whitney *U* test.

Abbreviations: BRN, bowel resection needed; CPK, creatine phosphokinase; CRP, C-reactive protein; SMA, superior mesenteric artery; WBC, white blood cell.

[a]The SMA occlusion site was divided into two regions: proximal occlusion, involving the main trunk, including the origin of the middle colic artery (MCA), and distal occlusion, involving the more peripheral portion from the MCA.

[b]There was one missing value regarding time from diagnosis to intervention in the BRN group and four in the non-BRN group (intervention was not performed in these cases).

[c]Of the four deaths, two were due to stroke and two were due to intestinal necrosis caused by reocclusion. These patients were included in the non-BRN group as the absence of intestinal necrosis was confirmed during the initial revascularization.

TABLE 2 Management approaches in 48 patients with superior mesenteric artery occlusion

	Overall	BRN group	Non-BRN group
N	48	28	20
Treatment			
Laparotomy only	35 (72.9%)	24 (85.7%)	11 (55.0%)
Laparotomy + EVT	6 (12.5%)	4 (14.3%)	2 (10.0%)
EVT only	2 (4.2%)	0 (0.0%)	2 (10.0%)
Conservative treatment	5 (10.4%)	0 (0.0%)	5 (25.0%)
Surgical procedures			
Bowel resection only		18 (64.3%)	
Bowel resection + Embolectomy		8 (28.6%)	
Other surgical procedure		2 (7.1%)	
Embolectomy only			13 (65.0%)

Note: Patients who had bowel resection and/or necrosis in the initial surgery were classified as the "BRN group" and the others as the "non-BRN group."

Abbreviations: BRN, bowel resection needed; EVT, endovascular treatment.

TABLE 3 Multivariable logistic regression model for predicting whether bowel resection is required in patients with acute superior mesenteric artery occlusion

Variables		OR	95% CI	Beta coefficient	SE of Beta coefficient	*P*-value
Time from onset to diagnosis (hour)	Continuous	1.04	0.99–1.09	0.037	0.024	.115
Proximal occlusion	No	Ref	—	—	—	—
	Yes	4.46	1.08–18.34	1.494	0.722	.039
Intercept	—	—	—	−1.309	0.784	.095

Note: Logistic regression formula: Score (linear predictor) = 0.037 × Time from symptom onset to diagnosis (hour) + 1.494 × Proximal occlusion (Yes = 1, No = 0) − 1.309.

The threshold of the linear predictor was 0.315, with a sensitivity of 78.6% and specificity of 55.0%.

Example 1 Using this model, it can be determined with 78.6% probability that bowel resection is not necessary for cases of proximal occlusion within 3.5 h.

Example 2 It can be determined with 78.6% probability that bowel resection is not necessary for cases of distal occlusion within 43.6 h.

Abbreviations: CI, confidence interval; OR, odds ratio; SE, standard error.

In this study, 75.5% of the SMA occlusions were caused by embolism, which was higher than the reported proportion of 40%–50% in Europe and the United States.[2] We presumed that this difference was due to racial variation; the annual report by the Japanese Society for Vascular Surgery states that emboli occur twice as often as thrombi in the Japanese population.[1] However, the prevalence of hypertension, diabetes, and hyperlipidemia is increasing in Japan, and we expect that the incidence of thrombosis will increase in the future.

Despite the improvements in vascular therapy over several decades, the mortality among patients with acute mesenteric ischemia remains alarmingly high, at 60%–80%.[22,23] Conversely, the mortality rate observed in this study (32.7%) was not worse than that reported in previous studies. Our study may have had comparatively low mortality rates because we did not include patients who may have died before visiting a professional facility with vascular and endovascular physicians for consultation.

No serum markers are accurate for the diagnosis of mesenteric ischemia.[8] D-dimer and lactic acid levels may be used to exclude the diagnosis of acute SMA occlusion; however, their specificities are reportedly low.[4,8,9,24–26] In one study, the highest lactate value within 24 h prior to surgery was an independent risk factor for mortality.[27] Preoperative lactic acid and D-dimer levels in the in-hospital death group were also significantly higher than those in the surviving group in our study (Table S2). However, the preoperative C-reactive protein level was the only marker that was significantly higher in the BRN group than in the non-BRN group.

No studies have considered acute SMA occlusion and $CHADS_2$ score (congestive heart failure, hypertension, 75 y of age or older, diabetes mellitus, and previous stroke or transient ischemic attack) in the past. Although the $CHADS_2$ and CHA_2DS_2-VASc scores (congestive heart failure, hypertension, age ≥75 y [doubled], diabetes, stroke/transient ischemic attack/thromboembolism [doubled], vascular disease [prior myocardial infarction, peripheral artery disease, or aortic plaque], age 65–75 y, sex [female]) were calculated and compared, there were no significant differences in any comparison in this study (Tables 1, S2).

This study has some limitations. First, the study used a retrospective design and only examined a small population of Japanese

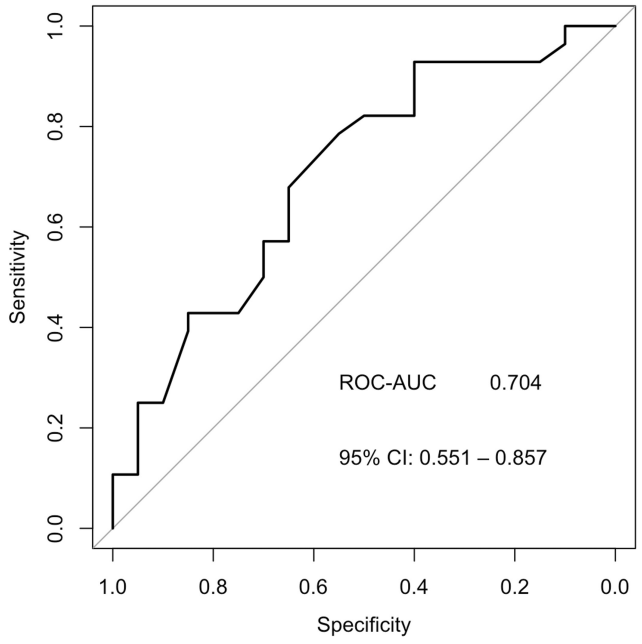

FIGURE 1 Receiver operating characteristic curve of a logistic regression model. AUC, area under the curve; CI, confidence interval.

patients. The study included 20 patients in the non-BRN group and 28 in the BRN group; therefore, the multivariable model was developed using only two covariates. Second, the selected treatment option might have been influenced by health insurance coverage. The physicians involved in this study may have opted for laparotomies because stent insertion for SMA is not reimbursed by the Japanese health insurance, and embolism accounts for a higher percentage of cases than thrombosis in Japan. Finally, the actual clinical impact of the model was not assessed in this proof-of-concept study. However, the results warrant a prospective validation of the model.

5 | CONCLUSIONS

Combining the time from symptom onset to diagnosis with the SMA occlusion site is expected to contribute to high sensitivity in determining the need for bowel resection in patients with acute SMA occlusion. Further prospective studies are required to investigate the clinical impact of this model.

DISCLOSURE

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Author Contributions: All authors contributed significantly; SW, HO, KH, and KM conceived the study. HO, JO, HH, and YK supervised the conduct of the trial and data collection. SW, KH, NF, TF, and TS collected data. SW and KH managed the data, including quality control. JO provided statistical advice on study design and analyzed the data. SW drafted the article, and all authors contributed substantially to its revision. SW, HO, and JO take responsibility for the paper as a whole. And all authors are in agreement with the content of the article.

Ethical Approval: The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. All IRBs waived the requirement for patient consent because of the retrospective study design. The study protocol was registered in the University hospital Medical Information Network Clinical Trials Registry (UMIN 000047179), which is one of the network members of the Japan Primary Registries Network and fulfills the WHO registry criteria. The study was conducted in accordance with the ethical standards of the Helsinki Declaration of 1975 and its subsequent revisions.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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