Spontaneous Intramural Intestinal Hemorrhage versus Acute Mesenteric Ischemia by CT Evaluation

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Abstract

Objective The purpose of our study was to differentiate the imaging findings of patients with spontaneous intramural intestinal hemorrhage (SIIH) from those with acute mesenteric ischemia (AMI) after abdominal computed tomography (CT) survey in the emergency department.

Methods We retrospectively included 83 patients diagnosed with SIIH or AMI after abdominal CT.

Results The mean ages of 30 SIIH patients and 53 AMI patients were 74.4 ± 14.6 years and 75.8 ± 11.2 years, respectively. Patients with SIIH had significantly thicker maximal intestinal wall thickening (14.8 ± 3.9 vs. 10.9 ± 4.1 , $p < 0.001$), a lower rate of ileum involvement (26.7% vs. 77.4%, $p < 0.001$) and a higher rate of ascites (96.7% vs. 64.2%, $p < 0.001$) compared with patients with AMI. Neither pneumatosis intestinalis ($p < 0.001$) nor portomesenteric gas ($p < 0.01$) were detected in SIIH patients but were observed in AMI patients. A receiver-operating characteristic (ROC) curve analysis showed that the optimal cut-off value for maximal intestinal wall thickening between groups was 10.4 mm and the area under the ROC curve between groups was 0.752 ($p < 0.0001$). A multiple logistic regression analysis showed that the independent predictors of SIIH were non-involvement of the ileum (odds ratio, OR, 6.998; $p = 0.001$), maximal intestinal wall thickening ≥ 10.4 mm (OR, 5.748; $p = 0.040$) and ascites (OR, 13.348; $p = 0.023$). The area under the ROC curve for the model was 0.854 ($p < 0.001$).

Conclusion The independent predictors of SIIH from AMI after abdominal CT in acute abdominal patients include non-involvement of the ileum, intestinal wall thickening ≥ 10.4 mm, and ascites.

Key words: spontaneous intramural intestinal hemorrhage, acute mesenteric ischemia, maximal intestinal wall thickening, non-involved ileum

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Introduction

Spontaneous intramural intestinal hemorrhage (SIIH) is a rare, acute abdomen condition, occurring with increasing frequency as a complication of warfarin anticoagulation overuse in emergency departments (EDs). Patients typically complain of abdomen pain (100%) (1, 2), and the rate of peritonitis is approximately 7.7-61.5% (1-3). Emergency

physicians (EPs) must exclude the possibility of surgical intervention. Abdominal computed tomography (CT) can help EPs to differentiate patients with acute abdominal pain due to its characteristics of rapid, first-line, imaging modality with high accuracy. However, abdominal CT occasionally is not useful to help EPs differentiate SIIH from acute mesenteric ischemia (AMI) due to similar findings, such as homogenous bowel wall thickening or the presence of a target sign on intravenous contrast-enhanced studies (4-6). Ap-

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Table 1. Demographic Information and Comorbid Medical in Patients with SIIH or AMI at ED.

	SIIH (n=30)(%)	AMI (n=53)(%)	p
Sex (male : female)	23:7	33:20	NS
Age (years)	74.4±14.6	75.8±11.2	NS
Duration before ED visits (days)	2.5±1.4	2.5±1.9	NS
Anticoagulant use	28 (93.3)	5 (9.4)	<0.001
Surgery	0 (0)	33 (62.3)	<0.001
Mortality	2 (6.7)	33 (62.3)	<0.001

proximately 17.9% of SIIH patients are transferred to medical centers for surgical intervention under the impression of AMI (2). Furthermore, approximately 32.1% of SIIH patients' formal abdominal CT reports by radiologists suggest the need for EPs to differentiate SIIH from AMI in clinical practice (2). It is critical for EPs to differentiate SIIH from AMI because the treatments are quite different, i.e., conservative medical treatment for SIIH (1, 3, 7, 8) and emergent surgical intervention for AMI (9-11). The purpose of our study was to discern the differences in abdominal CT findings and help EPs to differentiate SIIH from AMI.

Materials and Methods

We retrospectively reviewed the emergency medical charts of patients admitted to Taipei Veterans General Hospital from 2003 to 2013, which has an ED that sees approximately eighty thousand visits annually. Fifty-three cases that underwent abdominal CT in the ED were identified from a computer search of our hospital discharge codes (International Classification of Disease, ICD) of 557.0 and 557.9. The definition of AMI was bowel necrosis due to 4 types of pathophysiologic processes (12), including: 1) mesenteric arterial emboli (incidence 40-50%) from a cardiac source; 2) mesenteric arterial thrombosis (25%) due to severe atherosclerotic disease; 3) non-occlusive mesenteric ischemia (20%) due to a low cardiac output; and 4) mesenteric venous thrombosis (10%) due to an intraabdominal pathological condition or idiopathic. Initial resuscitation included intravenous fluid resuscitation, therapeutic intravenous heparin sodium and mesenteric arterial infusion of papaverine. Emergency laparotomy is typically needed to explore the possibility of bowel infarction and excision, except in non-occlusive mesenteric ischemia. The treatment for non-occlusive mesenteric ischemia is primarily medical conservative therapy. The diagnosis of AMI was made by surgical intervention (31/53) and an angiogram (6/53) and abdominal CT (53/53) with diagnostic criteria including bowel wall thickening, appearance of a target sign, lack of an enhanced bowel wall, pneumatosis intestinalis, arterial emboli and venous thrombosis. In AMI, patients with mesenteric ischemia secondary to mechanical obstruction, adhesions, volvulus, or clinically diagnosed AMI without abdominal CT were excluded, as were patients younger than 14 years of age. Thirty cases of SIIH that underwent abdominal CT in the

ED were identified of ICD 569.8 and 578. For the diagnosis of SIIH, the discharge diagnosis and non-traumatic spontaneous intramural hematoma after abdominal CT survey of homogenous bowel wall thickening, enhanced target sign and highly attenuated ascites were reviewed (30/30). The final diagnosis of SIIH was determined by abdominal CT (30/30) and a history of warfarin use (28/30) with prolonged activated partial thromboplastin time or hemophilia A (2/30). Two trained research assistants blinded to the study purpose entered the abstracted data into a new data bank and standardized abstractor forms used for study analyses. The findings of a CT scan, such as involved segment of the intestine, maximal intestinal wall thickening, bowel segments and the estimated length involved, ascites, pneumatosis intestinalis, portomesenteric gas, and mesenteric arterial or venous thrombosis were evaluated and analyzed by two abdominal radiologists who were blinded to the clinical diagnosis of AMI or SIIH. Categorical variables were compared between groups using the chi-square or Fisher's exact test for qualitative data. The Mann-Whitney non-parametric U-test or a *t*-test was used to analyze quantitative data. Multiple logistic regression analyses were applied to determine the accuracy of combinations of clinical significant variables in predicting patient outcomes. The Hosmer-Lemeshow test for lack of fit and likelihood ratio test used for model selection were performed. When applicable, tests were two-tailed. *p* values <0.05 were considered to be statistically significant.

Results

Among the 83 patients studied, 30 (23 men and 7 women) had SIIH and 53 (33 men and 20 women) had AMI. The mean ages were 74.4±14.6 years (range, 18-93 years) and 75.8±11.2 years (range, 38-95 years), respectively (Table 1). As compared with AMI patients, all included SIIH patients received conservative medical treatment without surgery (*p*<0.001). Only 2 (6.7%) SIIH patients died due to pneumonia and septic shock (*p*<0.001). In SIIH patients, anticoagulant use (28/30, 93.3%) was the major cause, while the other two patients had hemophilia A and suspected pancreatitis-induced coagulopathy. In AMI patients, there were 5 (9.4%) patients under anticoagulant treatment.

All included patients were diagnosed with SIIH or AMI after an abdominal CT examination in our ED. In the final formal reports, only 66.7% (20/30) suggested the diagnosis of SIIH alone, 23.3% (7/30) suggested that EPs must differentiate SIIH from AMI, and 10.0% (3/30) suggested the diagnosis of AMI alone (Table 2). Thus, the purpose of our study was to discern the differences in abdominal CT findings to differentiate SIIH from AMI.

With regard to the abdominal CT findings (Table 3), there was no difference between SIIH and AMI (*p*>0.05) in the degree of jejunum involvement or the estimated length. Maximal intestinal wall thickening was significantly thicker in SIIH patients as compared with AMI patients (14.8±3.9 vs. 10.9±4.1, *p*<0.001). The percentage of involved intestine

Table 2. The Formal Abdominal CT Reports in SIIH and AMI Suggested the Differential Diagnosis in Our ED.

	SIIH (n=30)(%)	AMI (n=53)(%)
SIIH only	20 (66.7)	0 (0)
Differentiate SIIH from AMI	7 (23.3)	0 (0)
AMI only	3 (10)	53 (100)
Enteritis or colitis	5 (16.7)	8 (15.1)
Partial intestinal obstruction	1 (3.3)	4 (7.5)
Acute pancreatitis	1 (3.3)	0 (0)

* 8 SIIH patients and 16 AMI patients have more than one differential diagnosis in formal abdominal CT reports

Figure 1. A ROC curve of the cut-off level of maximal intestinal wall thickening to differentiate SIIH from AMI.

was approximately 10.0% (≤ 15 cm) and 46.7% (16-30 cm) in SIIH patients (mean 33.2 cm), and 50.9% (>30 cm) in AMI patients (mean 36.7 cm) ($p>0.05$). SIIH patients also had a significant lower rate of ileum involvement (26.7% vs. 77.4%, $p<0.001$) and a significant higher rate of ascites (96.7% vs. 64.2%, $p<0.001$). Neither pneumatosis intestinalis nor portomesenteric gas was found in all SIIH patients, and these were only identified in AMI patients, at rates of 39.6% (21/53) and 20.8% (11/53), respectively. Intravenous medium aids in the detection of mesenteric arterial or venous thrombosis in abdominal CT. In our study, 100% (30/30) of SIIH patients and 75.5% (40/53) AMI patients underwent abdominal CT with intravenous contrast medium. The rates of mesenteric arterial or venous thrombosis in SIIH and AMI patients were 0% (0/30) and 52.5% (21/40), respectively.

A receiver-operating characteristic (ROC) curve analysis was performed to determine the potential role of maximal intestinal wall thickening in the discrimination between the SIIH and AMI groups. The area under the ROC curve between groups was 0.752 (95% confidence interval, 0.646-0.857; $p<0.0001$) (Fig. 1). The optimal cut-off value for maximal intestinal wall thickening between the groups was 10.4 mm. When maximal intestinal wall thickening was ≥ 10.4 mm, the sensitivity, specificity, positive predictive

Table 3. Summary of Abdominal CT Findings in SIIH and AMI at ED.

	SIIH (n=30)(%)	AMI (n=53)(%)	p
Duodenum involved ^a	1 (3.3)	0 (0)	NS
Jejunum involved	23 (76.7)	37 (69.8)	NS
Ileum involved	8 (26.7)	41 (77.4)	<0.001
Maximal intestinal wall thickening (mm) ^b	14.8 $\pm$ 3.9	10.9 $\pm$ 4.1	<0.001
Estimated length (cm)	33.2 $\pm$ 19.4	36.7 $\pm$ 27.4	NS
Ascites	29 (96.7)	34 (64.2)	0.001
Pneumatosis intestinalis	0 (0)	21 (39.6)	<0.001
Portomesenteric gas	0 (0)	11 (20.8)	<0.01
Mesenteric arterial or venous thrombosis ^c	0/23 (0)	21/40 (52.5)	<0.001

^a Number (%)

^b Mean $\pm$ SD

Figure 2. A ROC curve displaying the relationship between the sensitivity and specificity for the regression-model analysis of independent variables predicting SIIH from AMI after abdominal CT.

value (PPV) and negative predictive value (NPV) were 93.3%, 45.3%, 49.1% and 92.3%, respectively.

We conducted a multiple logistic regression analysis by entering backward and stepwise data for increased ileum involvement, ascites and whether intestinal wall thickening exceeded and included 10.4 mm. The independent predictors of SIIH were non-involvement of the ileum, (odds ratio, OR, 6.998; 95% confidence interval, CI, 2.180 to 22.457; $p=0.001$), maximal intestinal wall thickening ≥ 10.4 mm (OR, 5.748; 95% CI, 1.084 to 30.477; $p=0.040$) and ascites (OR, 13.348; 95% CI, 1.433 to 124.357; $p=0.023$). The area under ROC curve (Fig. 2) for the model was 0.854 (95% CI, 0.773 to 0.934; $p<0.0001$), suggesting good model discrimination. The sensitivity, specificity, PPV and NPV were 63.3%, 86.7%, 76.0% and 81.0%, respectively.

Discussion

SIIH is rare in the list of differential diagnoses, however, with the increasing overuse of warfarin for anticoagulation, SIIH is being reported more frequently. Unfortunately, abdominal CT occasionally does not help EPs differentiate

SIIH from AMI due to similar CT findings (4-6). It is critical for EPs to make the right decision because the optimal treatments are quite different, conservative medical treatment for SIIH (1, 7, 8) and emergent surgical intervention for AMI (9-11). In our study, 20% (6/30) of the SIIH patients were transferred to our hospital under the impression of AMI and for emergent surgical intervention. Approximately 33.3% (10/30) of our hospital formal abdominal CT reports for SIIH patients suggested AMI or the possibility of AMI (Table 2). In order to help EPs to differentiate SIIH from AMI by discerning the differences in abdominal CT findings, our retrospective study showed that the independent predictors of SIIH were non-involved ileum, intestinal wall thickening ≥ 10.4 mm and ascites.

The jejunum was the most commonly involved site of hematoma in SIIH patients (13). In previous studies of SIIH, the rates of intestinal segments involved were as follows: 50-69% in the jejunum, 38-61.1% in the ileum, and 5.6-23% in the duodenum (3, 14, 15), while in the present study they were 76.7%, 26.7% and 3.3%, respectively. In AMI, the ileum was the most common involved (84.2%), followed by the jejunum (47.4%), duodenum (10.5%), and colon (5.3%) (14). According to the above findings, the jejunum was the most common involved part of the intestine in SIIH (3, 15), whereas it was the ileum in AMI (14). The involvement of the jejunum may help EPs to differentiate SIIH from AMI. In our study, the involvement of the jejunum did not show significant difference between SIIH and AMI ($p > 0.05$), whereas the involvement of the ileum did. The rate of ileum involvement was significantly lower in SIIH patients ($p < 0.001$, Table 3). A multiple logistic regression analysis found that non-involvement of the ileum was an independent predictor of SIIH from AMI after abdominal CT. Non-involvement of the ileum may help clinical physicians to differentiate SIIH from AMI patients.

Wall thickening of the involved intestine was easily detected and estimated from CT. The mean maximal wall thickening of the involved intestine in SIIH was approximately 11.7-14.1 mm (7, 14) and 14.8 mm in our study. Regarding AMI, the mean maximal wall thickening was about 4 mm (14) and 10.9 mm in our study. The maximal intestinal wall thickening in SIIH was thicker than that in AMI ($p < 0.001$) (14), which is consistent with our study ($p < 0.001$). Whether maximal wall thickening of the involved intestine is greater or less than 10 mm has been previously proposed as a means to differentiate SIIH from AMI (14). Our study analyzed the abdominal CT findings of 30 SIIH patients, the largest series to date, and used statistical analyses to determine the cut-off value of maximal wall thickening. It has been shown that maximal wall thickening can indeed discriminate SIIH from AMI ($p < 0.0001$) and a thickness greater than 10.4 mm implies SIIH. A multiple logistic regression analysis found that maximal wall thickening ≥ 10.4 mm was an independent predictor of SIIH from AMI.

The estimated length of the involved intestine was previously discussed between SIIH and AMI. The percentage of

involved intestine was approximately 78% (≤ 15 cm) and 22% (16-30 cm) in SIIH patients, and 84% (> 30 cm) in AMI patients (14). The estimated length of the involved intestine was significantly longer in AMI than SIIH (14). However, in our study, there was no significant difference between SIIH and AMI patients. Perhaps due to advances in CT imaging and the early detection of AMI, the range and mean estimated length of involved intestines in AMI was 5-128 cm and 36.7 cm, respectively, which was not significant longer than that of SIIH.

Anticoagulant use history was also significantly different between SIIH and AMI ($p < 0.001$). We analyzed a subgroup of patients under anticoagulant treatment (28 SIIH patients vs. 5 AMI patients), however, there were no significant difference in sex, age, duration before ED visits or abdominal CT findings. Only ascites exhibited a significant difference between SIIH and AMI (27/28 (96.4%) vs. 2/5 (40.0%), $p = 0.007$).

Pneumatosis intestinalis (PI) is defined as the presence of gas in the bowel wall and CT has a high imaging sensitivity to identify intramural gas (16). PI can be detected in acute surgical (17, 18) and non-surgical abdomen disease (17-20). For AMI, the rate of PI in CT reports in previous studies was approximately 26.7-60% (17, 21) and 39.6% in our study. For SIIH, PI was not found in the CT reports in previous studies (1, 3, 5, 7, 14, 15) or in our study. Although SIIH had a significantly lower rate of PI as compared with AMI ($p < 0.001$), we could not analyze the odds ratio of PI since it was 0% in SIIH patients. Therefore, PI may help EPs to differentiate SIIH from AMI, however, more studies are needed to confirm this.

Hepatic portal venous gas (HPVG) is also easily detected in CT and associated with either benign medical disease (e.g., ulcerative colitis, intraabdominal abscess and gastric ulcer) or lethal surgical diseases (e.g., necrotic bowel and small bowel obstruction) (22). Approximately 16.1-35.7% of AMI patients had HPVG in previous studies (16, 21) and 20.8% in our study, however, HPVG showed no significant difference between the survivors and non-survivors in AMI patients (21). Regarding SIIH, HPVG was not found in previous studies (1, 3, 5, 7, 14, 15). A greater accumulation of data is needed to validate the effect of HPVG in discriminating between SIIH and AMI.

Study limitations

The strengths of this study include the large number of SIIH patients and statistical analyses for prognostic indicators to differentiate SIIH from AMI. There are some limitations associated with this study. First, this is a retrospective study and was limited to only a tertiary referral center. Second, AMI was diagnosed by operation, angiography and abdominal CT findings (pneumatosis intestinalis, portomesenteric gas, mesenteric arterial or venous thrombus). Third, this study could not provide clinical evidence of D-dimer, lactate or arterial gas in the differentiation between SIIH and AMI because the rates of these data were low, especially in

SIIH patients.

Conclusion

In conclusion, our retrospective study showed that SIIH patients had significant maximal intestinal wall thickening, a high rate of non-involvement of the ileum and ascites as compared with AMI. According to the ROC curve analysis, the optimal cut-off value of maximal intestinal wall thickening in SIIH was greater than 10.4 mm. The multiple logistic backward regression analysis showed that the independent predictors of acute abdomen patients with SIIH from AMI after abdominal CT were intestinal wall thickening ≥ 10.4 mm, non-involvement of the ileum, and ascites.

The authors state that they have no Conflict of Interest (COI).

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