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ORIGINAL RESEARCH

Clinical features of isolated superior mesenteric artery dissection in the emergency department: a single center retrospective study

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Abstract

Isolated superior mesenteric artery dissection (ISMAD) is a relatively rare disease and often lacks specificity in its clinical presentation, diagnosing it in emergency departments quickly and accurately is a challenge. The study was conducted to understand the basic characteristics of ISMAD including age of onset, risk factors, gender difference and whether D-dimer can be used as a biomarker for its detection. We retrospectively analyzed patients with ISMAD admitted to the emergency department of Xiangya Hospital of Central South University from September 1, 2017 to September 30, 2020. The data included the patient's basic information and the first laboratory test results after admission, including routine blood, liver function, renal function and coagulation function tests. Statistical analysis of results was done using GraphPad Prism 5. There were a total of 17 (15 male and 2 female) patients with a mean age of 52.53 $\pm$ 7.11 years diagnosed with ISMAD. Out of these, 7 (41%) patients had history of hypertension, 7 (41%) had history of smoking and/or alcohol intake, and almost all patients experienced significant abdominal pain and fullness. Four patients (24%) were initially misdiagnosed. The laboratory test results of renal, liver function tests and myocardial enzymology were in their normal ranges. In coagulation results, the positive rates of fibrinogen degradation products (FDP) and D-dimer were 29% and 35%, respectively. We compared these ISMAD results with our previous results for acute aortic dissection (AAD). D-dimer and FDP levels were lower in the ISMAD than in the AAD patients ($P = 0.0004$, $P = 0.0325$, respectively), and negative rates of D-dimer and FDP in ISMAD (65%, 71%) were higher than in AAD patients (14%, 24%) ($P < 0.0001$, $P = 0.0003$, respectively). In our study, ISMAD mostly occurred in middle-aged male patients with known hypertension or active smoking status. Misdiagnosis was common (24% of cases). Since D-dimer and FDP levels proved to be of limited diagnostic value, an abdominal Computed Tomography (CT) scan should be conducted in patients with unclear abdominal pain at an early stage of their diagnostic workup.

Keywords

Abdominal pain; Isolated superior mesenteric artery dissection; D-dimer; Fibrinogen degradation product

1. Introduction

Isolated superior mesenteric artery dissection (ISMAD) refers to the primary dissection of the superior mesenteric artery that does not involve the aorta [1], a relatively rare clinical disease. However, since the first report in 1947 [2] and with the advancement of imaging technology, its discovery rate has been increasing year by year. As an arterial dissection disease of the superior mesenteric artery, ISMAD's main hazard is that the false lumen of the dissection affects the blood supply of the true lumen of this artery, causing intestinal ischemia and even intestinal necrosis. The reasons causing ISMAD are not yet clear [3]. A larger angle between the superior mesenteric artery and distal aorta is considered to be related to the occurrence of ISMAD [4]. Abnormal flow dynamics at this particular site of the superior mesenteric artery are also an important factor in the development of ISMAD. Park *et al.* [5] used a computer model to simulate the hemodynamics of the superior mesenteric artery and found that a sharp change in the convex curvature of the artery resulted in abnormal mechanical stress on the anterior wall, which indicated abnormal shear stress on the anterior wall of the superior mesenteric artery as one of the potential causes of ISMAD [6]. According to previous literature, the risk factors of ISMAD mainly include

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middle age, male sex, high blood pressure, smoking history, hyperlipidemia, and coronary heart disease [4, 5].

Clinical manifestations of the disease lack specificity. It usually starts with sudden abdominal pain, which is obvious around the umbilicus and upper abdomen [7]. This symptom needs to be distinguished from other acute abdominal pain. Causes of abdominal pain are various, such as intestinal obstruction, appendicitis, digestive tract perforation, and urinary calculi. ISMAD is commonly misdiagnosed and mistreated in clinical practice. Unfortunately severe symptoms of ISMAD can manifest as intestinal ischemic necrosis, which can endanger the life of the patient in severe cases [8]. Since the clinical symptoms and laboratory test results of this disease are not specific, the diagnosis mainly depends on superior mesenteric artery computed tomographic angiography (CTA), which is an expensive test. Not all hospitals are equipped with a CTA machine so the diagnosis of ISMAD is easily missed or misdiagnosed in the emergency department.

Since ISMAD is a vascular disease, the pathological mechanism involves changes in bleeding and coagulation function and production of D-dimer and other fibrinogen degradation products (FDP). D-dimer is a specific protein fiber degradation product of cross-linked fibrin produced by the hydrolysis of fibrinolytic enzyme, and FDP are degradation products of fibrinogen/fibrin. It has been determined that D-dimer is the smallest fibrinolysis-specific degradation product in the circulation and is very sensitive to intravascular thrombus. D-dimer levels are increased in plasma in the stage of acute thrombosis due to simultaneous activation of coagulation and fibrinolysis [9]. The sources of D-dimer and FDP are different. FDP levels are elevated as activation of blood coagulation and fibrinolysis increases. In many vascular diseases such as aortic dissection, D-dimer is used as a biomarker [10] because it is very sensitive to intravascular thrombus and may be markedly increased in many diseases.

The purpose of this study was to retrospectively analyze the data of ISMAD patients in our emergency department to understand its main symptoms, laboratory test results, and whether D-dimer levels can be used as a biomarker for ISMAD.

2. Methods

2.1 Study population

We retrospectively analyzed patients with superior mesenteric artery dissection admitted to the emergency department of Xiangya Hospital of Central South University, China, from September 1, 2017 to August 31, 2020. The study protocols were approved by the ethics committee (No.202012198) of Xiangya Hospital of Central South University and complied with the Declaration of Helsinki. All patients were diagnosed by superior mesenteric artery CTA, and those with secondary superior mesenteric artery dissection due to aortic dissection were excluded.

2.2 Data collection

The following data were collected: patient's age, gender, initial symptoms, whether they had been misdiagnosed, and the first laboratory test results on admission to our hospital including routine blood, liver function, kidney function, and coagulation function tests. All the laboratory examinations were assayed on venous samples drawn from patients at the time of initial medical evaluation in the ED. The D-dimer assay was the Sysmex CS-5100, the other coagulation function tests including FDP used Dirui Automatic Biochemical Analyzer CS-1200. D-dimer normal range was 0-0.5 mg/L and the normal FDP range was 0-5 mg/L.

We did not classify the patient's ISMAD, and did not collect relevant data after the patient entered vascular surgery ward.

2.3 Statistical analysis

All results were statistically analyzed using GraphPad Prism 5 (GraphPad Software, Inc.) for evaluation. The results were expressed as mean $\pm$ standard deviation (SD). Continuous variables were compared using Student's t-test for normally distributed measures and the Mann-Whitney U test for non-normal distributions. Comparison of rates between groups was done using a chi-square test or Fisher's exact test, where suitable. $P < 0.05$ was considered statistically significant.

3. Results

There was a total of 17 (15 male and 2 female) patients with a median age of 55 years (IQR 47.50-56.50, range: 38-66 years) diagnosed with ISMAD. Typical CT imaging changes are showed in Fig 1. Seven patients (41%) had hypertension, seven (41%) had history of smoking and/or alcohol intake, and three patients had history of abdominal or pelvic surgery. The clinical symptoms of each patient are illustrated in Table 1. Almost all patients experienced significant abdominal (or back) pain and fullness. Four patients (24%) were misdiagnosed at first. Three patients were misdiagnosed with incomplete intestinal obstruction, and unfortunately 1 patient was misdiagnosed with appendicitis and underwent surgery.

Subsequently, we analyzed laboratory test results as illustrated in the Table 2. White blood cell (WBC) count was $10.95 \pm 5.77 \times 10^9$/L and neutrophil cell (NC) count was $9.22 \pm 5.8 \times 10^9$/L. Renal function assayss (BUN and Cr) were in their normal ranges (5.99 ± 2.83 μmol/L and 80.1 ± 16.2 μmol/L), and liver function assays (TBIL, ALT, AST) also did not show any obvious abnormality nor did myocardial enzymology. In coagulation test results, the mean value of PT, APTT, TT and INR were in their normal ranges. FIB level was 3.18 ± 1.44 g/L (normal range: 2-4 g/L), FDP level was 5.19 ± 4.48 mg/L (normal range: 0-5 mg/L) and D-dimer level was 0.42 ± 0.35 mg/L (normal range: 0-0.5 mg/L). Seven of 17 (41%) of patients exhibited FIB changes, 5 of 17 (29%) were positive for FDP, and 6 of 17 (35%) positive for D-dimer.

To understand the differences in positive rates of FDP and D-dimer between ISMAD and acute aortic dissection (AAD), we compared the results of ISMAD and AAD which we had published with data of 95 patients [11]. In AAD patients, D-dimer level was 1.696 ± 1.421 (range: 0.05 to 10.00) mg/L, the negative rate of D-dimer was 14% (13 in 95), FIB level was 3.662 ± 1.793 (range: 0.45~8.04) g/L, FDP level was 17.41 ± 23.1 (range: 1.6~131.8) mg/L, and the FDP negative rate was 24% (23 in 95). Therefore, D-dimer level was lower in ISMAD

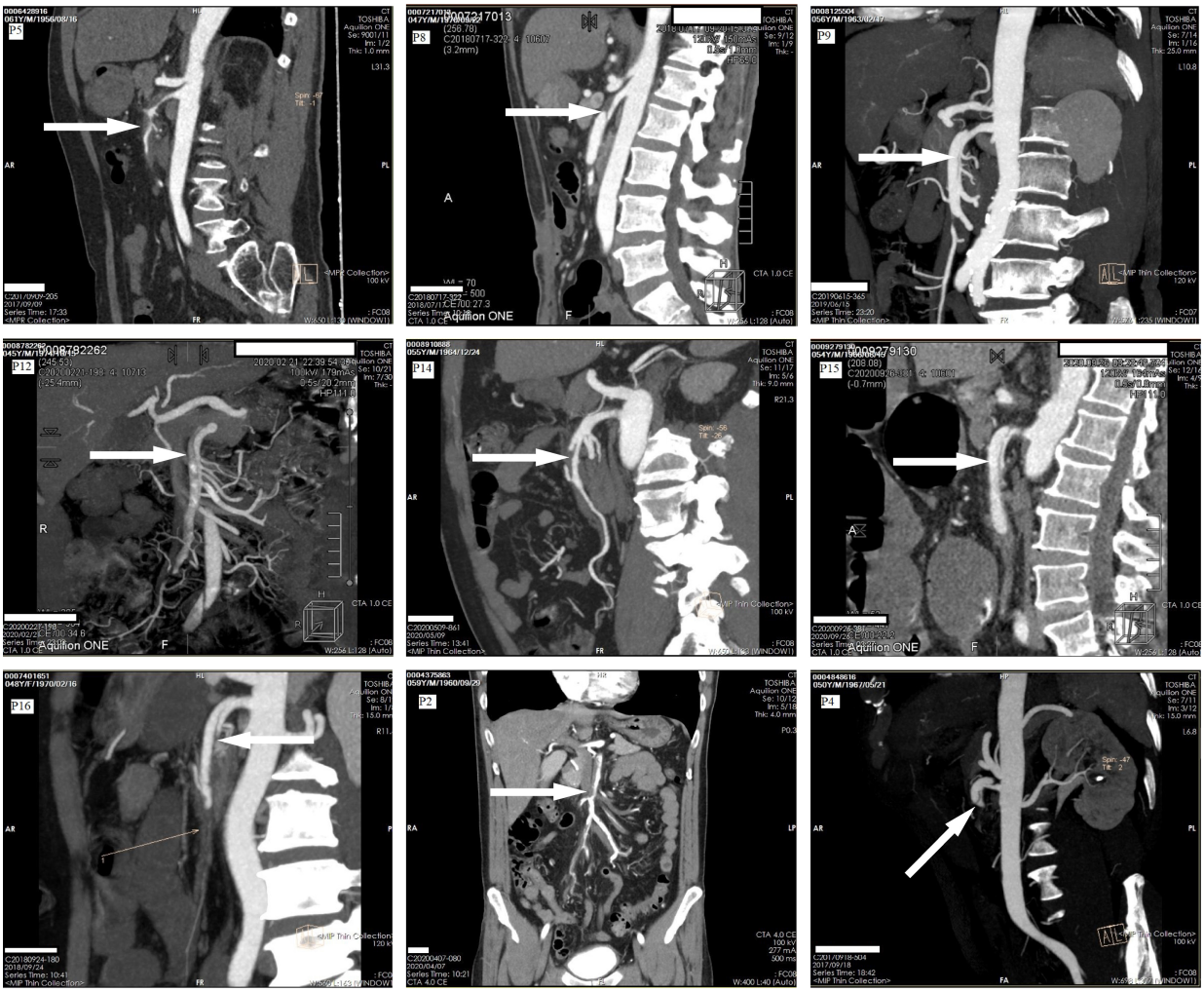

FIGURE 1. An example of a dissection of the superior mesenteric artery as indicated by the arrows, shown in a computed tomography angiography.

patients compared to that in AAD patients ($P = 0.0004$), and the negative rate of D-dimer in ISMAD patients (65%) was higher than that in AAD patients (14%) ($P < 0.0001$). However, the difference in FIB level between ISMAD and AAD patients was not statistically significant ($P = 0.3$). FDP level was lower in the ISMAD patients than in AAD patients ($P = 0.03$), while the negative rate of FDP (71%) was higher in ISMAD patients than in the AAD patients (24%) ($P = 0.0003$).

4. Discussion

ISMAD remains a rare condition but is being increasingly noted incidentally on diagnostic imaging. It is an arterial dissection of the superior mesenteric artery, where the main hazard is that the false lumen of the dissection affects the true lumen of the artery, leading to intestinal bleeding and even intestinal necrosis. The cause is not yet clear [12]. In our study, most patients were male, 41% had hypertension, 41% had a history of smoking and/or alcohol intake, all concordant with risk factors of ISMAD found in previous studies [6, 12]. The clinical manifestations of ISMAD are diverse. Most patients suffer from sudden abdominal pain or back pain and fullness, exhibited in almost all patients in the present study. The cause of abdominal pain may be intestinal deficiency of blood, the dissection itself, or an inflammation that stimulates the visceral arterial plexus. Severity of symptoms might be related to the length of vascular dissection and degree of true lumen stenosis [7, 13]. The clinical manifestations and physical examination of ISMAD have little specificity, mainly occurring as abdominal pain, and there are dozens or even hundreds of causes of abdominal pain. ISMAD leads to intestinal ischemia and weakened intestinal motility, which might cause partial or complete intestinal obstruction. Therefore it is easy to misdiagnose at the beginning of the disease. In the present study, 3 patients were misdiagnosed as having incomplete intestinal obstruction, and unfortunately, 1 patient was misdiagnosed with appendicitis and underwent surgery. Although the diagnosis of ISMAD depends on CTA of the superior mesenteric artery, many studies have proved that an ordinary CT scan can also be used to diagnose ISMAD [14, 15]. Therefore, it is necessary to perform CT examination for patients with persistent abdominal pain or abdominal pain that is not relieved after initial treatment to avoid misdiagnosis or missed diagnosis. In our study, the remaining 13 patients

TABLE 1. Patients' basic information

patient	gender	age	Clinical symptoms	Disease history	misdiagnosis
1	male	55	bloody stool for 20 days	Hepatitis B , drinking	Yes, Gastrointestinal bleeding, and hemorrhagic shock
2	male	59	abdominal pain for 3 days	Smoking, bronchitis	no
3	male	56	abdominal pain and back pain for 7 hours	hypertension, gastric ulcer, history of appendicitis surgery	no
4	male	50	abdominal fullness and pain for 8 days	hypertension	no
5	male	61	abdominal fullness for 4 hours	no	no
6	male	69	abdominal pain for 2 weeks	Drinking, smoking, history of inguinal hernia surgery	Yes, Incomplete intestinal obstruction
7	male	49	abdominal pain for 1 day	smoking	no
8	male	47	abdominal pain for 2 months	diabetes mellitus	Yes, Incomplete intestinal obstruction
9	male	56	abdominal pain for 3 days	Drinking, smoking, hypertension, head trauma history, epilepsy	No
10	male	42	abdominal pain for 5 hours	Drinking, hypertension	No
11	male	38	abdominal pain for 1 week	Kidney stones	No
12	male	45	abdominal pain for 2 days	smoking	No
13	male	57	abdominal pain for 1 day	no	No
14	male	55	chest and back pain for 6 hours	hypertension	No
15	male	54	abdominal fullness and pain for 8 days	hypertension, gout	Yes, appendicitis and surgery
16	female	48	abdominal pain for 1 day	hypertension, history of uterine fibroids surgery	Yes, Incomplete intestinal obstruction
17	female	55	abdominal pain for 10 days	no	no

TABLE 2. The results of the first laboratory test after entering the emergency department

patient	WBC	RBC	HGB	PLT	NC	LC	BUN	CR	UA	TBIL	TC	TG	HDL	LDL	CK	LDH	CKMB	Mb	ALT	AST	PT	APTT	TT	FIB	INR	FDP	D-dimer
1	5.2	1.27	38	6	3.8	0.9	13.3	112.4	398.1	20.2	2.12	0.77	0.38	1.56	40.5	181	20	30	9.6	30.6	19.5	40.6	17.8	1.07	1.56	14.5	0.84
2	11.5	5.09	149	228	9.7	1.1	5	91.3	398.3	12.6	4.1	0.74	1.36	2.37	61.1	175	17.2	40	18	20.8	12.8	38.6	24.1	4.4	1	2.6	0.22
3	10.6	5.07	157	175	8.1	2	7	78.5	313.3	11.6	6.14	1.94	1.4	4.06	117.6	203	18.9	32.8	44.6	32.3	11.5	29.7	16.3	2.29	0.99	1.3	0.07
4	6.7	4.7	136	105	5.2	0.5	6.7	94	374	9.9	4.56	1.8	1.08	2.95	114	126	10.7	33.4	7.8	15.1	15.6	35.6	19.3	4.3	1.33	1.8	0.12
5	11.8	4.3	144	158	10.8	0.7	3.62	100.5	342.1	8.9	5.06	0.4	1.37	3.01	109.5	201	15.7	38	26.5	23	15.1	30.9	18.1	2.63	1.19	3.3	0.58
6	5	3.9	125	184	3.4	1.1	4.98	70.5	305	9.8	3.1	1.01	0.87	1.94	163.8	164	9.4	12.3	11.7	18.4	13.6	35.3	17.33	3.18	1.07	3.1	0.05
7	14.6	5.24	147	280	13.4	0.7	4.53	66.2	345.1	14.3	6.79	1.1	1.1	4.6	86.2	201	22.3	24.1	17.6	16.4	18.9	37	44.5	0.45	1.5	15.9	1.13
8	5.5	3.4	100	438	3.2	1.6	3.91	56	257.1	11	2.14	1.51	0.77	1.09	10.7	90	7.6	8.2	8	8	13.3	36.6	19.6	2.94	1.04	2.6	0.35
9	6.6	3.97	134	196	4	1.8	3.7	92.1	211.2	28.5	5.45	2.26	0.96	3.69	58.4	169	10.7	23.5	17.3	14	13.4	28.8	17.4	3.51	1.05	3.1	0.13
10	15.1	4.76	160	192	13.6	0.7	3.79	74	453.8	13.2	5.65	1.21	1.21	3.84	140.3	195	13.4	34.2	78.1	47.2	12.7	26.1	20	2.23	0.99	4.2	0.13
11	12.7	4.57	148	361	11	0.8	5.21	67	275.7	24.1	5.12	2.04	0.93	3.6	56.8	245	7.7	17.4	163.3	55.7	14.8	28.7	18.3	5.44	1.16	10.6	1.02
12	12.4	4.72	138	199	10.3	1.3	4.34	66	241.4	14.1	4.39	1.36	0.78	3.18	170.8	165	2.7	26.9	18.3	23.9	12.9	26.3	15.6	3.61	1.12	7.4	0.82
13	5.8	4.51	128	132	4.4	1	6.71	81.8	374	25.4	4.69	0.58	1.88	2.47	66.3	160	8.9	31	8.7	17.1	13.8	35.9	16.8	2.82	1.08	4.6	0.46
14	12.5	4.68	150	237	11	0.9	6.03	75.4	361.5	11.7	5.26	1.26	1.48	3.21	126.6	182	15.6	40.3	14.2	18.8	11.2	21.2	16.2	2.34	0.96	0.6	0.3
15	21.8	3.75	114	259	20.2	1.3	12.59	101	370.3	50.5	3.65	3.3	0.44	2.38	89.7	562	53	65.5	24.6	55.3	14.3	33.6	14	8.84	1.24	6.5	0.54
16	24	4.67	146	216	21.9	0.7	5.63	56.5	166.1	19.3	3.61	0.68	1.3	2.04	120	395	62.5	30	29.2	43.3	17.2	41.8	15.9	5.98	1.36	3.2	0.24
17	4.3	3.52	107	150	2.7	1.3	4.8	78.6	298.6	6.5	6.17	6.38	1.08	3.37	82	205	11.8	24.3	16.4	23	12.4	34.3	15.6	3.71	0.97	2.9	0.19
Mean	10.95	4.242	130.6	206.8	9.218	1.082	5.991	80.11	322.7	17.15	4.588	1.667	1.082	2.904	94.96	212.9	18.12	30.11	30.23	27.23	14.29	33	19.23	3.181	1.148	5.188	0.4229
Std. Deviation	5.773	0.9408	29.31	97.01	5.799	0.4217	2.829	16.24	74.82	10.64	1.347	1.417	0.3789	0.9392	43.56	109.6	15.83	12.83	38.36	14.67	2.366	5.597	6.904	1.439	0.1907	4.48	0.345
Median	11.5	4.57	138	196	9.7	1	5	78.5	342.1	13.2	4.69	1.26	1.08	3.01	89.7	182	13.4	30	17.6	23	13.6	34.3	17.4	3.18	1.08	3.2	0.3

numbers with red color means the number is out of normal range.

with confirmed diagnosis had undergone an abdominal scan and enhancement CT at an earlier stage.

In our study, each patient's laboratory test data was collected, but the routine blood, renal function, liver function, and myocardial enzymology test results did not show obvious abnormalities and could not be used as biomarkers. As ISMAD has superior mesenteric artery dissection, as does AAD, in the process of tearing the dissection to form a true lumen and a false lumen, thrombosis and stenosis will be generated locally. It is well known that coagulation markers such as FDP and D-dimer increase dramatically with excellent sensitivity in AAD [16]. D-dimer is the smallest fibrinolysis-specific degradation product found in circulation, and FDP includes degraded fibrinogen. There is a variable rise in D-dimer level in active disease which indicates increased thrombosis risk. Elevated D-dimer levels following anticoagulation for a thrombotic event indicate increased risk of recurrent thrombosis [9]. In practice, simultaneous measurements of FDP and D-dimer levels are useful for more accurate estimation of hyper fibrinolytic states [17]. However, in the present study, neither D-dimer nor FDP levels were significantly elevated in ISMAD, and the positive rates were also lower than in AAD patients. Thus, D-dimer and FDP levels are of limited value for diagnosing ISMAD. The reason D-dimer and FDP levels were not as elevated as those in AAD might be because of the amount of thrombus in ISMAD is smaller owing to smaller vessel size than the aorta. Our study results were in line with those of Tanaka Y *et al*.'s study [18], which found that FDP and D-dimer levels were only slightly elevated in ISMAD and concluded that the utility of blood examination, especially for FDP and D-dimer levels, for diagnosis of ISMAD is limited.

For ISMAD a conservative or endovascular treatment is used in most patients, which can reduce surgery-related complications, mortality, and costs. Surgical management should be taken up in complicated patients who experience no relief after receiving conservative or endovascular treatment or when there are other compelling indications for surgery, such as complete tearing of the dissection or obvious intestinal necrosis [12]. In our study, we did not follow up the patients after they underwent surgical interventions and only included patients from the emergency department who received analgesia, nutritional supplements, and anticoagulant therapy, based on the advice of vascular surgery doctors.

Our study had several limitations. We only enrolled ISMAD patients who were admitted in our emergency department, only 17 cases. Furthermore, we did not classify ISMAD patients according to specifically superior mesenteric artery CTA since several patients had a general CTA performed in other hospitals. Ours was a retrospective study where we could not obtain the previous CTA information. Finally, we only collected the general data of patients in the emergency department and did not follow up after they were admitted to the vascular surgery ward.

5. Conclusions

In our study ISMAD mostly occurred in middle-aged male patients with known hypertension or active smoking status. Since D-dimer and DFP levels proved to be of limited diagnostic value, an abdominal CT scan should be conducted in patients with unclear abdominal pain at an early stage of their diagnostic workup.

AUTHOR CONTRIBUTIONS

GQH, XML and FJZ designed the study, GQH, XML and AMW collected the data, LPZ and XYM Analyzed the data, GQH and FJZ wrote this manuscript and FJZ revised this manuscript, all authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study protocols were approved by the ethics committee (No.202012198) of Xiangya Hospital of Central South University and complied with the Declaration of Helsinki.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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