Factors Associated with Failed Conservative Management in Symptomatic Isolated Mesenteric Artery Dissection

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WHAT THIS PAPER ADDS

Isolated mesenteric artery dissection (IMAD) is an uncommon but potentially catastrophic condition with variable and unpredictable outcomes. This condition is generally treated successfully by conservative management. Factors that may be associated with the failure of conservative management in patients with symptomatic IMAD have not been explored previously. The results of this study indicate that the risk factors for failed conservative management are type II IMAD (as defined by the Sakamoto classification: meaning that there is an entry tear, but no re-entry, and still no false lumen thrombosis), and ≥90% luminal stenosis.

Objective: The aim of this study was to assess factors associated with conservative management failure in patients with symptomatic isolated mesenteric artery dissection.

Methods: Patients with symptomatic isolated mesenteric artery dissection who underwent conservative therapy as first line treatment between February 2010 and May 2018 were included in this retrospective study. Conservative management failure was defined as the persistence or aggravation of symptoms and signs, increasing aneurysmal dilation, or new appearance of a dissecting aneurysm after conservative management. Univariable and multivariable analyses were performed to identify risk factors for failure of conservative management.

Results: A total of 123 patients (115 men, 8 women, mean age, 53.7 ± 6.1 years) were included in this study. Conservative management was successful in 89 (72.4%) patients but failed in the remaining 34 (27.6%) patients. Of the 89 for whom conservative management was successful, all of the symptoms were eliminated ($n = 81$) or relieved ($n = 8$) within 3.8 ± 0.7 days after conservative management. All of the 34 patients in whom conservative management failed underwent successful endovascular stenting. Failure of conservative management was associated with type II IMADs as defined by the Sakamoto classification (meaning that there is an entry tear, but no re-entry, and still no thrombosis of false lumen, odds ratio: 33.76; 95% confidence interval 8.65—131.85; $p < .001$) and with ≥90% luminal stenosis (odds ratio 40.70; 95% confidence interval: 3.76—440.07; $p < .01$).

Conclusions: Conservative management can be used successfully in most patients with symptomatic isolated mesenteric artery dissection. Risk factors for failed conservative treatment were type II IMADs and degree of luminal stenosis ≥90%.

Keywords: Mesenteric artery, Dissection, Management
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INTRODUCTION

Isolated mesenteric artery dissection (IMAD) is an uncommon but potentially catastrophic pathology with variable and unpredictable outcomes.[1,2] Most patients with IMAD are symptomatic (74%), with abdominal pain reported as the most common symptom (91%).[2,3] Although most cases of symptomatic IMAD resolve completely with conservative management, cases progressing to aneurysmal rupture, intestinal necrosis, and even patient death have been reported.[4—6] However, factors that may be lead to the failure

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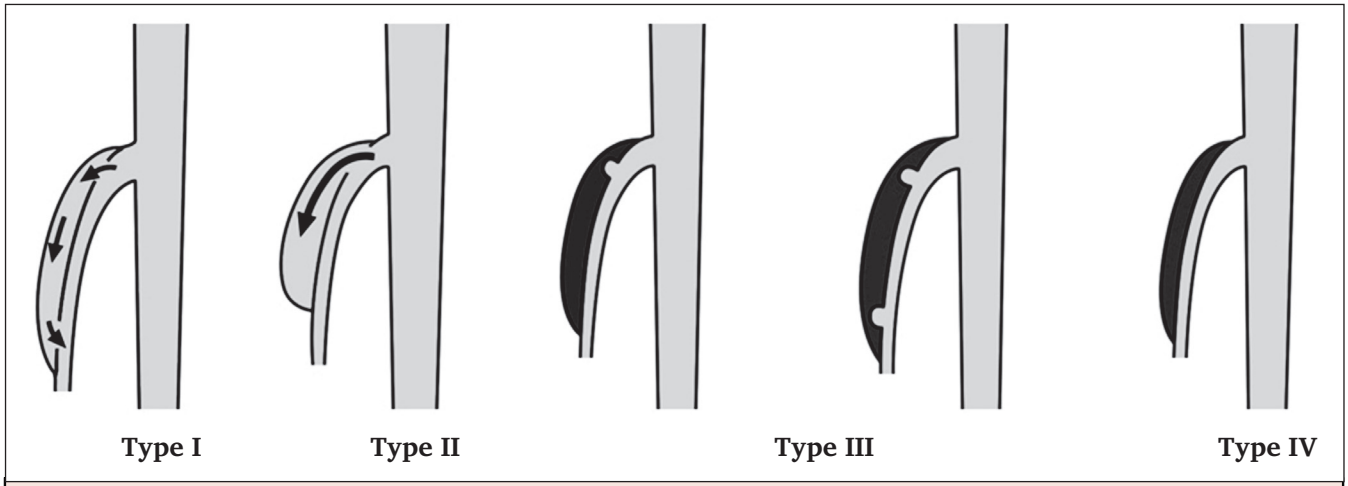

Figure 1. Sakamoto classification of isolated mesenteric artery dissection.[7] Type I: dissecting aneurysm with entry and re-entry tears; Type II: dissecting aneurysm without re-entry tear; Type III: thrombosed false lumen with an ulcer like projection; Type IV: occlusion of false lumen without ulcer like projection.

of conservative management in these patients have not been explored previously.

In this retrospective study, the aim was to evaluate factors that may be associated with failed conservative management in patients with symptomatic IMAD.

METHODS

Patients

This study was approved by all participating Institutional Review Boards with an informed consent waiver (2018KY023-01). Consecutive patients who were diagnosed with symptomatic IMAD (i.e., the presence of symptoms at the time of IMAD diagnosis) on contrast enhanced computed tomography (CT) scans and who underwent conservative therapy as first line treatment between February 2010 and May 2018 were included in this study. Patients who underwent other therapies (e.g., surgical treatment, endovascular stenting) as first line treatment, those who were asymptomatic, and those who were lost to follow up were excluded. Patient demographics and clinical information were collected from patients' medical records.

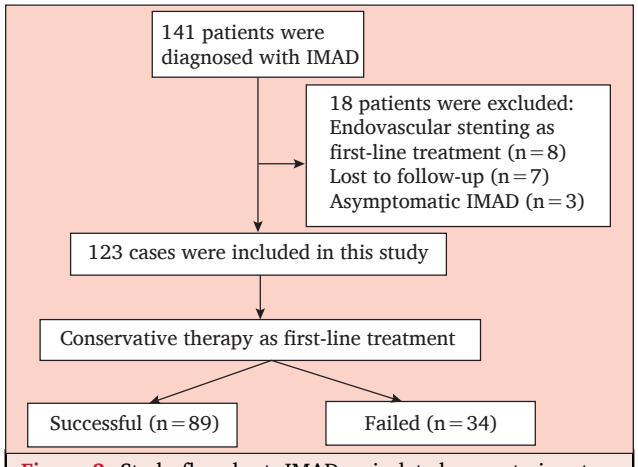

Figure 2. Study flowchart. IMAD = isolated mesenteric artery dissection.

Radiologic types of IMADs

The Sakamoto classification was used to identify the types of IMAD among study patients (Fig. 1).[7] The Sakamoto system is based on CT findings and describes IMADs as type I (dissecting aneurysm with entry and re-entry tears), type II

Table 1. Baseline characteristics of study patients (n = 123).

Characteristic	n (%) or median (IQR)
Age - years	54 (9)
Sex	
Female	8 (6.5)
Male	115 (93.5)
History of hypertension	31 (25.2)
Symptoms	
Abdominal pain	123 (100)
Nausea/vomiting	13 (10.6)
Back pain	6 (4.9)
Isolated mesenteric artery dissection	
Superior mesenteric artery dissection	123 (100.0)
Inferior mesenteric artery dissection	0 (0)
Dissecting aneurysm	
Yes	39 (31.7)
No	84 (68.3)
Diameter of dissecting aneurysm - mm	5.3 (2.1)
Radiological type of IMAD	
Type I	3 (2.4)
Type II	36 (29.3)
Type III	8 (6.5)
Type IV	76 (61.8)
Branch vessel involvement	
Yes	45 (36.5)
No	78 (63.5)
True lumen stenosis	
≥ 90%	21 (17.1)
< 90%	102 (82.9)

IMAD = isolated mesenteric artery dissection; IQR = interquartile range.

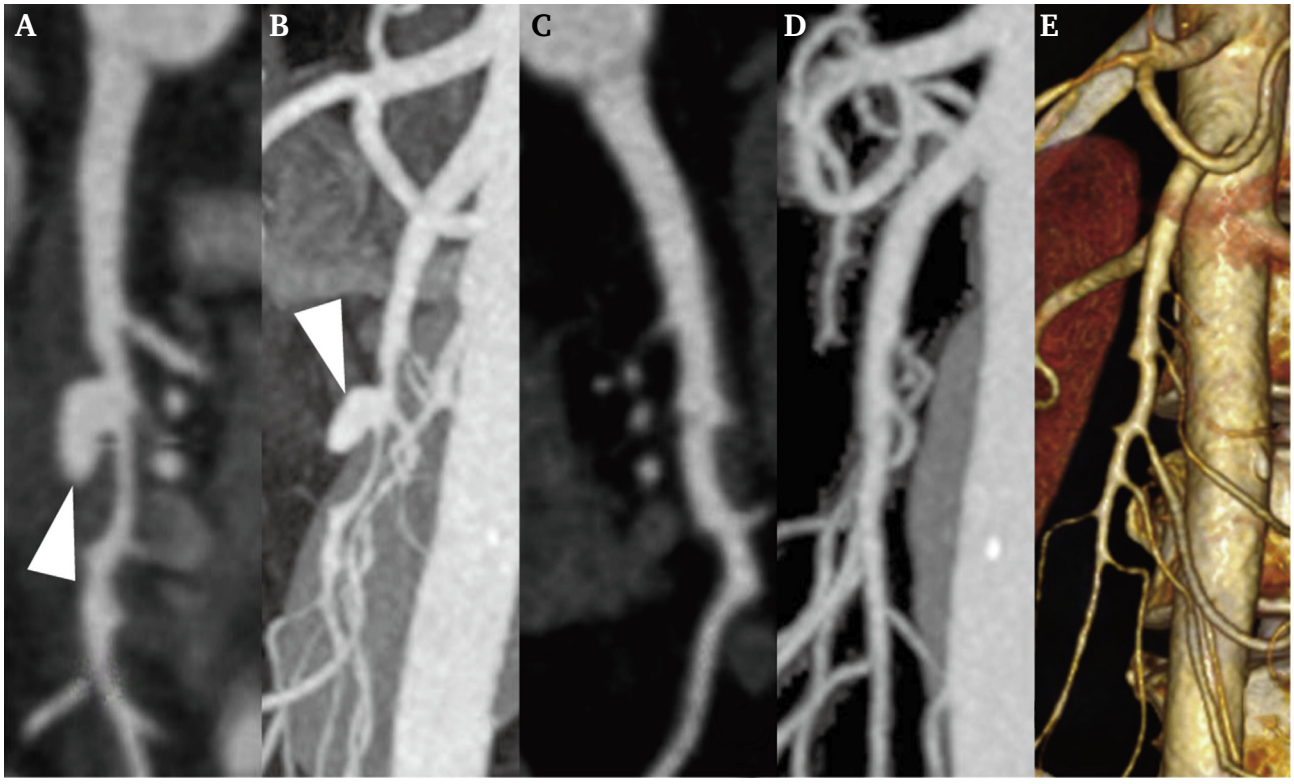

Figure 3. Conservative management was successfully used in a patient with type II symptomatic isolated superior mesenteric artery dissection aneurysm. A 53 year old man presented with acute abdominal pain that had lasted for three days. (A,B) A dissecting aneurysm was observed on contrast enhanced computed tomography (CT) images (arrowhead). (C–E) Complete remodelling of the superior mesenteric artery occurred after conservative management, as shown on a contrast enhanced CT scan performed six months later.

(dissecting aneurysm without re-entry tear), type III (thrombosed false lumen with an ulcer like projection), or type IV (occlusion of false lumen without ulcer like projection).

Management

Treatment decisions were based on patient symptoms and on the morphological characteristics of the IMAD on CT scan. Surgical treatment was used in patients with artery rupture and/or bowel necrosis. Endovascular stenting was used as first line treatment in patients with symptomatic IMAD with a large dissecting aneurysm (defined as an aneurysm diameter $\geq$ 1.5 times larger than the normal mesenteric artery diameter) and without a re-entry tear. These patients were excluded from the study. The remaining patients underwent conservative management as first line treatment; this management consisted of fasting, pain control, strict blood pressure control ($\leq$120/80 mmHg), and the intravenous administration of a vasodilator (Salvia miltiorrhiza, 8 mL/d). Failure of conservative treatment was defined as the persistence or aggravation of symptoms and signs, increasing aneurysmal dilation, or new appearance of a dissecting aneurysm after treatment. Patients in whom conservative treatment failed were considered candidates for endovascular stenting as second line treatment. Patients considered eligible for this second line treatment had a dissecting aneurysm diameter $\geq$1.5 times larger than the normal mesenteric artery diameter and no re-entry tear. The interval between diagnosis and stenting depended on each patient's symptoms. If patients have severe abdominal pain or bloody stools without relief after conservative management, the interval should be short to prevent intestinal necrosis; otherwise, the interval should be more than a week.

Follow up

Clinical follow up was scheduled for the first and sixth months after discharge and annually thereafter until complete remodelling of the mesenteric artery had occurred. For the patients who underwent endovascular stenting, clinical follow up was scheduled every 2–3 years after complete remodelling of the mesenteric artery had occurred. More frequent evaluations were performed when needed. During follow up, abdominal contrast enhanced CT scans were performed to assess the status of the IMAD and/or stent patency (Doppler sonography was performed in only one centre; follow up consisted of CT angiography in all study patients).

Imaging analysis

IMAD changes on CT were assessed and compared with the initial CT findings. Image interpretation focused on the morphological characteristics of the IMAD, including the presence of a dissecting aneurysm (defined as a dissection with aneurysm formation and with dissecting aneurysm diameter or length larger than the normal mesenteric artery

diameter), the presence of entry and re-entry tears, the presence of a thrombosed false lumen with an ulcer like projection, the presence of branch vessel involvement, and the degree of luminal stenosis. The degree of luminal stenosis was measured using the diameter of the unaffected mesenteric artery orifice and the diameter of the true lumen at the site of maximum stenosis and was classified as either ≥90% or <90%. All images were analysed separately by two independent radiologists.

Factor analysis

Uni- and multivariable analyses were used to assess factors that may be associated with the failure of conservative treatment. Patient sex, age, history of hypertension, radiological type of IMAD, presence of branch vessel involvement, and degree of luminal stenosis were chosen as potential factors associated with treatment failure.

Statistical analysis

Interobserver agreement values for the evaluation of the radiological type of IMAD and presence of branch vessel involvement were calculated using the percentage agreement between observers. Interobserver reproducibility for the evaluation of degree of luminal stenosis was analysed by Cohen's Kappa (κ) coefficient. A κ value of 0.0 or less was considered to represent poor agreement; 0.01—0.20, slight agreement; 0.21—0.40, fair agreement; 0.41—0.60, moderate agreement; 0.61—0.80, sufficient to good agreement; and 0.81—1.00, near perfect agreement. Factors associated with the failure of conservative treatment were assessed using univariable logistic regression analysis. Factors that were determined to be statistically significant ($p < .05$) in the univariable analysis were included in the multivariable analysis. Results are presented as odds ratios (OR) and 95% confidence intervals (CI). All statistical analyses were performed with SPSS version 17.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Patients

From February 2010 to May 2018, 141 patients were diagnosed with IMAD; in all of these patients, the dissections occurred in the superior mesenteric artery. Of these 141 patients, 18 (12.8%) were excluded because they underwent endovascular stenting, as first line treatment ($n = 8$), were lost to follow up ($n = 7$), or had asymptomatic IMAD ($n = 3$) (Fig. 2). No patients underwent surgical treatment. The remaining 123 (87.2%) symptomatic patients (115 men and 8 women; mean age, 53.7 ± 6.1 years; range, 35—75 years) underwent conservative therapy as first line treatment and were included in this study. Of these 123 patients, 2.4% (3/123) had type I IMAD, 29.3% (36/123) had type II, 6.5% (8/123) had type III, and 76 (61.8%) had type IV (Table 1). Branch vessel involvement and true lumen stenosis ≥90% were seen in 36.5% (45/123) and 17.1% (21/123) of patients, respectively. Of the 21 patients with true lumen stenosis ≥90%, the true lumen was compressed by a dissecting aneurysm in 19 patients and by a thrombosed false lumen in two patients.

Interobserver variability

Observers 1 and 2 recorded the same number of cases for each radiological subtype and for the presence of branch vessel involvement. Interobserver agreement for the degree of luminal stenosis was sufficient to good ($\kappa = 0.78$, concordance 93%).

Clinical outcomes

Conservative management was successful in 89/123 (72.4%) patients (Fig. 3); conservative management was considered to have failed in the remaining 34 (27.6%) patients due to stability of the dissecting aneurysm (type II) without relief of abdominal pain ($n = 15$), progression of the dissecting aneurysm (type II; $n = 14$), or new appearance of dissecting aneurysm ($n = 5$) (Fig. 4). Of the 89 patients in whom conservative treatment was successful, all of the symptoms were eliminated ($n = 81$) or relieved ($n = 8$) within 3.8 ± 0.7 days after conservative treatment. All of the 34 patients in whom conservative management failed underwent successful endovascular stenting. In these patients, the intervals between the diagnosis of IMAD and stenting were 5.5 ± 2.0 days (range 3—10 days) for 15 patients without relief of abdominal pain and 42.4 ± 9.4 days (range 35—70 days) for 19 patients with dissecting aneurysm progression ($n = 14$) or with new appearance of a dissecting aneurysm ($n = 5$). In the 15 patients with persistent abdominal pain before stenting, all of the symptoms were resolved within 2.4 ± 0.6 days after stenting. No patients experienced aneurysmal rupture, intestinal necrosis, or death.

Factors associated with failure of conservative management

Of the six factors analysed with a logistic regression model, univariable analysis identified two factors significantly associated with failure of conservative treatment: type II IMAD (OR 67.94; 95% CI 20.00—230.89; $p < .001$) and degree of luminal stenosis ≥90% (OR 125.71; 95% CI 15.61—1012.38; $p < .001$) (Table 2). Multivariable analysis confirmed the significant association of both of these factors with failure of conservative treatment (type II IMAD, OR 33.76; 95% CI 8.65—131.85; $p < .001$; degree of luminal stenosis ≥90%, OR 40.70; 95% CI 3.76—440.07; $p < .01$).

DISCUSSION

In this study, it was found that conservative management was successful in 72.4% of patients with symptomatic IMAD. Failure of conservative management was associated with type II IMADs (presence of a dissecting aneurysm without a re-entry tear) and a degree of luminal stenosis ≥90%.

Although most cases of IMAD can be managed successfully conservatively according to European Society for Vascular Surgery (ESVS) guidelines, approximately 20% of

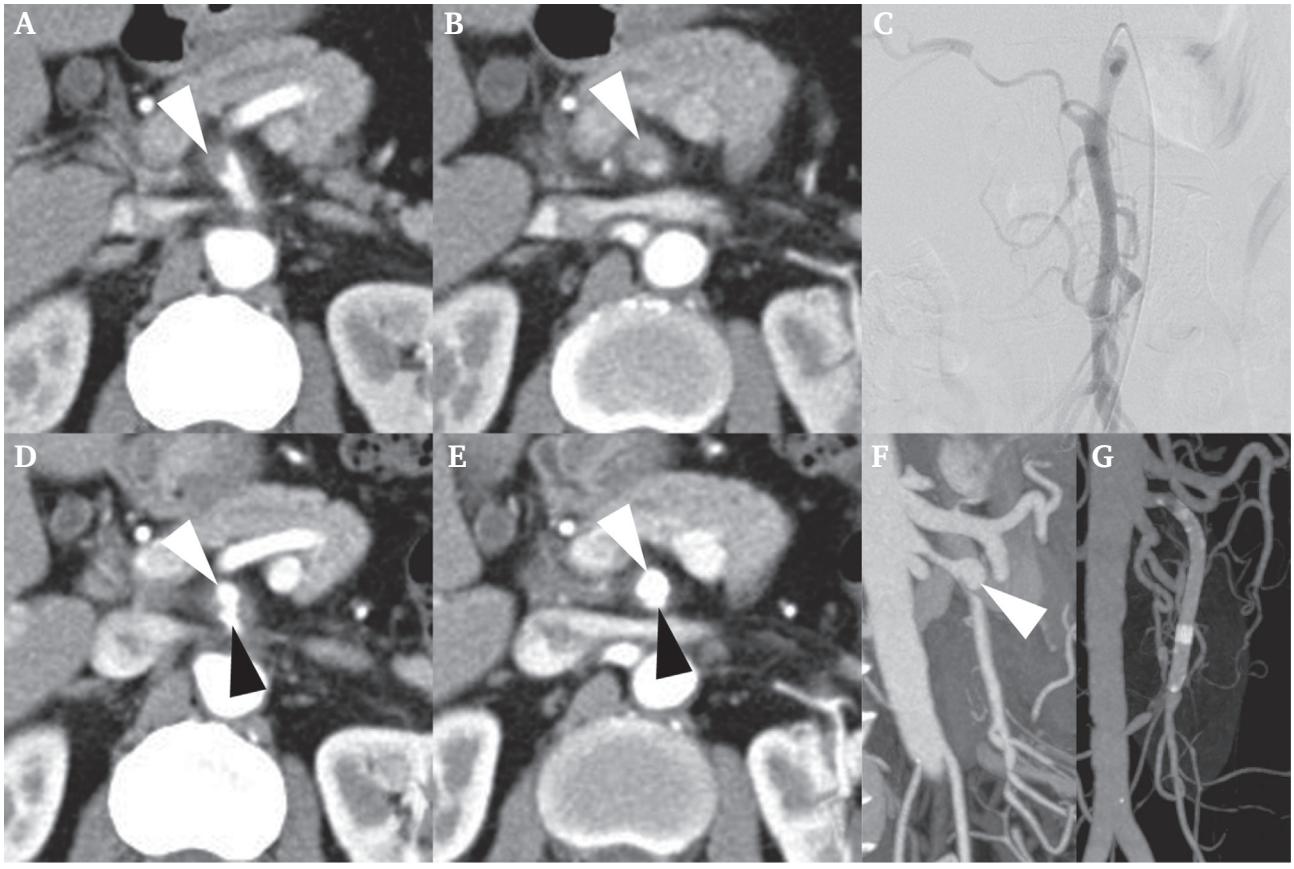

Figure 4. Example of failed conservative management of an isolated mesenteric artery dissection with development of a dissecting aneurysm (Sakamoto type III). A 47 year old man presented with acute abdominal pain that had lasted for 12 h. (A,B) Cross sectional computed tomography (CT) showed a thrombosed false lumen (arrowhead). (**C**) Superior mesenteric angiography demonstrated that the true lumen was compressed, and there was no dissecting aneurysm. (D,E) Cross sectional CT performed one month later showed a dissecting aneurysm (white arrowhead) and the true lumen (black arrowhead). (F) Multiplanar reconstruction showed a dilated dissecting aneurysm (arrowhead) with severe stenosed true lumen (≥90%). The dissecting aneurysm was dilated to distal branches of the superior mesenteric artery three days later (not shown), and endovascular stenting was performed. (G) Complete resolution of the dissecting aneurysm had occurred six months after the procedure.

patients ultimately need intervention.[2] In a previous study of clinical outcomes in 721 patients with IMAD, Kimura et al.[1] found that 82.1% of patients underwent conservative management as first line treatment; conservative management failed in 18.1% of these patients, and additional treatment was needed. Heo et al.[8] similarly observed a 20% failure rate for conservative management as first line treatment for patients with IMAD regardless of radiological type. In the current study, conservative management was successful in 72.4% of patients, a lower rate than has been reported previously.[1,9–13] The high conservative management failure rate in this study may have been related to the inclusion of patients with symptomatic IMAD only, as previous research has shown that conservative management is more likely to fail in patients with symptomatic IMAD.[14]

Endovascular stenting using bare stents alone or stent assisted coiling has been used successfully in the treatment of symptomatic patients with IMAD.[15] In this study, all 34 patients in whom conservative management failed underwent successful endovascular stenting, and all of the symptoms were resolved within 2.4 ± 0.6 days after treatment. These results suggest that endovascular stenting is an effective procedure for patients with symptomatic IMAD in whom conservative management failed.

This study suggests that the presence of a dissecting aneurysm without a re-entry tear (type II) is a risk factor for the failure of conservative treatment. Dissecting aneurysms are common in patients with IMAD, and these aneurysms may rupture by dilation or compress the true lumen.[4] This risk of aneurysmal degeneration is widely cited as the main indication for long term surveillance in patients with IMAD. Aneurysmal diameter enlargement has been noted in both asymptomatic and symptomatic patients, despite differing management strategies.[16] In this study, although no dissecting aneurysm ruptures occurred, the true lumen was severely compressed (≥90%) by a dissecting aneurysm without a re-entry tear in 19 patients. Progression of the dissecting aneurysm occurred in 14 patients, and new appearance of dissecting aneurysm occurred in five patients. These results suggest that a dissecting aneurysm without a re-entry tear can lead to luminal stenosis and intestinal ischaemia; therefore, the presence of a dissecting aneurysm without a re-entry tear appears to be a risk factor for failed conservative management.

Table 2. Results from bi- and multivariable analyses in 123 patients presenting with isolated mesenteric artery dissection.

Factors	Conservative management failure (univariable analysis)		Conservative management failure (multivariable analysis)	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Sex	–	–	–	–
Age	1.4 (0.94–1.11)	.82	–	–
History of hypertension	2.2 (0.65–7.31)	.26	–	–
Type of IMAD				
Type I	–	–	–	–
Type II	67.9 (20.00–230.89)	<.001	33.8 (8.65–131.85)	<.001
Type III	1.6 (0.37–7.21)	.52	–	–
Type IV[a]	0.01 (0.00–0.05)	<.001		
Branch vessel involvement (presence vs. absence)	0.4 (0.17–1.12)	.09	–	–
Degree of luminal stenosis (≥90% vs. < 90%)	125.7 (15.61–1012.38)	<.001	40.7 (3.76–440.07)	<.01

OR = odds ratio; CI = confidence interval.
[a] Type IV is a protective factor and was not included in the multivariable analysis.

This study also found that a degree of luminal stenosis ≥90% is a risk factor for failed conservative treatment. Severe luminal stenosis (≥90%) can lead to intestinal ischaemia or even intestinal necrosis.[17] Although there is collateral circulation between the mesenteric arteries and coeliac artery, most IMADs are cases of acute disease, and the formation of the collateral circulation requires time. Additionally, patients with symptomatic IMAD demonstrate increased inflammation and thrombus on diagnostic imaging with a trend toward increased stenosis when compared with asymptomatic patients.[10] In the current study, all patients had symptomatic IMAD, and conservative management was considered to have failed in the 15 patients with a degree of luminal stenosis ≥90% due to no relief in abdominal pain caused by intestinal ischaemia. These results suggest that a degree of luminal stenosis ≥90% is another risk factor for the failure of conservative management.

Limitations of this study include its retrospective nature. In addition, because of the rarity of IMAD this study is limited by its small sample size, however it remains one of the largest patient cohorts to be reported in the literature to date and is the first study to analyse factors associated with conservative treatment failure in patients with symptomatic IMAD. The morphological characteristics of IMAD were determined by CT rather than by mesenteric angiography. Additionally, the degree of luminal stenosis was difficult to determine precisely because of the tiny size of the true lumen, which may have biased the results. Finally, although Doppler ultrasound evaluation is useful in obtaining haemodynamic parameters, most of the study patients did not undergo this imaging assessment.

In conclusion, conservative management was successful in most patients with symptomatic IMAD. Risk factors for failed conservative treatment were type II IMAD (presence of a dissecting aneurysm without a re-entry tear) and a degree of luminal stenosis ≥90%. In the light of these findings, determining the type of IMAD and degree of luminal stenosis before the initiation of treatment may be useful in therapeutic decision making, as patients with a type II IMAD and a degree of luminal stenosis ≥90% may not benefit from conservative management.

CONFLICT OF INTEREST

None.

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COUP D'OEIL

Delayed Femoral Embolism of Biological Glue Following the Repair of Type a Aortic Dissection

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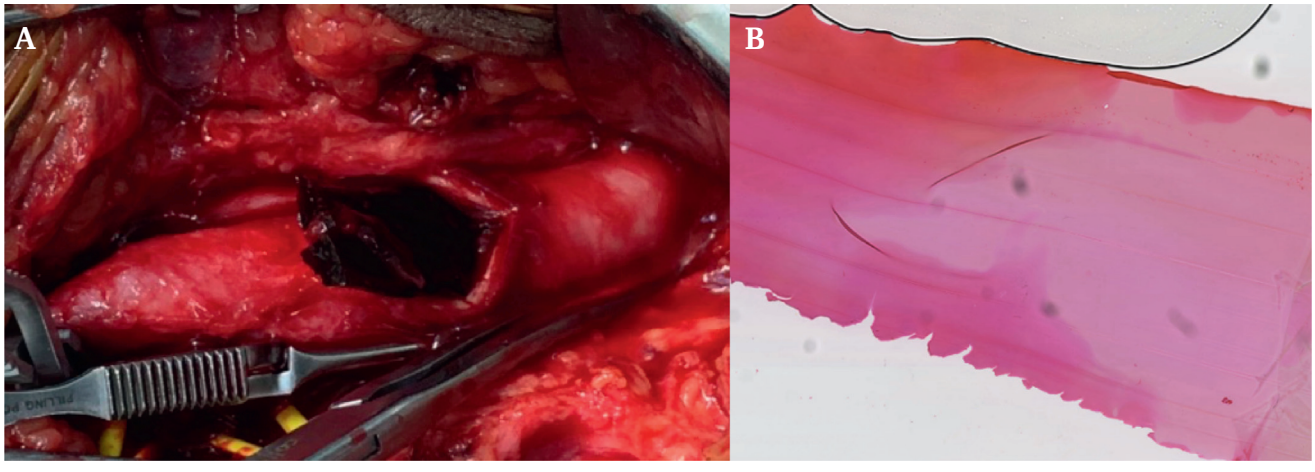

A 56 year old patient was referred with a diagnosis of acute left lower limb ischaemia. A month before, he had been treated successfully for acute type A aortic dissection. The false lumen had then been obliterated by Bioglue (Cryolife International, Kennesaw, GA, USA) injection between the dissected layers. Under general anaesthesia, the common femoral artery was explored and foreign material extracted from the posterior wall of the artery (panel A). Supplementary thrombo-embolectomy with a Fogarty catheter restored satisfactory distal arterial flow. Histopathological analysis confirmed that the embolic material extracted was indeed biological glue (panel B).

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