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Mid-Term Results of Endovascular Treatment for Spontaneous Isolated Dissection of the Superior Mesenteric Artery

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WHAT THIS PAPER ADDS

Endovascular treatment (EVT) has favourable short-term outcomes for spontaneous isolated dissection of the superior mesenteric artery (SIDSMA). However, evidence for this comes mainly from case reports and cohort studies with small patient numbers. This study, including 128 patients with up to five year follow up, showed that EVT was associated with a satisfactory superior mesenteric artery remodelling rate and stent patency. The cumulative event free survival rate in patients with stents was also superior to that in patents without stents, indicating that EVT could be an effective approach for SIDSMA.

Objectives: Endovascular treatment (EVT) is an alternative method to treat spontaneous isolated dissection of the superior mesenteric artery (SIDSMA). Although its short-term results are promising, few mid-term results have been reported. This study reports the five year follow up of EVT for SIDSMA.

Methods: A total of 128 consecutive patients with SIDSMA admitted to the study hospital between 2011 and 2016 were enrolled in this retrospective study. Their demographic information, clinical findings, EVT outcomes, and follow up results were analysed.

Results: Conservative treatment and pre-operative preparation were given immediately after admission, then digital subtraction angiography was performed. Stents were deployed in 112 out of 128 patients. The 16 patients who did not receive stents then continued conservative treatment. Peri-procedural complications occurred in three patients, including one death and two pseudoaneurysms at puncture sites. Mean follow up was 29.7 months (range 6–60 months) in patients with stents and 31.4 months (range 14–45 months) in patients without stents. During follow up, the overall complete remodelling rate in the stent group was 88.3%. Most took place within three months of stenting. The cumulative primary stent patency rate was 99.1%, and the cumulative event free survival rate was 99.0%, 95.8%, and 95.8% at one, three, and five years in patients with stents, compared with 62.5% at both one and three years in patents without stents ($p < .001$).

Conclusions: EVT for SIDSMA is clinically successful. The event free survival rate, primary patency, and complete remodelling are satisfactory during mid-term follow up. Endovascular treatment is an effective approach for SIDSMA.

Keywords: Spontaneous isolated dissection of the superior mesenteric artery, Endovascular treatment, Remodelling
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INTRODUCTION

Spontaneous isolated dissection of the superior mesenteric artery (SIDSMA), without associated aortic dissection, remains a rare condition. However, an increasing number of case reports and retrospective studies have been published recently because of the development and popularisation of computed tomography (CT), which suggests that the incidence of this disease might have been underestimated previously.[1,2] It can be an occasional incidental CT finding, and no treatment may be needed. Alternatively, onset of this disease often presents as acute abdominal pain and can progress to arterial rupture, occlusion, or bowel necrosis. Several classifications of SIDSMA have been proposed, but none covers all anatomical types of this disease. Treatment options usually include conservative, surgical, or endovascular treatments,[3] but there is no consensus on first line management strategy. Open surgical repair usually takes place when bowel resection is indicated. Conservative management as initial treatment has been reported more frequently, with the symptom relief rate ranging from 66.8% to 86.6% in recent published reviews.[1,2,4] It may take several days to evaluate effects, thus there may be severe

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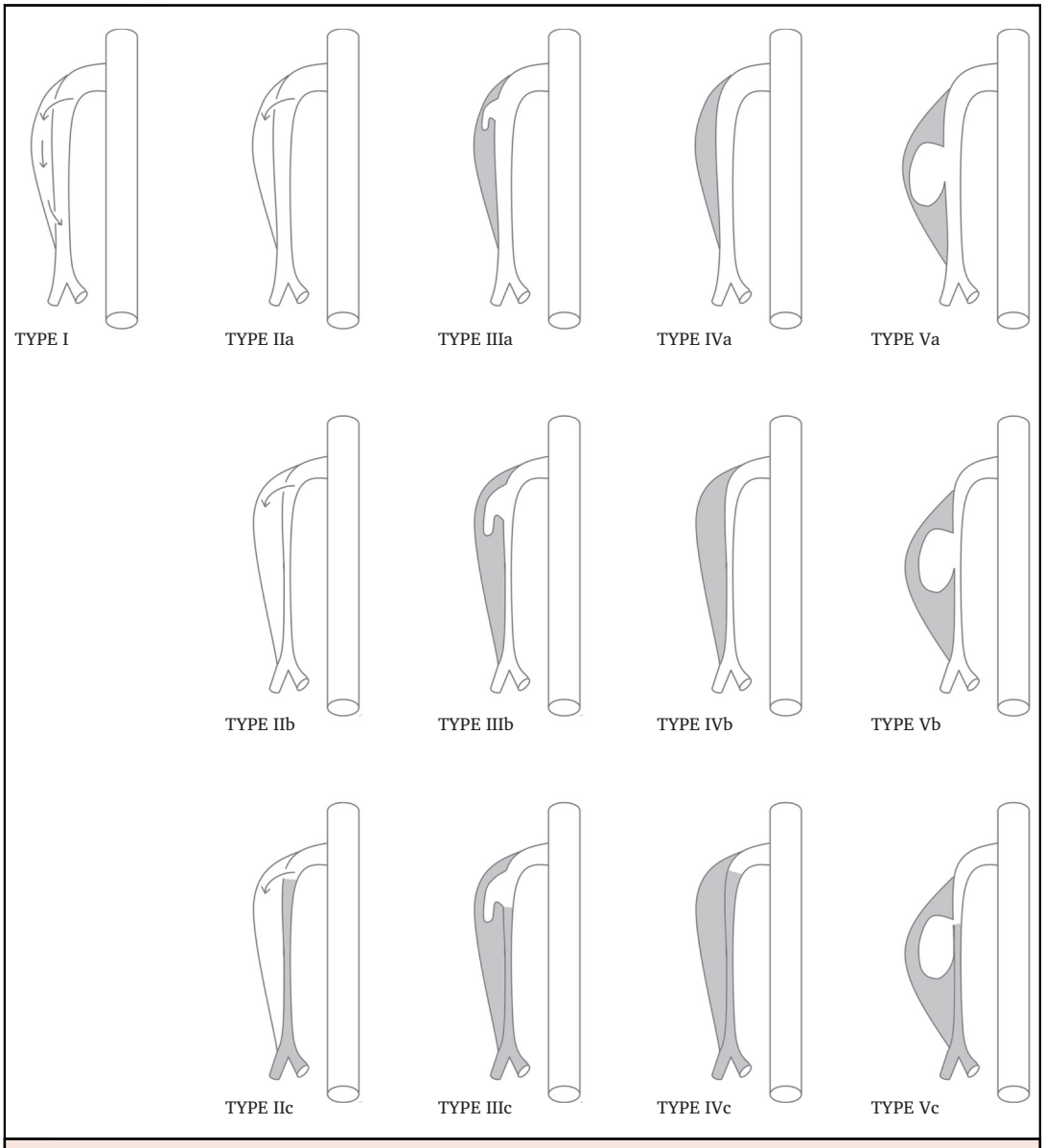

Figure 1. Morphologic classification of spontaneous isolated dissection of the superior mesenteric artery (SIDSMA). Type I, patent false lumen with both entry and re-entry; type II, "cul-de-sac" shaped false lumen without re-entry (subdivided into IIa, patent true lumen; IIb, severe stenosis of the true lumen; and IIc, occlusion of the true lumen); type III, thrombosed false lumen with an ulcer like projection (ULP) (subdivided into IIIa, patent true lumen; IIIb, severe stenosis of the true lumen; and IIIc, occlusion of the true lumen); type IV, completely thrombosed false lumen without an ULP (subdivided into IVa, patent true lumen; IVb, severe stenosis of the true lumen; and IVc, occlusion of the true lumen); and type V, dissecting aneurysm (subdivided into Va, patent true lumen; Vb, severe stenosis of the true lumen; and Vc, occlusion of the true lumen). Types I, IIa, IIIa, IVa, and Va were considered to be patent true lumen flow whereas types IIb, IIc, IIIb, IIIc, IVb, IVc, Vb, and Vc were considered to be true lumen stenosis and occlusion.

consequences for those in whom conservative methods fail, and additional treatments will be needed. During follow up the complete remodelling rate varies from 15.2% to 64%,[5–8] resulting in concerns over recurrent of symptoms in the long term. Endovascular treatments provide approximately 95% symptom relief,[1] but the long-term stent patency and remodelling rate remain unclear.

Therefore, essential issues when determining optimal treatment are effectiveness of symptom relief and follow up prognosis such as high complete remodelling rate and good patency if stents are placed. In this study, the efficacy and follow up results of endovascular treatments for SIDSMA were assessed, and an updated classification is proposed, with the goal of addressing the issues mentioned above.

MATERIALS AND METHODS

Study population

This retrospective study included 128 consecutive patients with SIDSMA at the study hospital, First Affiliated Hospital,

School of Medicine, Zhejiang University, between August 2011 and October 2016. The follow up closing date for all patients was July 2017. The diagnosis of SIDSMA was made from findings on spiral computed tomography angiography (CTA), such as an intimal flap in the superior mesenteric artery (SMA) and/or thrombosis of the false lumen. In addition, diameters of the normal proximal and distal parts of the SMA lesions as well as the length of the lesion and other relevant information were collected. The morphological classification of CTA findings was adopted with a minor modification from a previous publication.[9] In brief, SIDSMA was categorised into five types (Fig. 1): type I, patent false lumen with both entry and re-entry; type II, "cul-de-sac" shaped false lumen without re-entry; type III, thrombosed false lumen with an ulcer like projection (ULP); type IV, completely thrombosed false lumen without an ULP; and type V, dissecting aneurysm. Types II, III, IV, and V have three subtypes: subtype a, patent true lumen; subtype b, severe stenosis of the true lumen; and subtype c, occlusion of the true lumen. Types I, IIa, IIIa, IVa, and Va are considered to be patent true lumen flow and types IIb, IIc, IIIb, IIIc, IVb, IVc, Vb, and Vc are considered to be true lumen stenosis and occlusion. Patients with concomitant aortic dissection, coeliac dissection, vasculitis, or recent abdominal operation or trauma were excluded from this study. Demographic information, imaging features, treatment modalities, and follow up records including stent patency and SMA remodelling data were collected. Complete remodelling was defined as the absence of residual arterial dissection with no SMA stenosis and total thrombosis of false lumen on the follow up CTA. Incomplete remodelling was defined as improved true luminal patency of the SMA compared with pre-operative status. The false lumen was narrowed but not fully thrombosed. An aneurysm was defined as a focal SMA diameter increase of $>$50% compared with normal adjacent SMA.

Treatment strategies

Conservative treatments and pre-operative preparations including combinations of blood pressure control, fasting, bowel rest, and parenteral nutritional support with anticoagulation were given immediately. Then, on the next available operating day irrespective of symptomatic control, patients were sent to the catheter laboratory for digital subtraction angiography (DSA) under local anaesthesia. The time delay between admission and digital subtraction angiography examination usually was 2—3 days (mean 2.3 days, range 1—4 days). During the endovascular treatment (EVT), a femoral or brachial approach was used. A 6F vascular sheath was inserted via the puncture site and a bolus of 5000IU heparin was injected. Then, selective superior mesenteric arterial angiography was performed via a 5F MPA multifunction catheter (Cordis, Miami Lakes, USA), based on which the morphological classification was checked and the distal stent landing zone was ascertained. For patients with type I, IIa, IIIa, IVa, and Va (patent true lumen), the pros and cons of stent deployment and solely conservative treatments were explained to the patient, and their wishes were followed. For the remaining types, stent implantation was recommended. If stents were to be deployed, a 0.018 in guide wire (V18, Boston Scientific, Marlborough, USA) was used for recanalisation of the true SMA lumen, and bare self expanding stents were deployed with the proximal end extending beyond the ostium of the SMA into the aorta. In addition, coil embolisation was employed in patients with type V and some with type II and III if the false lumen and/or entry tear were overwhelmingly large. Finally, DSA was repeated to examine the improvement of distal blood supply. After the stents were deployed successfully, low molecular weight heparin (100U/kg, twice a day) was used for three days for anticoagulation, and aspirin was continued indefinitely. For those patients who did not receive stents, conservative treatments continued. For follow up, CTA was repeated at three, six and 12 months and yearly afterwards, and relevant information was also collected at these time points.

Statistical analysis

Statistical analysis was performed with the Student *t* test, chi-square test, or Fisher's exact test. The cumulative event free survival rate and cumulative primary patency were calculated using a Kaplan—Meier curve generated with GraphPad Prism (5.0v; GraphPad Software Inc, La Jolla, USA). Events included recurrent abdominal pain, aneurysm formation, new dissection, death, and SMA occlusion if it was patent at the beginning of follow up. A figure for the overall complete remodelling rate was also generated by this software. The follow up index was calculated describing follow up completeness at a given study end date as the ratio between the investigated and the potential follow up period.[10] A p value of $<$ .05 was considered to be statistically significant.

RESULTS

A total of 128 patients were enrolled in this retrospective study. Their demographic information and other relevant data are summarised in Table 1. The mean patient age was 53.5 years old (range 34—72 years). Most patients were male, and presented with abdominal pain. Hypertension was the most common comorbidity. Six patients were asymptomatic and had incidental SIDSMA diagnoses on contrast CT. Abdominal pain was the most prominent symptom in SIDSMA and accounted for all symptomatic patients. Other symptoms included nausea (eight patients), vomiting (five patients), and haematochezia (one patient). There was no intestinal infarction or necrosis. The mean dissection length was 6.2 cm.

All patients received conservative treatments and pre-operative preparation as soon as their diagnosis of SIDSMA was suspected. Severe pain re-occurred in three patients, even though symptoms had previously been relieved and they were under strong conservative management. One patient with type IIIb progressed to IIIc one day after admission (Fig. S1). The other two patients

Table 1. Characteristics of patients treated for spontaneous isolated dissection of the superior mesenteric artery

Variable	Patients (n = 128)
Male	112 (87.5)
Mean age (range) − y	53.5 (34–72)
Median time before admission (range) − d[a]	5.0 (0.3–90)
Smoking	41 (32.0)
Comorbidities	
Hypertension	49 (38.3)
Diabetes	5 (3.9)
Hyperlipidaemia	7 (5.5)
Asymptomatic patients	6 (4.7)
Symptomatic patients	122 (95.3)
Symptoms	
Abdominal pain	122 (95.3)
Haematochezia	1 (0.8)
Nausea	8 (6.3)
Vomiting	5 (3.9)
Bowel infarction	0 (0)
Mean dissection length − cm	6.2

Data is given as n (%) unless otherwise stated.
[a] Time delay between the onset of symptoms and admission to the department.

requested conservative management and voluntarily declined DSA when their diagnoses of SIDSMA were suspected. CTA was repeated after abdominal pain re-occurred, showing that one patient with type IVa had progressed to type Vc in six days (Fig. S2), with the other patient progressing from type IVa to IVb in 10 days (Fig. S3). Emergency endovascular treatments were performed in all three cases, and their symptoms were relieved. The morphological classification via CTA is summarised in Table 2. For the three patients mentioned above, this is the classification after the condition had deteriorated.

DSA data are summarised in Table 3. All patients were sent to the catheter laboratory for DSA, and stents were successfully implanted in 112 patients (87.5%). Sixteen patients (12.5%) received angiography only. Catheterisation was unsuccessful in seven patients (5.5%) (two type IIc, five type IIIc) because of failed access to the true lumen of the

Table 2. Morphology based types of spontaneous isolated dissections of the superior mesenteric artery that were treated.

Type	n (%)
I	4 (3.13)
IIa	0 (0)
IIb	16 (12.5)
IIc	10 (7.81)
IIIa	3 (2.34)
IIIb	55 (42.97)
IIIc	12 (9.38)
IVa	3 (2.34)
IVb	12 (9.38)
IVc	0 (0)
Va	0 (0)
Vb	8 (6.25)
Vc	5 (3.91)

Table 3. Characteristics of digital subtraction angiography for treatment of spontaneous isolated dissection of the superior mesenteric artery

Variable	Patients[a]
Successful implantation of stent	112 (87.5)
Asymptomatic patients	6 (4.7)
Symptomatic patients	106 (82.8)
Angiography only	16 (12.5)
Technical failure	7 (5.5)
Narrow distal outflow artery precluding stent deployment	5 (3.9)
Choice of conservative management without attempt to stent deployment[b]	4 (3.1)
Brand of stents	
Xpert, ABBOTT	83 (74)
Lifestent, BARD	32 (28.6)
Pulsar-18, BIOTRONIK	23 (20.5)
SmartControl, CORDIS	15 (13.4)
Embolisation	29 (25.9)
Mean number of stents deployed per patient (range)	1.37 (1–2)
Complications[c]	3 (2.3)
Mean delay to improved symptoms − d[d]	2.3
Median length of hospital stay − d	7.1
Asymptomatic patients	8.3 (5.36)
Symptomatic patients	7 (94.6)

Data is given as n (%) unless otherwise stated.
[a] For successfull implantation of stent, angiography only and complications, the number of patients were 128. For brand of stents, embolization and median length of hospital stay, the number of patients who successfully received stent, were 116.
[b] Patient symptoms in this group were relieved before angiography. After discussion with the patient and family, conservative management was chosen. One case of type I, type II b, type IV a, and type IV b, respectively, made up this group.
[c] One death, and two pseudoaneurysms at puncture sites.
[d] In successfully stented symptomatic patients who were still suffering abdominal pain at the time of digital subtraction angiography. There were nine patients in this group. Mean delay to improved symptoms represents the time delay between the implantation of stents and the relief of symptoms.

distal SMA. Stents could not be deployed in five patients (3.9%) because of a narrow distal outflow artery. Thus, no attempt was made to deploy stents in these patients and they continued their conservative treatment. For the remaining four patients (3.1%), who achieved symptomatic relief before angiography, conservative treatment was preferred over EVT. No stents were implanted with respect to these patients' autonomy. Peri-procedural complications occurred in three patients. One patient died several hours after the procedure. Intra-operative DSA footage was later analysed and it was found that the stent deployed in this patient did not extend proximally into the aorta. As the SMA pulsed, the proximal end of the stent might have torn the vessel wall, resulting in internal bleeding and haemorrhagic shock. Pseudoaneurysm at the puncture site occurred in the other two patients, who were treated accordingly with no severe consequences. Symptoms were relieved in most patients before DSA. Except for the patient who died as mentioned earlier, there were nine other

Table 4. Follow up of patients treated for spontaneous isolated dissection of the superior mesenteric artery

Variable	Patients with stents (n = 111)	Patients without stents (n = 16)	p
Mean follow up time (range) − mo	29.7 (6–60)	31.4 (14–45)	> .05
Follow up index[a]	0.87	0.90	> .05
Remodelling of dissections			
Complete remodelling	98 (88.3)	1 (6.3)	< .001
Incomplete remodelling	12 (10.8)	1 (6.3)	
Unchanged dissection	0 (0.0)	12 (75.0)	
Adverse event			
Recurrent abdominal pain	1 (0.9)	4 (25.0)	< .001
Aneurysm formation	0 (0.0)	2 (12.5)	.015
New dissection	1 (0.9)	0 (0.0)	> .05
Patent false lumen	4 (3.6)	14 (87.5)	< .001

Mean follow up time (range) − mo P=0.65.
Follow up index P=0.26.
New dissection P=1.0.
[a] The follow up index is defined as the ratio between the investigated and the potential follow up period, indicating follow up completeness at the study end date. Data is given as n (%) unless stated otherwise.

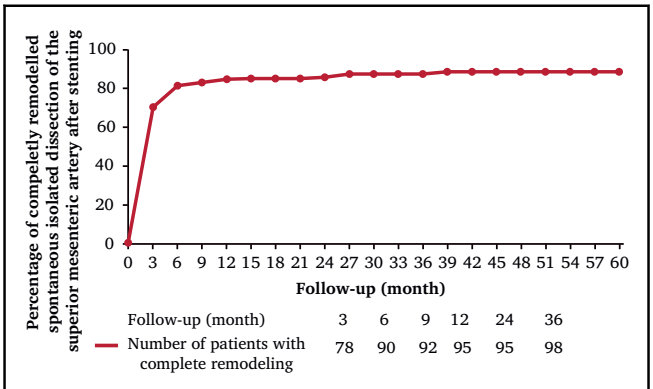

Figure 2. Overall complete remodelling rate in patients with stents confirmed by computer tomography angiography. The number of patients with complete remodelling is given in table. The last confirmed complete remodelling took place at 38 months after stent implantation. The population comprised 111 patients, resulting in an overall complete remodelling rate of 70.3% at three months, 81.1% at six months, 84.7% at one year, 87.4% at three years, and 88.3% at five years.

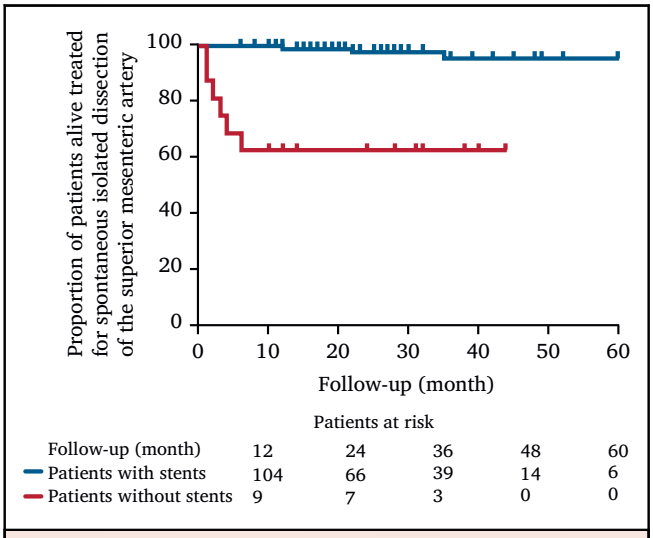

Figure 3. Cumulative Kaplan-Meier curve of event free survival rate of patients treated for spontaneous isolated dissection of the superior mesenteric artery. The cumulative event free survival rate was 99.0%, 95.8%, and 95.8% at one, three and five years in patients with stents, compared with 62.5% at both one and three years in patients without stents (p < .001).

patients who remained symptomatic when DSA was performed. They received stents successfully. In this group, the mean time delay between the implantation of stents and the relief of symptoms was 2.3 days, which indicated a lag between restoration of patency and recovery. A total of 29 coil embolisations was deployed in the false lumen in all cases with type V and in some cases with type II and type III if the sizes of entry tear and/or false lumen were overwhelmingly large.

Summaries of follow up data are shown in Table 4, Figs 2 and 3, and Table S1. The complete remodelling rate was significantly higher and the unchanged dissection rate significantly lower in patients with stents. The mean follow up index (±SD), on the study closing date was 0.87 (±0.08) in patients with stents vs. 0.90 (±0.14) in patients without stents (p = .26). The overall complete remodelling rate was 88.3% in patients with stents vs. 6.3% in patients without stents (p < .001). Most of the complete remodelling took place within three months of stenting. During this time, 78 cases of complete remodelling were observed, resulting in an overall complete remodelling rate of 70.3%. The rate was 81.1% at six months, 84.7% at one year, 87.4% at three years, and 88.3% at five years. The incidence of adverse events at follow up, such as recurrent abdominal pain (one in patients with stent group vs. four in patients without stents, p < .001) and aneurysm formation (none in patients with stent group vs. two in patients without stents, p = .015), was also significantly lower in the stent group, along with the rate of patent false lumen. For patients with recurrent abdominal pain in the stent group, DSA was performed and stent patency confirmed. It was suggested that patients have frequent smaller meals rather than a fewer larger ones, with the aim of better abdominal pain control. The pain was subsequently relieved with no further medication. For patients without stents, abdominal pain had a tendency to recur and conservative management was always needed. For the two patients with aneurysm formation, no other symptoms were identified. These patients remained under close observation.

Primary patency was favourable. Occlusion of stents occurred in one patient at three month follow up, resulting in cumulative primary patency of 99.1%. Another case of new dissection in the stent group was also noted at the patient's four month follow up. Both cases were asymptomatic, with no additional treatments. Cumulative event

free survival rates were 99.0%, 95.8%, and 95.8% at one, three and five years in the stent group compared with 62.5% at both one and three years in the conservative management group ($p < .001$).

DISCUSSION

Treatment of SIDSMA aims to control symptoms and prevent complications (e.g. intestinal necrosis). Usually patients present with acute abdominal pain, and the majority of cases described in the literature have been managed conservatively.[3,11] However, SIDSMA can also be identified as an incidental finding on CT scans performed for other conditions and does not necessarily suggest acute mesenteric ischaemia. This could be managed by careful observation without additional treatments.[12–14] First line therapy for SIDSMA, however, is still under debate. Open surgery is useful in patients with severe complications such as bowel necrosis. Conservative management decreases the demand for SMA bloody supply, thus providing a time window for patients to establish collateral circulation. Apart from these two approaches, EVT is also an option. With the help of stents, EVT can re-open the SMA compressed by false lumen and solve intestinal ischaemia directly. As early as 2000, a case report was published on use of EVT for SIDSMA,[15] and since then, several published case series have shown promising results.[16–19] In the present authors' practice, use of EVT has a high technical success rate and high efficiency at restoring blood supply and controlling symptoms. In addition, it has a satisfactory primary patency and complete remodelling rate at follow up, up to five years.

More than five classifications of SIDSMA have been proposed with no consensus reached.[20,21] All are based on SIDSMA imaging, such as the extent of the false lumen and presence of thrombosis in the false and/or true lumen. These classifications, however, are based on small to medium sample sizes and therefore are unable to cover all anatomical variants of SIDSMA. The present study had twice the patient number compared with a previous publication by the same study group, and also found similar subtypes in type V, thus putting forward a more precise and complete classification system.

Of note, symptoms in most of the patients were relieved before DSA. One reason for this is that there was a time delay between onset of symptoms and admission to the department. The median delay was 5.0 days. During this time, patients were at primary care centres or local hospitals receiving conservative treatment and their symptoms were relieved to some extent. After admission, the pre-operative preparation patients received was similar to the conservative treatments. However, once SMA blood supply demand increased (e.g. resuming oral intake), symptoms such as abdominal pain were likely to recur. Use of additional treatment (e.g. EVT or surgery) besides conservative management was 18.1%,[2] indicating that SIDSMA can deteriorate even with adequate conservative management. Stents contribute significantly to restoration of patency with low peri-procedural mortality.[2] This is why most patients were still willing to receive stents even if they became asymptomatic after several days of conservative treatment. At the present authors' centre, if SIDSMA is suspected, patients immediately receive conservative management and pre-operative preparation, awaiting EVT on the next available operating day. Stents were placed during the EVT for most patients and restoration of patency was achieved. Coil embolisation was used in large false lumens to facilitate their thrombogenesis and prevent rupture. However, even though the waiting time was short (mean 2.3 days, range 1–4 days), SIDSMA in three patients deteriorated and emergency EVTs were administered. The treatment strategy explained the lack of bowel necrosis in this cohort.

EVT can achieve a success rate up to 97.6%.[20] In this study, technical failures occurred in seven patients (5.5% of 128), with all of these the result of failed access to the true SMA lumen. No attempt was made to deploy stents in nine patients (7.0% of 128), five of these because of a narrow distal SMA. Even the tiniest stents seemed extremely oversized, and were likely to lead to a tear in the distal SMA. Thus, stent implantation had to be aborted. For the other four patients, because conservative managements had been useful in controlling symptoms, patients were willing to continue the same treatments and their wishes were followed. Complications occurred in three patients (2.3% of 128 patients) including one death, which was caused by an unexpected proximal SMA rupture. It was later found that the stent deployed in this patient did not extend proximally into the aorta, which might have led arterial pulsation to cause the stent to tear the arterial wall leading to arterial rupture, internal bleeding, and haemorrhagic shock. Other rare complications such as blocking off branches originating from the false lumen[22] did not occur, nor did bowel necrosis or peritonitis.

Although conservative management may be useful at controlling symptoms,[23] pain resolution does not complete the cure of this disease. One study reported that the maximum SMA diameter could continue to enlarge in some patients in the following six months even if the symptoms had relieved.[24] Another study with 83 symptomatic patients and mean follow up of 53 months found that 20% of patients developed late recurrence of abdominal pain after pain resolution from conservative treatment.[8] The present study showed 25.0% pain occurrence (4 out of 16 patients without stents). Therefore, even if all symptoms have disappeared, the high incidence of adverse events during follow up remains a concern. This is why the present authors would deploy stents even if the morphological classification was type I, IIa, IIIa, or IVa. For the complete remodelling rate, one study reported that 64% of patients with symptomatic SIDSMA achieved this via conservative management at two year follow up.[7] Other articles reported a much lower complete remodelling rate, ranging from 15.2% to 41.7%.[5,6,8,13,25] This study reports both the complete remodelling and primary patency rates of patients who underwent stents and had follow up of up to five years. Both results are quite satisfactory. The five year cumulative complete remodelling rate was 88.3%. Except for the patient with

SMA occlusion, the rest of the patients had incomplete remodelling, with none left unchanged. Most complete remodelling took place within three months of the procedure, and the rates were higher than for previously published conservative treatments. In terms of patency of SMA stents, one case series with five patients showed 100% on follow up CT up to 8.5 months (range 4–38 months).[26] Another cohort with 10 patients published recently showed 90% patency during follow up (range 11–99 months, median 53 months).[27] The present study showed cumulative primary patency up to 99.1%. Only one occlusion of a stent took place three months after endovascular treatment. For all other patients, their stents remained patent during follow up.

This study had several limitations. First it is a retrospective study not a randomised controlled trial, thus the level of evidence could be improved further. Another shortcoming is that as most patients were enrolled within the past five years, only six patients reached five year follow up. This may have led to inaccurate estimation of the five year cumulative event free survival rate and cumulative primary patency, and these results should be interpreted with caution.

CONCLUSION

EVT for SIDSMA has a high clinical success rate. The cumulative event free survival rate, primary stent patency, and complete remodelling rate are all satisfactory during midterm follow up. Endovascular treatment is an effective approach to cure SIDSMA and could be considered as a first line therapy.

CONFLICTS OF INTEREST

None.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2018.11.013.

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