

Primary Endovascular Intervention for Acute Mesenteric Ischemia Performed by Interventional Cardiologists – A Single Center Experience

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The current standard care for acute mesenteric ischemia (AMEI) involves urgent revascularization and resection of the necrotic bowel. Since 2012, we have used an AMEI protocol of our own design, which focused on early treatment and allowed interventional cardiologists to become involved when interventional radiologist was not available. A total of 8 patients were treated, and two interventional cardiologists performed all the stenting procedures. The procedure success rate was 100% in patients with non-calcified lesions (6/8). The 30-day survival rate was 100% in patients with angiographic success, and was 0% in patients with failed procedure. In two patients with total occlusion of the superior mesenteric artery, laparotomy was avoided when interventions were successful and completed within six hours of protocol activation. Four surviving patients were discharged after short intensive care unit stays (less than 48 hours); these patients returned to and remained at home throughout their 90-day follow-up. The overall procedure success rate and 30-day survival rate were both 75%. There was no access site or intervention-related complications. Using our protocol, we believe that primary endovascular treatment for AMEI is feasible. In geographic regions where healthcare resources are lacking, a time-efficient strategy adopted by interventional cardiologists should be considered for the purpose of saving lives and possibly even avoiding open laparotomy.

Key Words: Angioplasty and stenting • Endovascular treatment • Mesenteric ischemia • Mesenteric necrosis • Percutaneous coronary intervention • Peripheral artery disease

INTRODUCTION

Acute mesenteric ischemia (AMEI) is uncommon, with an incidence of around 1/100,000 per year.¹ AMEI has high mortality and morbidity rates (75-100%).² A systematic review showed that survival rates of patients who underwent bowel resection and vascular bypass surgery remained unchanged between 1966-2002.³ However, this poor outcome was shown to be improved with early diagnosis and revascularization.⁴ In general, angiography is underutilized because many patients present with non-specific symptoms, and many hospitals lack 24-hour angiographic services.^{4,5} Unless mesenteric artery stenosis or occlusion is confirmed early, the mesenteric ischemia can progress into systemic in-

Received: March 29, 2016 Accepted: November 30, 2016
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flammatory response syndrome (SIRS). Early revascularization using the endovascular approach has been reported to improve in-hospital survival rate to 80-82%, but it remains underutilized.⁵⁻¹¹ Previous studies on AMEI focused on techniques in surgical treatment such as placing stents retrogradely via direct puncture to the mesenteric artery during open laparotomy.^{12,13} However, only surgeons in the tertiary centers have experience performing mesenteric artery bypass surgery and retrograde open mesenteric stenting (ROMS). Once diagnosed, the time required for transfer may increase the extent of mesenteric ischemia or necrosis.

All these situations strongly suggested that an early invasive protocol is important in real-world practice. In our hospital, interventional cardiologist is available 24-hour a day. We performed our first mesenteric artery stenting in 2012, after which we then designed and revised our protocol to allow activation of interventional cardiologists when interventional radiologist was not available. Here we report our results.

METHODS

Study design

In this single center, retrospective study, we reviewed data from patients who received endovascular treatment for AMEI at our institution between 2012 and 2014. The informed consent for endovascular procedure was obtained from all patients, and our institutional review board approved this retrospective study (IRB Number 104-021-E). The inclusion criteria were emergency department (ED) visit for abdominal pain and confirmed thrombus formation, stenosis > 50% or decreased flow in one of the mesenteric vessels. The exclusion criteria were definitive pathology other than ischemia found by computed tomography (CT), or mesenteric ischemia associated with aortic dissection.

The AMEI protocol

Our hospital is a community hospital with a catchment area population of about 600,000 in Hsinchu, Taiwan. We developed a protocol in August 2012; an interventional radiologist (Chih-Horng Wu) and two interventional cardiologists (Kuei-Chin Tsai and Mu-Yang Hsieh) were recruited emergently to treat the index

case. We have 11 interventional cardiologists, but only one interventional radiologist. After our index case, an interventional cardiologist (Mu-Yang Hsieh) wrote a draft. The draft was reviewed and completed by interventional radiologist (Chih-Horng Wu). As the protocol evolved, the interventional cardiologist and interventional radiologist discussed different possibilities regarding guiding catheter selection and treatment options. The interventional radiologist thereafter trained the interventional cardiologist to perform selective bowel angiography in the initial three cases. Ultimately, the protocol evolved to enable the interventional cardiologist's active participation in the procedure.

Originally, the AMEI protocol was modeled from the acute coronary protocol. The primary goal is to facilitate urgent bowel revascularization; Figure 1 is a schematic representation of the protocol. For patients with evident bowel necrosis and peritoneal signs, a surgical team was directly consulted (group 1 patients). The endovascular team can be activated to perform endovascular revascularization after the surgical procedure. For patients with no evident bowel necrosis by CT, team members can activate the protocol immediately in the ED (group 2 patients). In suspected patients with possible CT findings (group 3 patients), the decision-making team reviewed the CT images separately and voted whether to proceed with diagnostic angiography. The protocol required that patient outcome should be disclosed to every member of the decision-making team.

Medical treatment

Prior to undergoing angiography, patients were orally loaded with aspirin 300 mg and clopidogrel 300 mg. Additionally, a heparin bolus with a 3000 U loading dose and a 12 U/kg/hour maintenance dose were initiated. If resuscitation or oral endotracheal intubation was not necessary, the patient was directly sent for angiography.

Angiography

Angiography was performed in either the catheterization lab or in the angiography room, depending on space availability. A 6-Fr sheath was placed in the femoral artery, and then a 5-Fr diagnostic catheter (RC-1 or JR) was used to perform selective angiography to the celiac trunk, superior mesenteric artery (SMA), or inferior

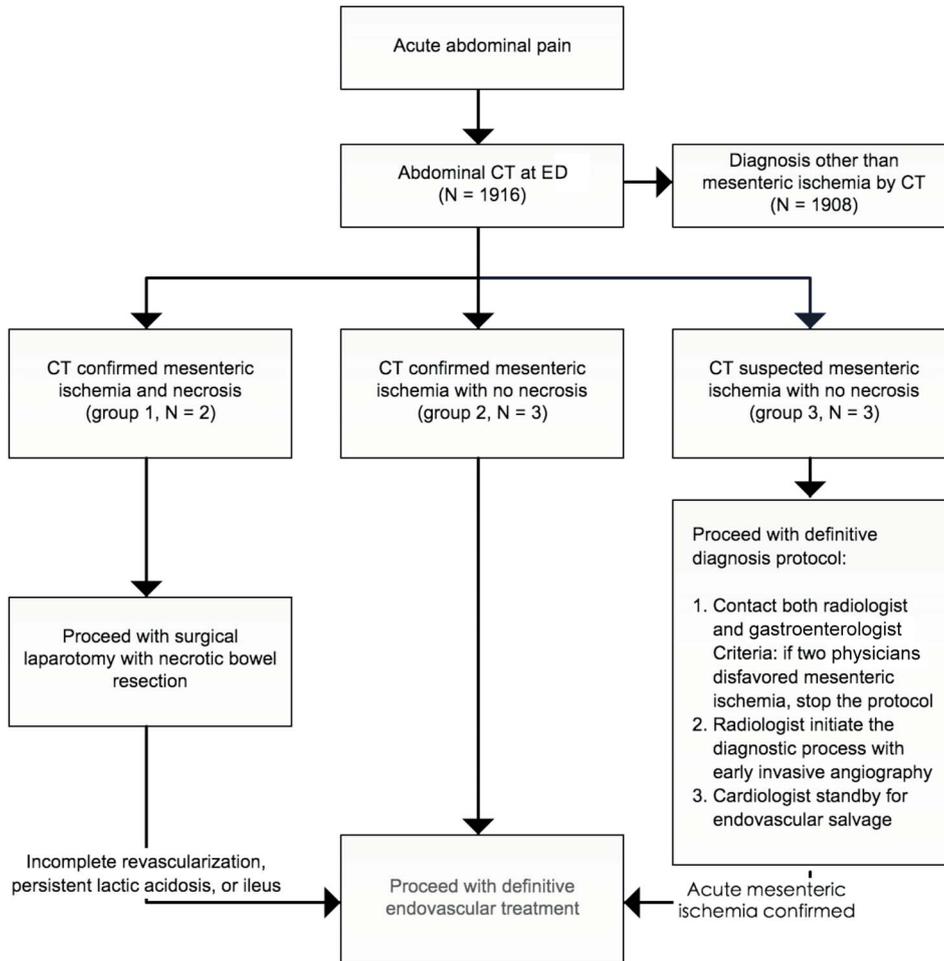


Figure 1. Flow chart of our acute mesenteric ischemia protocol.

mesenteric artery (IMA), depending on the CT findings. The flow was rated using the TIMI (thrombolysis in myocardial infarction) flow scale, as it was used in primary percutaneous coronary intervention.¹⁴ The mesenteric artery was considered diseased if there was diameter stenosis over 50%, and occluded if stenosis was 100% with 0 TIMI flow.

Endovascular intervention

After the culprit lesion was identified, thrombosuction, balloon angioplasty, and stenting were performed as indicated. The femoral sheath was changed to 7-Fr sheath, and a 7-Fr JR4 or IMA guiding catheter was used to engage the target artery. A guiding catheter with a side hole was used for ostial lesion, and an activated clotting time of at least 250 seconds was achieved with heparin (3000-5000 U). A standard 0.014-inch soft

coronary wire (SION from Asahi, Runthrough from Terumo, or BMW-U2 from Abbott) was used to cross the lesion. Distal contrast injection was used to confirm that true lumen was reached in 100% of the occluded cases. Thrombosuction was performed with a dedicated coronary thrombosuction device (Thrombuster, Terumo, Tokyo, Japan). A coronary balloon catheter (Maverick, Boston Scientific, Natick, MA, USA) was used for balloon dilatation. Then, the vessel diameter was estimated in comparison to the balloon size. If the lesion had a residual mural thrombus or stenosis exceeding 50% after the thrombosuction or balloon angioplasty procedure, the operator could decide to deploy a coronary bare-metal stent (Multi-Link, Abbott, Abbott Park, IL, USA or Integrity, Medtronic, Minneapolis, MN, USA). If the lesion had persistent TIMI 0 flow after repeated thrombus aspiration, bailout stenting was performed at the discre-

tion of the operator. A thrombolytic agent was not used in our protocol due to concerns that it could lead to uncontrolled peri-procedural gastrointestinal bleeding. Because our protocol was designed to include patients after surgical treatment, the protocol prohibited the use of thrombolytics or glycoprotein IIB/IIIA inhibitors. Distal protection device was not used.

Post-stenting care

Patients were sent to the intensive care unit (ICU) directly after stenting. Electrolyte imbalances were corrected, hourly urine output was recorded, and arterial pressure was monitored for 48 hours. Broad-spectrum antibiotics were used at the discretion of the critical care specialist. Abdominal check-ups were performed by the surgeon daily, or as needed. Changes in pain scale were recorded if the patient could make a clear report. Aspirin (100 mg) and clopidogrel (75 mg) were administered daily. An anticoagulant was administered within three days if the patient had a diagnosis of atrial fibrillation.

Follow-up

Data on demographic and clinical characteristics, cardiovascular risk factors, angiography findings, treatment results, complications, and outcomes were collected. Angiographic success was defined as residual

stenosis less than 40% and with TIMI 3 flow. Total clinical success was defined as total relief of pain at 48 hours or improvement in gastric emptying time if the patient was intubated. Partial clinical success was defined as residual abdominal pain upon discharge. Patients with recurrent abdominal pain were evaluated by the vascular Duplex, and underwent invasive angiography if re-stenosis was suspected. The primary outcome was 30-day survival. The secondary outcomes included definitive diagnosis rates, angiographic success, clinical success, avoidance of laparotomy, complication rates, and length of hospital stay.

RESULTS

Demographics and presentation

A total of 1916 abdominal CT scans were ordered by ED physicians between August 2012 and August 2014 to evaluate the cause of acute abdominal pain. Of these, eight patients fulfilled the inclusion criteria. The demographic, clinical characteristics, and presentation of acute abdominal pain are described in Table 1. All study participants presented with new-onset or acute worsening of abdominal pain within one week. All the patients who could grade their pain at ED reported a score of at least 7 on a pain scale of 10, where 1 was the minimum

Table 1. Demographics, clinical characteristics, and presentation of acute abdominal pain of the study participants

No	Age	Sex	Comorbidities	CHADS ₂ -VASc	Shock	Resting dyspnea	Food avoidance	Diarrhea	Nausea/vomiting	Ileus, diffuse	Ileus, localized	Lactate (mmol/L)
1	79	Female	Cirrhosis, gout	2	+	+	-	-	-	-	+	8.8
2	61	Male	PAOD, ESRD, DM, dyslipidemia, smoking	2	+	-	-	+	+	-	+	2.5
3	74	Female	HTN, dyslipidemia, gout	2	-	-	-	+	-	-	+	1.7
4	72	Female	DM, HTN	3	-	+	-	-	-	+	-	7.4
5	63	Female	Afib, VHD, mechanical valve, CVA, DM, HTN, dyslipidemia	5	-	+	-	-	-	-	+	2.4
6	74	Female	CAD, old MI, PAOD, ESRD, DM, HTN, dyslipidemia	4	+	+	-	-	-	-	+	5.0
7	86	Male	CAD, Afib, VHD, DM, HTN	3	-	-	-	-	-	-	+	2.6
8	80	Female	CAD, ESRD, DM, HTN	4	-	-	+	-	-	-	+	1.0

Afib, atrial fibrillation; CAD, coronary artery disease; CVA, cerebrovascular accident; DM, diabetes mellitus; ESRD, end-stage renal disease; HTN, hypertension; MI, myocardial infarction; PAOD, peripheral artery occlusive disease; VHD, valvular heart disease.

and 10 was the maximum pain. All study participants showed normal amylase and lipase levels in the initial laboratory tests in the acute setting. The lactate levels were elevated in patients who presented with hypotension or shock.

Treatment results and outcomes are summarized in Table 2. Two patients were stratified into group 1 (definitive mesenteric ischemia with evident bowel necrosis), three patients into Group 2 (definitive mesenteric ischemia without bowel necrosis), and three patients into Group 3 (suspected mesenteric ischemia by CT and no evidence of bowel necrosis).

The median time of protocol-to-angiography was 12 hours (range 3.4-24.5 hours). The delay to angiography was mainly due to: 1) time taken for intubation and fluid resuscitation to achieve target central venous pressure and stable hemodynamics; and 2) time taken to review the CT images by multiple team members.

Selective diagnostic angiography confirmed AMEI in all the patients. Five patients had 100% total occlusion of embolic etiology, which were all located in the main trunk of the SMA. The other three patients had an etiol-

ogy of thrombotic or non-occlusive mesenteric ischemia, with stenosis of at least 50% in diameter (range, 50-90%), and were all ostial disease of the SMA or IMA.

Endovascular intervention was attempted in all cases, and there were no difficulties in engaging the guiding catheters. Wiring was successful in seven patients, but failed in one patient who had severe calcification and total occlusion. During the thrombus aspiration phase, four patients with total occlusion of the SMA had TIMI 1 flow despite multiple attempts at aspiration. These patients received bare-metal stenting, with balloon expandable coronary stents with a median size 4.0 mm (range 2.5-4.5 mm). Thereafter, stenting immediately restored the flow to TIMI 3 flow.

The two cases with heavy calcification and a high thrombus burden had failed procedures. These patients developed profound shock along with multiple organ failure and died within one day. Of the six patients with successful procedures, one patient (Case 6) underwent a laparotomy with resection of necrotic bowel segment before angiography. The endovascular balloon angioplasty and stenting of the SMA resulted in resolution of

Table 2. Procedure details and outcomes

No	Culprit vessel	Lesion character	Vessel diameter (mm)	Lesion length (mm)	Calcification	Protocol to angiography (hour)	Treatment	Laparotomy	Angiography to discharge (days)	Follow-up duration (days)	Angiographic/ clinical success	30-day survival
1	SMA	100%, main trunk	4.0	28	Minimal	24.5	A + S	Yes (after stenting)	45	33	Yes/Yes	Yes
2	SMA & CT	100%, ostial	3.0	NA	Severe	11.9	W	No	NA	1	No/No	No
3	IMA	80%, ostial	3.0	15	Minimal	22.2	S	No	2	905	Yes/Yes	Yes
4	SMA	100%, main trunk	2.5	40	Minimal	16.3	A	No	NA	1	No/No	No
5	SMA	100%, main trunk	4.0	30	Minimal	3.4	A + S	No	2	781	Yes/Yes	Yes
6	SMA	50%, ostial	4.0	5	Minimal	12.1	S	Yes (before stenting)	21	166	Yes/Yes	Yes
7	SMA	100%, main trunk	4.5	50	Minimal	5.5	A + S	No	3	627	Yes/Yes	Yes
8	SMA	90%, ostial	4.5	8	Moderate	9.0	S	No	2	530	Yes/Yes	Yes

A, aspiration; BMS, bare-metal stent; CT, celiac trunk; IMA, inferior mesenteric artery; S, direct stenting; SMA, superior mesenteric artery; W, wiring.

ileus and shock. Another patient (Case 1) underwent laparotomy and resection of necrotic bowel after the stenting procedure. The remaining four patients recovered well, and there was no need to proceed with exploratory laparotomy after stenting.

There were no procedure-related complications, including aortic dissection, target vessel dissection, puncture site hematoma, uncontrolled gastrointestinal bleeding, respiratory failure, or new onset renal failure.

Follow-up

No patient was lost to follow-up. The in-hospital mortality in our study population was 37.5% (3/8). Two patients with angiographic failure declined laparotomy and died of multiple organ failure syndrome (2/8). One patient died in a chronic care facility due to ventilator-acquired pneumonia. One patient who survived (Case 6) had recurrent abdominal pain and developed new mesenteric ischemia in a previously untreated vessel (IMA). Repeated CT and angiography confirmed restenosis of a previously placed SMA stent (in-stent 40% stenosis), and a 100% occluded IMA from ostium. Recanalization of the IMA failed due to severe calcification. Due to a prior abdominal operation, retrograde open mesenteric stenting (ROMS) was not attempted. The patient expired at 166 days of follow-up.

After a confirmed diagnosis of AMEI, the overall mortality rate during the follow-up period was 50%. The other four patients who received intervention within 24 hours were discharged after short durations of ICU stay (less than 48 hours) and appeared well up to 90-day follow-up. Angiographic success correlated with 30-day survival. The 30-day survival rate was 100% in patients who had successful stenting (6/8) and 0% in patients with failed procedure (2/8).

DISCUSSION

Most coronary intervention centers operate 24 hours a day. Our current study showed that a strategy similar to that used in acute coronary care could be used for AMEI. In our study, the main findings were: 1) a dedicated protocol and team can improve the definitive diagnosis rate in patients with suspected AMEI; 2) an endovascular approach to treat AMEI without evident

bowel necrosis was safe and had acceptable success rates; 3) early angiographic success significantly improved patient outcome and may avoid laparotomy, even in patients who had total occlusion of the main trunk of the SMA; 4) when resection of the necrotic bowel was not accompanied by complete revascularization, post-operative endovascular salvage could still improve patient outcome (group 1, Case 6).

A number of studies have investigated the results of vasodilators,¹⁵ thrombolytics,^{3,11} balloon angioplasty,^{6,7} and stenting.^{6,7,11} Endovascular treatment has already been established as an alternative approach for chronic mesenteric ischemia.¹⁶ Although previous studies suggested that the endovascular approach can reduce complications and improve outcome, it is used in a minority of patients.⁸⁻¹⁰ In this study, our early invasive protocol was effective. Without concomitant revascularization, the two patients in group 1 had poor recovery even after surgical resection of the necrotic bowel segment. They had persistent ileus and lactic acidosis in the immediate post-operative period. Revascularization with endovascular techniques made it possible to wean these patients off the ventilator. The three patients in group 2 had their total occlusions treated urgently; this resulted in shorter ICU stays and avoided laparotomy for two of the patients. Use of the early invasive strategy in the three group 3 patients demonstrated that our protocol could confirm diagnosis and make timely treatment possible.

Our results showed that TIMI 0-1 flow persisted in three patients despite repeated thrombosuction. The flow improved to TIMI 3 flow in all three cases after deployment of a bailout balloon-expandable stent. Ultimately, we found no no-reflow phenomenon. In coronary artery disease, the no-reflow phenomenon was related to distal microembolization from a clot or ulcerative plaque consisting of thrombi or lipid materials. We can postulate that the incidence of no-reflow may be decreased because mesenteric arteries have many collaterals (Drummond artery, marginal arteries, or distal arcade).

It is important to note that treatment techniques vary between medical centers. The primary mode of endovascular treatment in the hands of an interventional radiologist is aspiration thrombectomy and thrombolysis,^{9,11} while the vascular surgeon would advo-

cate ROMS.^{12,17} A previous study where six AMEI patients were treated with ROMS had a technical success rate of 100% and peri-procedural mortality rate of 17%.¹² However, the use of the ROMS technique required an initial exploratory laparotomy. The same study showed that the mortality of percutaneous antegrade endovascular therapy was 100% (2 cases), because all attempts failed. Another study where 50 patients received endovascular revascularization by interventional radiologists had a success rate of 88%, a mortality rate of 32%, and an endovascular therapy-related complication rate of 10%.¹⁸ With advances in technique and device technology, Zhao and et al. reported that endovascular-first treatment leads to improved patient outcomes after systemically reviewing 28 articles with a total of 1110 patients. The in-hospital mortality was 26.9% in the endovascular group, versus 40.3% in the open surgery group.¹⁹ In another registry involving 439 patients, Branco and et al. reported that endovascular strategy decreased the risk of death (with a 2.5-fold decrease) when compared to open surgery, avoiding laparotomy in 16 patients.²⁰ Our results were comparable to these studies (technical success rate 75%, in-hospital mortality 25%, and complication rate 0%).

Our study has several limitations. The study was small and included only eight patients, which reflects the low incidence of AMEI in the real world. Patients who signed a do-not-resuscitate consent early in the course would be missed in the registry. We were not able to obtain whole abdominal visceral angiograms since some procedures were performed in the cath lab and we had only small image panels. Unfortunately, this leads to difficulty in detecting distal embolization. Although distal embolization might occur, the majority of our group 2 and 3 patients avoided laparotomy. We did not perform post-stenting pressure gradient measurements, which made documentation of angiographic success incomplete. The stents we deployed were all smaller in comparison to those referenced in prior reports. Vasospasm secondary to shock and small body habitus of Asian females may be the reasons of smaller stent size. As our experience further lays the groundwork for improved procedure quality, more accurate sizing may lead to better patient outcomes. Additionally, it is difficult to perform a randomized study not only because of small case numbers, but also because our surgeons have

little experience in mesenteric bypass operation. Finally, since endovascular techniques varied from center to center, it may be difficult to compare our results to other studies. Our results need to be validated in a larger multi-center study.

CONCLUSIONS

An early invasive strategy utilizing coronary techniques and devices can be an alternative method to ensure urgent bowel revascularization. Despite the limitations in our study, we believe that our experience can ultimately improve the quality of patient care. Our protocol can be implemented in any hospital with established acute coronary care. In addition to validating our protocol in a larger trial, it is also necessary to design a randomized trial to compare surgical-first techniques to endovascular-first strategies.

ACKNOWLEDGMENTS

This study was supported by Grants from the National Taiwan University Hospital, Hsin-Chu Branch (HCH 104-021).

FUNDING

No disclosure.

CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

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