

Chapter 19

In Patients with Acute Mesenteric Ischemia Does an Endovascular or Hybrid Approach Improve Morbidity and Mortality Compared to Open Revascularization?

Mark Wyers and Fahad Shuja

Abstract Acute mesenteric ischemia (AMI) covers a broad range of vascular pathologies ranging from acute arterial embolism or thrombosis, to the eventual manifestation of untreated chronic mesenteric ischemia. In recent decades, with improved anticoagulation management, the incidence of SMA embolism has declined. Currently, the most common presentation is an acute exacerbation of chronic atherosclerotic mesenteric vessel occlusion. The clinical manifestations and time course of this are much more variable and difficult to stratify. Regardless of the cause, in the absence of timely restoration of blood flow, there will be progression to bowel ischemia, peritonitis and death. The entity was first described in 1895, however it was not until the 1950s that techniques for restoration of mesenteric blood flow were described. Initial operative strategies included SMA embolectomy, SMA thromboendarterectomy and aorto-mesenteric bypass. Angiography was used primarily for diagnostic purposes but early reports of intra-arterial thrombolysis using heparin and streptokinase were published in the 1970s. With further advancements in endovascular techniques, percutaneous revascularization has become the preferred modality for treating patients with chronic mesenteric ischemia. However, the standard of care for AMI remains unclear and mortality rates remain quite high. Traditionalists would argue that there is no substitute for an open abdominal exploration and assessment of bowel viability. They are skeptical of recent publications citing favorable outcomes with purely percutaneous treatments for AMI, maintaining that it does not allow for assessment of bowel viability, requires advanced technical skills and is more time consuming compared to open approach. Alternatively, a combined open and endovascular, or “hybrid” approach can be viewed as a compromise that still honors traditional surgical principles to evaluate bowel viability. Milner et al. were the first to publish a case report on a “hybrid” approach to

M. Wyers, MD, FACS (✉) • F. Shuja, MD
Department of Vascular and Endovascular Surgery, Beth Israel Deaconess Medical Center,
Boston, MA, USA
e-mail: mwyers@bidmc.harvard.edu

AMI. They combined open and endovascular strategies to establish mesenteric blood flow. Briefly, the SMA is exposed at the base of the transverse mesocolon. A patch angioplasty is then performed at the site of intended arterial puncture site, through which, an SMA stent is deployed via retrograde cannulation. Proponents of this technique assert that it allows for assessment of bowel viability, and offers direct access to SMA revascularization rather than the long and sometimes challenging transbrachial or transfemoral approach. Since the first description of this technique in 2004, several groups have published their experience with this approach. In this chapter, we aim to summarize the literature on endovascular techniques (including hybrid approach) for treating acute mesenteric ischemia, and how they compare to the traditional open revascularization strategies.

Keywords Mesenteric ischemia • Mesenteric stent • ROMS • Mesenteric bypass • Reterograde mesenteric stent • CT diagnosis mesenteric ischemia • Bowel ischemia • SMA embolectomy • SMA stent • SMA bypass

Introduction

Acute mesenteric ischemia (AMI) covers a broad range of vascular pathologies ranging from acute arterial embolism or thrombosis, to the eventual manifestation of untreated chronic mesenteric ischemia. In recent decades, with improved anticoagulation management, the incidence of SMA embolism has declined. Currently, the most common presentation is an acute exacerbation of chronic atherosclerotic mesenteric vessel occlusion. The clinical manifestations and time course of this are much more variable and difficult to stratify. Regardless of the cause, in the absence of timely restoration of blood flow, there will be progression to bowel ischemia, peritonitis and death. The entity was first described in 1895 [1], however it was not until the 1950s that techniques for restoration of mesenteric blood flow were described. Initial operative strategies included SMA embolectomy [2], SMA thromboendarterectomy [3] and aorto-mesenteric bypass [4]. Angiography was used primarily for diagnostic purposes but early reports of intra-arterial thrombolysis using heparin and streptokinase were published in the 1970s [5]. With further advancements in endovascular techniques, percutaneous revascularization has become the preferred modality for treating patients with chronic mesenteric ischemia [6]. However, the standard of care for AMI remains unclear and mortality rates remain quite high. Traditionalists would argue that there is no substitute for an open abdominal exploration and assessment of bowel viability. They are skeptical of recent publications citing favorable outcomes with purely percutaneous treatments for AMI [7–10], maintaining that it does not allow for assessment of bowel viability, requires advanced technical skills and is more time consuming compared to open approach. Alternatively, a combined open and endovascular, or “hybrid” approach can be viewed as a compromise that still honors traditional surgical principles to evaluate bowel viability. Milner et al. were the first to publish a case report on a “hybrid”

approach to AMI [11]. They combined open and endovascular strategies to establish mesenteric blood flow. Briefly, the SMA is exposed at the base of the transverse mesocolon. A patch angioplasty is then performed at the site of intended arterial puncture site, through which, an SMA stent is deployed via retrograde cannulation [12]. Proponents of this technique assert that it allows for assessment of bowel viability, and offers direct access to SMA revascularization rather than the long and sometimes challenging transbrachial or transfemoral approach. Since the first description of this technique in 2004, several groups have published their experience with this approach [12–20]. In this chapter, we aim to summarize the literature on endovascular techniques (including hybrid approach) for treating acute mesenteric ischemia, and how they compare to the traditional open revascularization strategies.

Search Strategy

A literature search of English language publications from 1990 to 2014 was used to identify published data on endovascular or open approaches to AMI using the PICO outline (Table 19.1). Databases searched were PubMed, Medline, and Cochrane Evidence Based Medicine. Terms used in the search were “mesenteric ischemia treatment”, “mesenteric ischemia endovascular”, “acute mesenteric ischemia revascularization”, acute mesenteric ischemia AND endovascular approach”, and “mesenteric ischemia stenting”. Articles were excluded if they limited their analysis to chronic mesenteric ischemia. We did not find any prospective, randomized controlled trials on this subject. Eight case series, three reviews, one consensus paper and two case reports were included in our analysis. The data was classified using the GRADE system.

Results

Incidence and Risk Factors for AMI

Contemporary population-based studies on the epidemiology of this disease entity are lacking. According to a Swedish study based on autopsy and operating room data, the incidence of AMI in the city of Malmo was 12.9/100,000 person-years.

Table 19.1 PICO table for interventions on acute mesenteric ischemia

P (patients)	I (intervention)	C (comparator)	O (outcomes)
Patients with acute mesenteric ischemia	Endovascular revascularization	Open revascularization	Mortality, morbidity, bowel resection

More than two third of the cases had thromboembolic etiology, while the remainder was venous occlusions or non-occlusive mesenteric ischemia [21]. Clinical risk factors include atrial fibrillation, recent myocardial infarction, congestive heart failure and peripheral arterial emboli [22]. Up to 40% of patient with acute mesenteric ischemia have a history of post-prandial abdominal pain in the past, suggesting an acute-on-chronic process [23].

Presentation and Diagnosis of AMI

Common manifestations of AMI include abdominal pain, nausea and vomiting. Unless transmural bowel involvement is present, there may be minimal tenderness to palpation upon initial presentation. Unfortunately, these symptoms overlap with several other intra-abdominal pathologies and commonly lead to a delay in diagnosis or misdiagnosis. This diagnostic challenge is one of the main reasons why mortality from acute mesenteric ischemia has remained 50–70% over the years [19, 21, 24]. Therefore, physicians need to maintain a high index of suspicion. Once suspected, a multi-detector row computed tomography angiography (MDCTA) forms the cornerstone of the diagnostic algorithm [25–28]. It provides excellent visualization of the celiac artery and the SMA and aids in excluding other causes of abdominal pain. Furthermore, it allows for assessment of bowel wall thickness, pneumatosis, mucosal, and bowel wall enhancement pattern that support the diagnosis of AMI. There is no single radiographic finding that is perfectly sensitive or specific, but using a combination of CT criteria achieves a positive and negative predictive value of 100% and 96% respectively [29].

Treatment of AMI

Once suspected, treatment is divided into three aspects; appropriate resuscitation, prompt restoration of blood flow and resection of non-viable bowel. Resuscitation usually involves isotonic crystalloid fluids. Various clinical parameters are used as objective evidence of adequate resuscitation, including mentation, heart rate, blood pressure, urine output and degree of metabolic acidosis. AMI is a surgical problem, however and resuscitation should not delay revascularization and abdominal exploration, if needed. Based on the pre-operative CT and clinical exam, it can be determined whether the patient has peritonitis or not, and whether the occlusion is embolic or thrombotic in nature. Presence of peritonitis necessitates laparotomy to assess bowel viability and need for resection. Grossly necrotic bowel is resected. The bowel ends may be stapled off and anastomosis or stoma formation performed at a second-look laparotomy.

Mesenteric revascularization in the acute setting is typically focused on the SMA only and precedes bowel resection in order to minimize the length of intestine

removed. Revascularization may take one of three forms depending on the etiology of the occlusion, suspicion for bowel infarction and available resources:

Open – SMA embolectomy, mesenteric bypass, endarterectomy

Endovascular – aspiration embolectomy, rheolytic thrombectomy, catheter-directed thrombolysis, angioplasty and stent

Hybrid – retrograde open mesenteric stent

Endovascular Therapeutic Options

The SMA can be approached percutaneously via femoral or brachial artery. Brachial approach is preferred if there is a sharp downward angle between the SMA and the aorta. If percutaneous access fails, the SMA can be accessed in an open, retrograde fashion by exposing it at the base of the mesocolon. Once access is established, there are different endovascular options to treat an SMA occlusion:

Aspiration Embolectomy

This is a viable option in patients without any need for bowel resection. Briefly, over a stiff 0.035-in. wire, a 7-Fr sheath with a removable hub is placed proximal to the embolus. A hydrophilic 0.035-in. guidewire is then passed through the embolus. Over this wire, the tip of a 6-Fr guiding catheter is passed through the embolus. After removing the guidewire, a 20-ml syringe aspiration is applied manually to the guiding catheter accompanied with catheter withdrawal. Several passes are usually required. A small series out of Sweden reported 9 cases of percutaneous aspiration embolectomy of the SMA [7]. Technical success (defined as restoration of SMA blood flow) was achieved in all 7, however all patients had residual embolus in at least one branch of SMA upon completion. There was one case of SMA dissection, treated with stent. One patient went on to require bowel resection. In-hospital mortality was 10%. Another small series from Germany reported 6 cases of percutaneous aspiration embolectomy [8]. SMA blood flow was restored to normal in 5, while 1 patient had diminished blood flow upon completion due to a dissection. In-hospital mortality was 33%.

Catheter-Directed Thrombolysis

In cases of incomplete aspiration embolectomy or distal embolization, percutaneous SMA thrombolysis is an option in patients without peritonitis or high risk of bleeding. With the sheath placed in proximal SMA, a multiple side-hole infusion catheter or a microcatheter is advanced in the embolus and a thrombolytic agent infused, with repeat angiography at 12–24 h interval. A paper from the Swedvasc registry

reported cases of percutaneous thrombolysis for acute SMA occlusions [9]. Between 1987 and 2009, 34 patients underwent this intervention. No one had peritonitis. Notably, 47% of patients underwent an adjunctive endovascular procedure at the time of thrombolysis (aspiration embolectomy, angioplasty/stenting, mechanical thrombectomy, papaverine infusion). Complete or partial lysis was achieved in 30 patients (88%). Six bleeding complications were noted, which were all self-limiting. In-hospital mortality was 26%. Successful thrombolysis was associated with decreased mortality.

Antegrade Angioplasty and Stenting

This allows treatment of underlying stenotic or occlusive lesions primarily or after thrombolysis. For ostial or heavily calcified lesions, balloon-expandable stents are preferred over self-expanding ones owing to their superior radial force. A completion angiography is performed after stent placement, as well as pressure measurement. If the residual pressure gradients across the lesion/stent exceeds 10 mmHg, additional angioplasty and/or stenting is performed.

Retrograde Recanalization and Stenting of the Superior Mesenteric Artery

This “hybrid” approach was first described by Milner et al. in 2004 and has since been described by various groups in North America and Europe [11–20]. Variations in the technique have been described but in general, the SMA is punctured anteriorly with a micropuncture needle and 0.018” wire. The inner cannula of the micropuncture set can be used instead of a sheath. Lateral fluoroscopy is used to advance the wire to the level of the obstruction. Retrograde arteriography is performed. A torque device and minimal shaping of the wire is the default, trying to maintain luminal position of the wire. A guiding catheter may also provide some necessary support and steerability. Once the lesion is crossed and aortic access is obtained, the arteriotomy is made to include the wire, with the wire left in place. The arteriotomy should be kept as proximal on the SMA as possible. The artery is carefully inspected. Occasionally there is thrombus in the proximal SMA that can be retrieved with a clamp. A limited endarterectomy is performed and a patch angioplasty is performed with either vein or bovine pericardium. Prior to completion of the patch a 6 or 7 Fr sheath is advanced over the wire in through the side of the arteriotomy. The sutures are secured with a rubber shod while the artery is stented. Usually a 3–4 mm predilation is performed with repeat retrograde contrast injection to identify the SMA origin. If visualization of the SMA origin or aorta remains poor, a femoral puncture can be used to place a flush catheter in the aorta for imaging purposes. Most often a 6 or 7 mm balloon expandable stent or stentgraft is required. This approach allows the surgeon to evaluate the bowel and intervene on the vasculature at the same time.

Furthermore, in case of bowel perforation, it avoids the use of a prosthetic bypass in a contaminated operative field. The largest case series on retrograde open mesenteric stenting comes from a Dutch group, published in 2014 [20]. They analyzed 68 patients with AMI presenting between 2007 and 2011. In this report, percutaneous mesenteric artery stenting was the preferred treatment in patients without peritonitis, while retrograde open mesenteric stenting (ROMS) was reserved for cases of percutaneous technical failure. Technical difficulty, including the inability to cross the lesion with a wire, was the most common reason for failure of percutaneous revascularization. Fifty of these patients were able to undergo percutaneous mesenteric artery stenting, while 15 required retrograde stenting. Technical success (defined as successful completion of the procedure and <30% residual stenosis) was achieved in 14 of 15 patients despite the preceding percutaneous failure. One patient underwent bowel resection despite successful revascularization. Two patients had progression of bowel ischemia and required a second laparotomy and bowel resection. The mortality rate in ROMS group at 30 days was 20% and primary stent patency (defined as uninterrupted patency) was 91%. At 12 months, mortality rate for ROMS patients was still 20%, while primary stent patency was 83%. Primary assisted patency (defined as revision of the revascularization method to prevent impending occlusion) was 91% while secondary patency (defined as restored patency after occlusion by thrombectomy or angioplasty) was 100%. Unfortunately, patient outcomes in the percutaneous stenting group were not reported in this study.

Open Versus Endovascular Revascularization for AMI

To date, there is no randomized clinical trial for comparison of open versus endovascular mesenteric revascularization for acute ischemia. Available data is limited to single center studies [12, 30] and nationwide reports [6, 29] (Table 19.2). Block et al. published the national trends in Sweden for revascularization for AMI [29] and

Table 19.2 Results of endovascular or hybrid repair for acute mesenteric ischemia

Study	Patients	Outcome classification	Typical risk for endovascular technique	Relative risk for open technique	Quality of evidence
Arthurs et al. [30]	Endo=56 Open=14	Mortality	36%	50%	Low
Wyers et al. [12]	Endo=8 ROMS=6 Open=5	Mortality	100% endo 17% ROMS	80%	Low
Ryer et al. [18]	Endo=49 Open=17	Mortality	15%	23%	Low
Block et al. [29]	Endo=42 Open=121	Mortality	28%	42%	Low
Blauw et al. [20]	Endo=50 ROMS=15	Mortality	Endo not reported 20% ROMS	NA	Low

ROMS retrograde open mesenteric stenting, NA not applicable

demonstrated an increasing trend towards endovascular strategies. In 2009, endovascular treatment surpassed open surgery (29 versus 24 cases respectively). A similar analysis of the National Inpatient Sample (NIS) database from 2000 to 2006 also showed a significant increase of endovascular treatments for AMI but still more open procedures. In that 6-year period 64.5 % of patients with AMI underwent open surgery compared to 35.5 % who underwent endovascular revascularization [6]. In Swedvasc [29], there was no difference in 30-day mortality between open and endovascular surgery for embolic occlusions (37 versus 33 %). However, for thrombotic occlusions, mortality rate was significantly higher after open than endovascular treatment (56 versus 23 %). Similar trends were reported in the North American study by Schermerhorn et al. [6], where endovascular interventions had a 16 % in-hospital mortality compared to 39 % mortality after open surgical repair. Notably, those undergoing percutaneous revascularization had significantly higher rates of medical co-morbidities but a lower rate of bowel resection. The difficulty in these large database reviews and retrospective AMI studies resides in the ability to stratify patients between truly acute and subacute presentations and to overcome the selection bias between the two treatments.

Block et al. published their analysis of all SMA revascularization procedures performed for acute mesenteric ischemia between 1999 and 2006 as recorded in the Swedvasc registry [29]. Their experience appears to mirror other modern reports of the treatment of AMI with a transition to more endovascular treatments over the study period. A total of 163 patients were analyzed (121 open, 42 endovascular). Treatment strategies differed significantly depending on the type of occlusion with 85 of 99 embolic occlusions undergoing surgical embolectomy. In contrast, patients with thrombotic occlusion were treated more often treated with percutaneous endovascular procedures in 20 of 54 patients; an additional 4 were treated with retrograde open mesenteric stenting (ROMS); the remaining 21 patients underwent bypass or thromboendarterectomy. The time from symptom onset to treatment was shorter in open treatment arm, a statistic heavily influenced by the number of embolic presentations in that group. Bowel resection and incidence of short bowel syndrome were higher in patients undergoing open surgery. Thirty-day mortality rates were 42 % vs 28 % ($p=0.03$) for open and endovascular surgery. The two groups however are likely very different in terms of their disease severity at presentation. Patients in the endovascular group had greater delays to treatment yet had a lower incidence of bowel resection and better survival, suggesting a more subacute or acute on chronic presentation. Technical failure was 21 % in the endovascular group and 14 % in the open group. In both subgroups, revascularization failure was a harbinger of very poor outcome with 30-day mortalities of 56 % and 87 % in the endovascular and open cohorts respectively. This discrepancy also highlights the selection bias between the open and endovascular groups.

In a small case series of 13 AMI patients, Wyers et al. [12] noted that the intervention with the lowest mortality (17 %) was retrograde mesenteric stenting, compared to 80 % mortality for open bypass. Despite the small sample size of the study, it established ROMS as a viable revascularization method. ROMS technical success

was 100% including 4 patients that had failed a previous antegrade percutaneous approach.

Arthurs et al. reviewed the Cleveland Clinic experience of 70 AMI patients over a 9 year period [30]. They report a very aggressive endovascular approach in 81% of the total, using prolonged lytic therapy, mechanical thrombectomy and primary stenting. As in the Swedvasc registry, endovascular procedures were applied more commonly to thrombotic (72%) than to embolic occlusions (28%). Technical failure in endovascular therapy group was 13% overall and did not differ significantly between thrombotic (11%) and embolic (15%) disease. Patients undergoing open revascularization also had significantly longer segments of bowel resection, and were almost twice as likely to develop pulmonary or renal failure post-operatively. The mortality difference between the two treatment arms, 39% for endovascular and 50% for open treatment, did not reach statistical significance. Only when endovascular failures were excluded, however, did this difference reach statistical significance (36% versus 50%, respectively $p < 0.05$). Such exclusion however is not sound when comparing two treatment strategies and the former intention to treat analysis is more appropriate. There were no revascularization failures in the open revascularization group.

When reviewing literature on the subject, it is critical to distinguish between acute and sub-acute ischemia, and the time to intervention. The selection bias in the available retrospective analyses is evident but difficult to control for. The outcomes of interventions are highly likely to be dependent on these patient variables rather than the treatment they received. It is evident that patients with embolic occlusions, who are more likely to have more acute and critical symptoms, are treated more often with traditional open thrombectomy. Treatment delay with prolonged thrombolytics and a higher endovascular treatment failure rate, as demonstrated in the Cleveland Clinic experience, is not well tolerated in this group. Patients with thrombotic occlusions of the SMA tended to have a more insidious presentation [29] this built-in delay in diagnosis and presentation selects out a more heterogeneous patient group that may tolerate the occlusion better and therefore have more ability to undergo less invasive endovascular procedures and still have a lower rate of abdominal exploration and bowel resection [29]. Similarly, patients treated with endovascular means had a median duration of symptoms of 62 hours, compared to 26 hours for open surgery. Yet, traditional therapy group had a 3 fold longer segment of bowel resection than endovascular arm (160 cm versus 52 cm, $p < 0.05$) [30]. Sixty hours of ischemia without death and shorter length of bowel gangrene would again indicate a sub-acute presentation and favorably, but incorrectly, biases the outcomes of endovascular therapy. The Swedvasc registry data showed similar findings [29], where 24% of patients receiving endovascular therapy had a history of abdominal angina, and therefore, an indication that there was an element of sub-acute or acute-on-chronic presentation. Such pitfalls are inevitable in retrospective case series and can only be addressed by a well-designed prospective, randomized clinical trial. Due to the low incidence of AMI and emergent presentations, such a trial is unlikely to take place.

Recommendations

Because endovascular revascularizations can be technically challenging, time consuming and have a technical failure rate of 13–20%, they are best reserved for patients with sub-acute presentations without suspicion of bowel infarction. In patients without peritonitis, endovascular revascularization is associated with lower morbidity and mortality (GRADE; Moderate). Furthermore, patients undergoing successful endovascular revascularization have a better survival than open surgery (GRADE; Low). These observations however, more likely reflect a selection bias rather than the superiority of the percutaneous endovascular approach broadly applied to AMI patients. Survival in patients with failed endovascular intervention is not statistically different than open surgery (GRADE; Low). Most importantly, prolonged attempts at percutaneous intervention should not be allowed to delay laparotomy and bowel assessment/resection.

Once the need for bowel assessment has been established, the decision between a traditional bypass and hybrid retrograde stenting of the SMA are both good options. In patients with severe AMI presenting with peritoneal signs, immediate laparotomy and assessment of bowel viability is imperative. From a technical viewpoint, there are likely some advantages that favor a hybrid approach to the treatment of acute mesenteric ischemia. In these cases, a hybrid procedure with retrograde SMA revascularization has some potential advantages over open revascularization. This technique has a high rate of technical success, and allows prompt attention to the bowel. In the setting of peritoneal sepsis, the use of a prosthetic graft and the time and complexity of saphenous vein harvest can also be avoided. While not conclusive, the small series of carefully selected patients treated with ROMS may suggest a survival advantage. More widespread experience with this technique and further comparison is necessary. (GRADE; Moderate).

A Personal View of the Data

The data published on the topic of acute mesenteric ischemia is insufficient to be able to make a firm treatment recommendation in the treatment of acute mesenteric ischemia. Both reporting bias and patient selection bias are evident. All of the reports are relatively small retrospective case series from single centers. Patient acuity at the time of presentation is highly variable and likely represents the single largest effect on the outcome rather than the mode of treatment. Patients that present with an acute SMA embolus may have a more acute presentation and may develop bowel ischemia more rapidly. On average, there may be more of a need for bowel exploration in this group. Also in this group, surgical embolectomy likely confers a more expedient revascularization than endovascular mechanical or pharmacomechanical treatments that can be time consuming and have a higher rate of technical failure. Therefore a traditional surgical approach is favored for acute embolic presentations.

Patient acuity and the incidence of bowel ischemia are most variable in patients that present with acute on chronic or thrombotic mesenteric ischemia. It is this variability, combined with patient selection bias and such small numbers that makes it impossible to make any strong recommendations between treatment modalities for this acute on chronic group that presents with terminal mesenteric thrombosis.

Patient selection bias is most notable in reports of percutaneous endovascular interventions. Early detection and treatment before the onset of irreversible bowel ischemia is the key to patient survival. Ironically, at the opposite end of the spectrum, the patients in this group that present in the most delayed fashion, may also have improved outcomes. Because they have well developed collaterals, given the same degree of mesenteric vascular occlusion, they may have fewer symptoms and a lower incidence of bowel necrosis. Certainly the morbidity and mortality from AMI is associated with extent of bowel ischemia. Although difficult to assess based on exam, vessel involvement and laboratory tests (which tend to be non-specific), if there is low suspicion of non-viable bowel, low enough that abdominal exploration is not necessary, then an endovascular approach seems reasonable.

Recommendations

- Endovascular therapy for the treatment of AMI is not broadly applicable. **(Evidence quality: low; weak recommendation)**
- Because of the rapid degree of progression with embolic presentations of AMI a traditional operative approach with embolectomy is likely the safer approach. **(Evidence quality: low; moderate recommendation)**
- For acute on chronic presentations where there is little concern for bowel ischemia, an initial percutaneous endovascular approach is reasonable. **(Evidence quality: moderate; moderate recommendation)**
- If there is any concern about bowel viability, enough to warrant abdominal exploration then an operative bypass or hybrid ROMS procedure is the better revascularization choice. **(Evidence quality moderate; recommendation strong)**

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