

## The surgical management of acute bowel ischemia in octogenarian patients to avoid Short Bowel Syndrome: a multicenter study

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**SUMMARY: The surgical management of acute bowel ischemia in octogenarian patients to avoid Short Bowel Syndrome: a multicenter study.**

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**Background.** This is a multicenter study performed in two Italian tertiary care centers: General Emergency Surgery Unit at St. Orsola University Teaching Hospital - Bologna and Department of Surgical Sciences at Umberto I University Teaching Hospital - Rome. The aim was to compare the results of different approaches among elderly patients with acute bowel ischemia.

**Methods.** Sixty-three patients were divided in two groups: 1) DSgroup- 28 patients treated in Vascular Unit and 2) GEgroup- 35 patients treated in Emergency Surgery Unit.

**Results.** Mean age was 80 years, significantly higher for the GEgroup ( $p < 0.001$ ). Gender was predominantly female in both groups, without statistical difference. Pre-operatively, laboratory tests didn't show any difference in white blood cell count, serum lactate levels or serum creatinine among patients, while increase of c-reactive protein was observed in DSgroup with significant difference ( $p < 0.001$ ). The

main cause of acute bowel ischemia was embolism in DSgroup ( $p = 0.03$ ) and vascular spasm in GEgroup ( $p < 0.001$ ). On CT scan, bowel loop dilation was present in 58.7% of patients without statistical difference in both groups. The time lapse from diagnosis to operation didn't show significant differences between two groups (mean 349.4 min). Pre-operative heparin therapy was administered in DSgroup more frequently ( $p < 0.001$ ). Among DS patients, thrombectomy was the most frequent procedure (19 patients) associated with bowel resection in 9 cases. In GEgroup, 22 patients had an explorative laparotomy ( $p < 0.001$ ), 8 had a bowel resection with anastomosis and 5 a bowel resection plus stoma. A second look was required more significantly in DSgroup ( $p < 0.002$ ). Post-operative morbidity affected significantly GEgroup ( $p = 0.02$ ). The 3-day survival was significantly higher in the DSgroup ( $p < 0.001$ ). At discharge 32 patients (50.8%) were alive, 21 in DSgroup ( $p < 0.001$ ). Only one patient among both groups (1.6%) developed a short bowel syndrome.

**Conclusions.** In octogenarian patients with acute bowel ischemia, surgery should be always pursued whenever the interventional radiology is not assessed as a viable option. Both groups of patients showed an excellent outcome in terms of avoiding a short bowel syndrome. A multidisciplinary management by a dedicated team could offer the best results to prevent large intestinal resections.

KEY WORDS: Intestine ischemia - Short bowel syndrome - Octogenarian patients - Bowel rescue - Surgery.

### Introduction

Intestinal vascular emergencies are life-threatening conditions with disastrous prognosis, currently difficult to diagnose at the early stages of the diseases; a rapid diagnosis is mandatory to avoid irre-

versible ischemia, extensive bowel resection, sepsis and death. They include all bowel ischemic injuries due to acute or chronic vascular and/or hemodynamic diseases related to the mesenteric vascular compartment. They can be occlusive or non-occlusive (NOMI, non-occlusive mesenteric ischemia), arterial or venous, localized or generalized, superficial or trans-mural, reversible or irreversible. Any sudden, continuous and unusual abdominal pain must be suspected for this diagnosis, even though uncommon (1). Reversible acute mesenteric ischemia is treated conservatively with bowel rest, in-

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travenous fluids, heparin iv, oral aspirin, and oral antibiotics (2): an isolated superior mesenteric artery dissection should not be considered irreversible as long as signs of acute bowel injury are absent (3, 4). On the other hand, it is difficult to predict bowel necrosis due to mesenteric inadequate blood supply: in a recent French study (5, 6), factors significantly associated with it were organ failure ( $P=0.03$ ), serum lactate levels  $>2$  mmol/l ( $P=0.01$ ) and bowel loop dilation on computerized tomography scan ( $P=0.02$ ). Necrosis rate increased from 3 to 38, 89, and 100% in patients with 0, 1, 2, and 3 factors, respectively. Apart from lactate (7-11), representing an early un-specific sign of tissue hypo-perfusion and gut barrier dysfunction, and widely used as “marker” of mesenteric irreversible ischemia, other factors have been considered as early and predictive of bowel necrosis such as intestinal fatty acid-binding protein-FABP (expression of villi injury) and citrulline (marker of enterocyte mass) (11): to this day, no study has produced a high enough or convincing level of evidence supporting one biomarker over another, and none is currently available in routine practice (12); a normal serum lactate level does not exclude irreversible acute mesenteric ischemia and should not be used for diagnosis. Mesenteric venous thrombosis is an uncommon cause of acute mesenteric ischemia (9-16%), typically affecting the superior mesenteric vein and more rarely the inferior mesenteric vein (13-15): the etiology can be categorized based on Virchow’s triad of venous stasis, hypercoagulable state and endothelial injury. Contrast-enhanced computed tomography (CT) scan has become the cornerstone of the diagnosis by showing features of vascular disorders and of intestinal ischemic or venous injury (16). As far as concerns ultrasound, it has certainly a limited role in this critical condition while magnetic resonance imaging could be important especially in NOMI to monitor an effective reperfusion (17). Diagnosis must be as early as possible, because intestinal viability could be achieved in up to 100% of patients if the duration of symptoms is less than 12 hours (18) and because mortality is heavily affecting this category of patients: up to the ’90, it was still in a range of 60-90% (18). More recently, mortality has consistently been reported in the range of 50% (19, 20). Poor functional status, “do not resuscitate” order, low albu-

min, open wound, and dirty *versus* clean-contaminated cases were reported as pre- and intra-operative variables significantly associated with post-operative mortality (21). In 2015, a study among 4527 patients showed a pooled in-hospital mortality of 63% with no significant reduction of the rate in the last decade (22): there was a significant difference about in-hospital mortality between acute arterial mesenteric infarction (73.9%) compared with acute venous mesenteric infarction (41.7%) ( $P < 0.001$ ), and NOMI (68.5%) compared with acute venous mesenteric infarction (44.2%) ( $P < 0.001$ ). One year survival for mesenteric venous thrombosis was reported to be 83.7% (15, 16). Acute mesenteric ischemia in Intensive Care Unit (ICU) patients was associated, in a multicenter French report, with a 58% ICU death rate: older age and an higher sequential organ failure assessment (SOFA) severity score at diagnosis were risk factors for mortality (23). The risk of short bowel syndrome (SBS) following extensive bowel resection for mesenteric ischemic or venous infarction is high: a recent study reported up to 25% of patients affected by SBS, requiring parenteral nutrition in 18% of the cases (24), especially due to type I acute intestinal failure (25). In other reports, the incidence of SBS after mesenteric venous thrombosis was 13.9% (15, 16). The incidence of acute mesenteric ischemia increases exponentially with age (26) and the significance of it as a differential diagnosis in elderly patients with acute abdomen may be underestimated. In a study, the in-hospital incidence rate of acute mesenteric ischemia was 7.3/100,000/year, more common than ruptured abdominal aortic aneurysm, and the age-specific incidence was higher than the incidence of acute appendicitis in patients over 75 years with acute abdomen: during the follow-up, the age-adjusted risk of death was 1.8 times higher in this category of survivors than in survivors of acute cholecystitis (26). In order to evaluate the impact of surgery (revascularization and/or bowel resection) in a very elderly population (octogenarian patients), we performed a multicenter study in two Italian tertiary care centers: General Emergency Surgery Unit at St. Orsola University Teaching Hospital-Bologna and Department of Surgical Sciences at Umberto I University Teaching Hospital-Rome. The aim was to compare the results of different surgical approaches in case of acute bowel ischemia.

## Methods

Sixty-three patients were divided in two groups: 1) DS group- 28 patients treated in Vascular Unit and 2) GE group- 35 patients treated in Emergency Surgery Unit. Results were expressed as median (range) unless otherwise stated. Comparisons between categorical variables were determined using the chi-square or Fisher's exact test, as appropriate. Continuous variables were assessed with the Mann-Whitney U-test. Logistic backward regression was undertaken to determine factors independently associated with mortality, morbidity and discharge at home including all factors where the P-value was less than 0.05 on univariate analysis. A statistical software package (SPSS Version XX.0; IBM Co, Armonk, NY, USA) was used for the analysis, with  $p < 0.05$  considered statistically significant.

## Pre-operative results

Mean age was 80 years, significantly higher for the GE group ( $p < 0.001$ ). Gender was predominantly female in both groups, without statistical difference. Pre-operatively, laboratory tests didn't show any difference in white blood cell count, serum lactate levels or serum creatinine among patients, while increase of c-reactive protein was observed in DS group with significant difference ( $p < 0.001$ ). The main cause of acute bowel ischemia was embolism in DS group ( $p = 0.03$ ) and vascular spasm in GE group ( $p < 0.001$ ). Venous ischemia was simultaneously present in 12 cases among all patients. Colonic involvement was reported in 41.3% of patients. Chronic ischemia affected 2 patients among GE group and none in DS group. On CT scan, bowel loop dilation was present in 58.7% of patients without statistical difference in both groups. The time lapse from diagnosis to operation didn't show significant differences between two groups (mean 349.4 min). Pre-operative heparin therapy was administered in DS group more frequently ( $p < 0.001$ ) (Table 1).

## Intra- and post-operative results

Among DS patients, 3 surgical patients had no treatment with viable bowel at laparotomy and were

not considered for statistical analysis. In DS group, thrombectomy was the most frequent procedure (19 patients) associated with bowel resection plus anastomosis in 9 cases: notably, 7 out of 19 patients underwent thrombectomy with patch. Aorto-mesenteric bypass was performed in 4 cases among DS patients, while 5 subjects underwent a retrograde ilio-mesenteric bypass. In GE group, 22 patients had an explorative laparotomy ( $p < 0.001$ ): 17 of them (77.2%) had no bowel resection because of massive intestinal infarction and at multivariate analysis explorative laparotomy correlated significantly with post-operative mortality. Among the remaining 13 patients, 8 had a bowel resection with anastomosis and 5 a bowel resection plus stoma. A second look was required more significantly in DS group ( $p < 0.002$ ): 7 out of 8 were represented by thrombectomy plus intestinal resection. Post-operative morbidity affected 32 patients (50.8%), more significantly in the GE group ( $p = 0.02$ ). The 3-day survival was significantly higher in the DS group (89.3 *versus* 48.6%,  $p < 0.001$ ). At discharge 32 patients (50.8%) were alive, 21 in DS group ( $p < 0.001$ ). Only one patient among both groups (1.6%) developed a short bowel syndrome (Tables 2, 3).

## Discussion

Acute mesenteric ischemia is an emergency with a high mortality rate and survivors have high rates of intestinal failure. Intestinal Stroke Centers were developed worldwide as a multimodal management strategy involving gastroenterologists, interventional radiologists, vascular and abdominal emergency surgeons, and intensive care specialists, in order to increase survival and reduce intestinal insufficiency (Figure 1). All patients receive: 1) a specific medical protocol; 2) endovascular and/or open surgical revascularization whenever possible; and/or 3) resection of non-viable small bowel. One of the first report related to an Intestinal Stroke Center (27) showed a 30-day survival of 95% with rates of intestinal resection decreasing to 18% and to a mean length of 7 cm when the disease was treated at early stages. In few follow-up studies from the same group (24, 28, 29), among 124 patients (mean age 63 years) the management of intestinal ischemic in-

TABLE 1 - PRE-OPERATIVE DATA.

	Overall (n=63)	DS Group (n=28)	GE Group (n=35)	P-value
Age (years)	79.9±7.1	76.4±6.5	82.7±6.3	<0.01
Male sex	31 (49.2)	17 (60.7)	14 (40.0)	0.13
<b>Laboratory tests</b>				
WBC (x10 <sup>9</sup> /L)	20.7±11.2	21.3±6.4	20.2±14.0	0.70
PCR	20.3±15.2	29.8±10.6	11.6±13.7	<0.01
Lactate	6.4±4.6	6.8±1.1	5.8±6.8	0.44
Creatininemia	1.7±1.2	1.8±0.6	1.6±1.6	0.53
<b>Pre-operative imaging</b>				
bowel dilatation at CT scan	37 (58.7)	16 (57.1)	21 (60.0)	1.00
colonic involvement	26 (41.3)	8 (28.6)	18 (51.4)	0.08
ACUTE INTESTINAL ISCHEMIA	61 (96.8)	28 (100.0)	33 (94.3)	0.50
CHRONIC INTESTINAL ISCHEMIA	2 (9.0)	0	2 (5.7)	0.50
Venous ischemia	12 (19.0)	3 (10.7)	9 (25.7)	0.20
Arterial ischemia	58 (92.1)	28 (100.0)	30 (85.7)	0.06
1) athero-thrombosis	30 (47.6)	17 (60.7)	13 (37.1)	0.08
2) embolism	22 (34.9)	14 (50.0)	8 (22.9)	0.03
3) arterial dissection	0	0	0	-
4) other mechanisms (spasm, unspecified, etc.)	13 (20.6)	0	13 (37.1)	<0.01
Pre-operative Heparin therapy	33 (52.4)	28 (100.0)	5 (14.3)	<0.01
Time: FROM symptoms in hospital TO surgery	349.4±266.8	334.3±122.7	365.4±345.4	0.65

WBC = white blood cell count; PCR = c-reactive protein

Values in parentheses are percentages unless indicated otherwise; Values are mean ± standard deviation (range)

juries in a dedicated Intestinal Stroke Center allowed to reduce overall mortality and intestinal resection rates to less than 20 and 30%, respectively. The first line should be represented by radiology endovascular therapy (aspiration thrombectomy and local thrombolytic therapy, often associated with angioplasty and stent placement) whenever possible: a recent review using PubMed reported a technical success rate up to 100% among patients with arterial mesenteric ischemia and around 75-100% in case of venous mesenteric ischemia (30). Whenever interventional radiology is not possible among the subset of patients who are poor candidates for endovascular intervention (like those with flush mesenteric vessel occlusion, long segment occlusive disease, and a

thrombosed mesenteric stent and/or bypass), vascular surgery represents the second line: a single center 40-year experience on 48 patients (mean age 64 years), operated for atherosclerotic mesenteric ischemia with a mesenteric artery reconstruction (bypass grafting, local endarterectomy and transaortic endarterectomy), showed (31) nine deaths due to bowel infarction with a perioperative (<30 days) mortality rate of 52% in acute cases and of 0% in chronic cases (P < 0.001). In a more recent single-center report (32) 82 patients (age 63±12 years) underwent antegrade or retrograde aorto-mesenteric bypass (aortoceliac/superior mesenteric or aortomesenteric) for acute mesenteric ischemia. Concurrent bowel resection was necessary in 45% of cases, and

TABLE 2 - INTRAOPERATIVE DATA.

	Overall (n=63)	DS Group (n=28)	GE Group (n=35)	P-value
<b>Operation</b>				
1) Bowel resection	28 (44.4)	15 (53.6)	13 (37.1)	0.40
2) Bowel anastomosis	23 (36.5)	15 (53.6)	8 (22.9)	<b>0.03</b>
3) Stoma creation	11 (17.5)	6 (21.4)	5 (14.3)	0.74
4) Explorative laparotomy	22 (34.9)	0	22 (66.9)	<b>&lt;0.01</b>
5) Thrombectomy	10 (15.8)	10 (35.7)	-	-
6) Thrombectomy + intestinal resection	9 (14.3)	9 (32.1)	-	-
<b>Second Look</b>	10 (15.8)	8 (28.6) (7/8 thrombectomy+ intestinal resection)	2 (5.7)	<b>&lt;0.02</b>

Values in parentheses are percentages unless indicated otherwise; Values are mean ± standard deviation (range)

TABLE 3 - POSTOPERATIVE DATA.

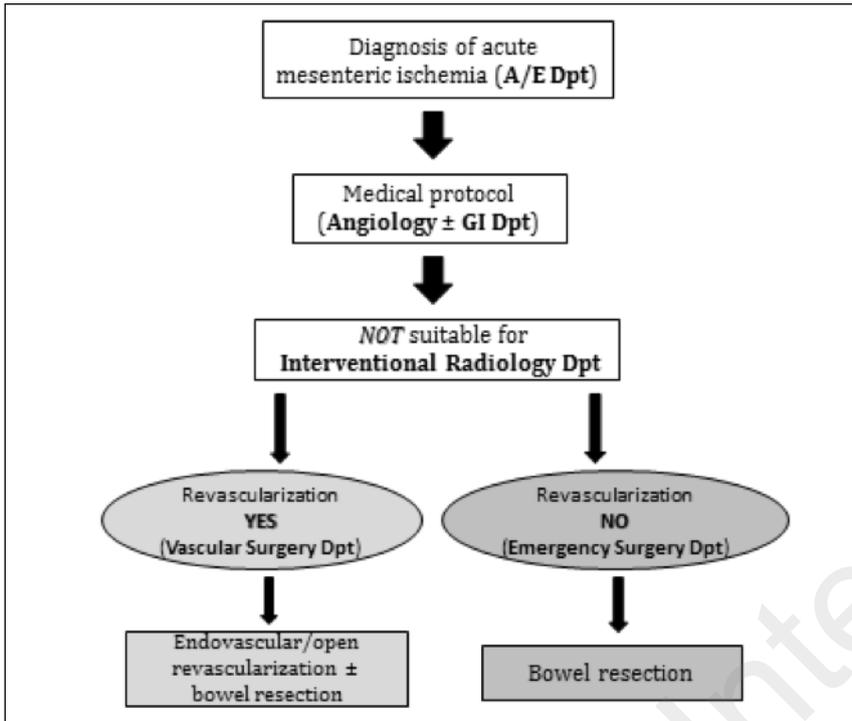
	Overall (n=63)	DS Group (n=28)	GE Group (n=35)	P-value
<b>3-day survival</b>	42 (66.7)	25 (89.3)	17 (48.6)	<b>&lt;0.01</b>
<b>Post-operative surgical complications</b>	32 (50.8)	8 (28.6)	24 (68.6)	<b>0.02</b>
<b>Alive at discharge</b>	32 (50.8)	21 (75.0)	11 (31.4)	<b>&lt;0.01</b>
<b>SBS+TPN</b>	1 (1.6)	0	1 (2.9)	1.000

SBS = short bowel syndrome; TPN = total parenteral nutrition

Values in parentheses are percentages unless indicated otherwise; Values are mean ± standard deviation (range)

37% of patients required a second-look operation. The 30-day mortality was 26%. A 1988-2006 review among 6342 mesenteric angioplasty +/- stenting and 16071 open surgical mesenteric revascularization (bypass, endarterectomy, or embolectomy) has been reported in international literature (33). Mortality was lower after mesenteric angioplasty +/- stenting than bypass for both chronic (3.7 versus 13%, P<0.01) and acute cases (16 versus 28%, P<0.01). Bowel resection was more common after bypass than mesenteric angioplasty +/- stenting (7% versus 3%, P<0.01) and this subgroup showed an increased in-hospital mortality for both repair types

(54 and 25%). Retrograde open mesenteric stenting (ROMS) is a hybrid technique that combines the advantages of open surgical and endovascular approaches: 1) prompt blood flow restoration with an endovascular approach and 2) inspection and resection of the small bowel. Two recent papers (34, 35) reported the results related to this technique. Fifteen (mean age 66 years) and twenty-five patients (mean age 64.9±11.6 years) were respectively included. In the first study (34) technical success was achieved in 14 patients and the mortality rate at 30 days was 20%. Ten patients underwent unplanned re-laparotomy. Two cases needed resection of the small bowel.



**Figure 1 - Algorithm: acute mesenteric ischemia management in “S. Orsola” (Bologna) and “Umberto I” (Rome) University Hospitals.**  
 Dpt = Department; A/E = Accident and Emergency; GI = Gastrointestinal

In the second report (35), technical success was 92% but thirteen patients (52%) required bowel resection and the 30-day operative mortality rate was 25%. The three techniques (endovascular, open and hybrid) were compared in a recent systematic review among 1110 patients (36) and in a meta-analysis among 3020 subjects (37). In the first report (36), hybrid technique seemed to have the lowest mortality and acceptable second-look laparotomy rate. The overall bowel resection rate was lower in the endovascular group. The second study (37) reported that endovascular or hybrid intervention were associated with a reduced risk of in-hospital mortality with a prevalence of it around 19%. Moreover they showed a benefit impact on risk of bowel resection and second-look laparotomy. In our combined experience in Umberto I and S. Orsola University Hospitals, endovascular treatment may serve as a first-line therapy for selected patients when there is a low suspicion for intestinal necrosis. Open vascular surgery should be reserved for emergency conditions requiring exploratory laparotomy and thrombectomy represented the most frequent procedure (19 patients). Hybrid technique may be an especially effective approach for treating acute mesenteric ischemia with low morbidity. In our series, we experienced only one case of

short bowel syndrome in a very elderly population: in case of SBS, superior mesenteric artery re-vascularization is sometimes unfeasible and celiac artery vascularization (if stenotic or occluded) may improve blood supply to the remnant bowel. Roussel A et al. (38) reported 11 anterograde aorto-hepatic bypass, 1 ilio-hepatic bypass and 1 case of celiac artery endarterectomy (mean age  $47.2 \pm 12.1$  years): technical success was 92% allowing for digestive surgical rehabilitation with continuity restoration in 7 patients (54%). Parenteral nutrition was weaned in 2 patients and one year survival rate was 73.8%. Two further studies (39, 40) analyzed the factors influencing mortality rates after re-vascularization for acute mesenteric ischemia: in the first report (39) open surgical intervention, bowel resection and age were associated with increased mortality, while the second one (40) underlined as multivariable predictors of mortality the impaired functional status, increased age, and postoperative sepsis. In our experience, the increased age (octogenarian patients) influenced the rate of bowel involvement, up to 17 cases (out of 63 patients - 27%) of explorative laparotomies for extensive bowel infarction. Interestingly, Beaulieu RJ et al. (41) analyzed rates of bowel resection following endovascular *versus* open vascular repair after acute

mesenteric ischemia, evaluating 4665 treated patients from 2005 through 2009 (mean age 70.5 years): during the study time period, 14.4% of patients undergoing endovascular procedures required bowel resection compared with 33.4% for open revascularization ( $P < 0.001$ ). In a recent paper, Ding et al. (42) promote a systematic use of “open abdomen” approach secondary to acute superior mesenteric artery occlusion, reporting a reduced sepsis-related complication rate together with improvement of the clinical outcomes in case of peritonitis. Other Authors (43) do not support this strategy of “damage-control” surgery because the systematic routine use of it and of the second-look procedures pose a substantial risk of blank laparotomies, which may result in unjustifiable increased rate of hemorrhages, repeated discontinuation of antithrombotic therapy, as well as specific complications linked to the management of an open abdomen (infection, fistula, impaired fascial closure). Therefore, most Authors recommend selective (rather than systematic) second-look procedures based on surgeons assessment of questionable bowel viability during initial operation. Even then, negative findings during repeat surgery (second look) have been reported in >50% and up to 93% of cases (43). In our experience, a second look was required more significantly in DS group ( $p < 0.002$ ): 7 out of 8 cases were managed by thrombectomy plus intestinal resection.

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## Conclusions

In octogenarian patients with acute bowel ischemia, surgery should be always pursued whenever the interventional radiology is not assessed as a viable option. In our experience post-operative mortality was still high (50%) but both groups of patients showed an excellent outcome in terms of avoiding a short bowel syndrome (1.6%). A multidisciplinary management by a dedicated team offers the best results in order to prevent large intestinal resections.

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*Conflict of interest/Financial support and sponsorship*  
None.

### *Author contribution*

All Authors gave substantial contributions to the conception, design, acquisition, analysis, and interpretation of data for the work.

All Authors drafted the work, revising it critically for important intellectual content.

All Authors gave their final approval of the version to be published.

All Authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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