The Egyptian Journal of Hospital Medicine (October 2017) Vol. 69 (4), Page 2366-2372

Types and Management of Chronic Intestinal Ischemia

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ABSTRACT

Background: chronic intestinal ischemia is unusual but important cause of abdominal pain. Although this condition accounts for only 5% of all intestinal ischemic events, it can have significant clinical consequences

Aim of the Work*:* the objective of this systematic review was to assess the value of different types of management of chronic intestinal ischemia (Open surgery versus endovascular interventions). PubMed and EBSCOHost electronic databases were methodically searched for English-language articles published between 1996 and 2015.

Conclusion*:* chronic mesenteric ischemia is a condition characterized by postprandial abdominal pain, which is ascribed to intestinal hypoperfusion. Patients were frequently malnourished and develop significant weight loss due to sitophobia. Traditionally, open surgery has been the treatment of choice; however, endovascular surgery was gaining wider acceptance. Based on the data, open surgeries surpass endovascular procedures in terms of symptom amelioration and long-term vessel patency, along with less significant symptomatic recurrence. Patients undergoing open procedures do, however, have a higher rate of complications. Nonetheless, there was no statistically significant difference in mortality rates between the two approaches.

Keywords: celiac artery, mesenteric vasculitis, chronic mesenteric ischemia.

INTRODUCTION

Chronic intestinal ischemia is uncommon condition that accounts for about 2% of revascularization procedures in patients with atheroma. Most patients are older than 60 years; women are affected three times more often than men. Ischemia occurs when the blood supply to the intestines is inadequate as a result of lesions affecting one or more of the three mesenteric arteries: the celiac artery, the superior mesenteric artery and inferior mesenteric artery [(1)].The most common cause of chronic intestinal ischemia is atherosclerotic occlusion or severe stenosis of the mesenteric arteries. A stenosis of >50% is present in 18% of patients older than 65 years, but very few were symptomatic [(2)].The clinical presentation was seen in patient mostly between 60 and 80 years old, with or without concurrent disease in other vascular beds. This manifestation of systemic arteriosclerosis carries the risk factors of: smoking, hypertension, dyslipidemia and coronary artery disease. Some of these patients have associated comorbidities including chronic obstructive pulmonary disease, diabetes, aortic artery aneurysm and peripheral vascular disease. The severity of clinical presentation depends on:

1. The site, grade, and cause of vascular obstruction.
2. The degree of collateralization.
3. The stage of the disease [(3)].

Diagnosis can often be made by non- invasive methods such as computerized axial tomographic angiography, magnetic resonance angiography, and duplex ultrasonography as well as by invasive catheter angiography [(4)]. Angiography was traditionally the gold standard for the diagnosis of intestinal ischemia. The development of multidetector row computed tomography (CT), however, has permitted detailed analysis of vascular flow that was never before possible [(5)].

The use of endovascular therapy for intestinal ischemia is predominantly limited to treatment of chronic form the disease [(5)].Various surgical techniques are available for splanchnic revascularization including transaortic endarterectomy, antegrade or retrograde bypass grafting, angioplasty with or without stenting [(6)].

PATIENTS AND METHODS

Search strategy

The PubMed and EBSCOHost electronic databases were methodically searched for English-language articles published between 1996 and 2015.

Inclusion Criteria

1. Only series with >10 patients undergoing endovascular therapy or open revascularization were used for data analysis.

Received: 9 / 8 /2017
Accepted: 18 /8 /2017
DOI : 10.12816/0041543

2. Studies including small numbers of patients presenting with acute on chronic ischemia or arcuate ligament syndrome were included, as it was not possible to identify and exclude these patients because the original studies did not differentiate patients on the basis of diagnoses.

Exclusion Criteria

1. Case reports were excluded to minimize possible bias in reporting only successful outcomes.
2. Population based studies were excluded as their data might have overlapped with the single center reports.
3. Studies reporting combined results for acute and chronic intestinal ischemia were excluded.

Data Extraction

Full length articles for all selected studies were evaluated by at least 2 reviewers. Data on age, presentation, procedure details, and outcomes were entered in an electronic database. The outcome definition was adopted from each individual study, and the number of patients was considered the denominator for all outcomes.

The outcomes extracted include:

1. 30-day mortality
2. Postoperative complications
3. Symptom improvement, and
4. Need for a secondary procedure.

Patency outcomes following surgery were documented at:

1. 6 months
2. 1, 2, 3, and 5 years
3. Mean follow-up.

Symptom recurrence following surgery was documented at 1 and 3 years and at mean follow-up. Assisted primary patency at 1 and 5 years following surgery and freedom from symptoms at 1, 2, and 5 years and at mean follow-up were also documented.

The study was approved by the Ethics Board of Ain Shams University.

Statistical Analysis for Meta Analysis

Data from all eligible studies were pooled for analysis. Weighted means were calculated.

As there have been appreciable methodological improvements in the past 2 decades and a significant increase in the numbers of patients receiving endovascular procedures in the last decade, the overall results for open and endovascular operations were analyzed by treatment type along with a comparison of results from 1996 to 2005 with outcomes from 2006 to 2015 for each treatment method.

Associations were tested with categorical analysis, reported as the odds ratios (OR) with the 95% confidence intervals (CI) or the absolute difference for variables with a 100% incidence (values may be negative in these cases). $P<0.05$ was considered to indicate a significant difference.

RESULTS

Examination of the 20-year literature on CMI identified 1939 patients (mean age 65 years) in whom abdominal pain (93.1%) was the most common presenting symptom **(Table 1).** The pain was postprandial in 84.3% of the patients and was associated with weight loss (76.1%), diarrhea (36.16%), nausea/vomiting (32.9%), and constipation (19.7%).

Patients undergoing open surgeries (**Table 2)** were significantly more likely to be smokers and less likely to have a history of diabetes, coronary artery disease, myocardial infarction, hypertension, hyperlipidemia, and renal insufficiency.

There was no statistically significant difference between the 2 groups with regard to age, angina, congestive heart failure, coronary artery bypass grafting, stroke, chronic obstructive pulmonary disease, hypercoagulable state, or peripheral vascular disease.

Of the 1163 patients (mean age 63.2 years) who underwent open surgery, 714 patients were operated upon between 2006 and 2015 and 449 between 1996 and 2005. Overall, 1.7 vessels per patient were revascularized (1.6 in the 2006-2015 period and 1.9 in the 1996-2005 period).

Overall mean follow-up was 43.8 months (34.9 for the latter decade and 57.9 for the former). Symptoms improved in 96.5% of the cases (94.4% in the latter decade and 99.6% in the former; **Table 3).** Complication and mortality rates were 32.7% and 5.6%, respectively, (34.7% and 4.5% from 2006-2015 and 28.6% and 7.4% from 1996-2005).

Based on the 13 studies that enumerated complications, respiratory sequelae were the most common, accounting for 40%, followed by cardiac (18%), infectious (16%), and renal (10%).

Table 1: clinical presentation of chronic mesenteric ischemia

Study	N/Mean Age, y	Abdominal Pain	Postprandial Pain	Weight Loss	Diarrhea	Nausea/ Vomiting	Constipation
Lee 2015	31/70	81%	84%				
Sarac 2014	65/70	95%		68%	26%		
Silva 2013	59/67	100%	78%	68%	22%	22%	
Sivamurthy 2012	60/66		82%	47%	39%		
Brown 2011	47/73	92%		75%			
Park 2010	98/66	97%		94%			
Cho 2009	25/64	100%		84%	32%	36%	
Leke 2008	17/—	100%		65%		47%	24%
Jimenez 2007	47/62	98%	85%	83%	64%		21%
Matsumoto 2006	33/63	70%	88%				
Farber 2005	18/64	78%		83%			
Mateo 2004	85/62	92%		87%	44%		17%
Kihara 2003	42/60	100%	93%	93%	40%	61%	10%
Moawad 2002	23/60	74%	78%	61%	30%	35%	17%
McMillan 2001	25/61	100%		84%	40%	25%	12%
Johnston 2000	21/58	100%		100%	57%		29%
Harward 1999	18/68	100%	100%	94%	61%	11%	11%
Calderon 1998	20/58.6	100%	80%	65%	40%	5%	
Cormier 1997	20/—	100%	100%	90%	60%		
Geelkerken 1996	14/42.9	100%	79%	75%			
Totals	1112/65.4	93.1%	84.3%	76.1%	36.2%	32.9%	19.7%

Table 2: comparison of risk factors

	Open (n)	Endovascular (n)	OR (95% CI)	p
Smoking	78.5% (715)	61.0% (402)	2.3 (1.78-3.05)	<0.001
Diabetes	9.1% (515)	15.1% (352)	0.6 (0.37-0.86)	0.007
CAD	37.5% (562)	58.9% (322)	0.4 (0.32-0.55)	<0.001
Angina	26.1% (172)	31.5% (67)	0.8 (0.41-1.43)	0.41
MI	24.7% (172)	38.6% (67)	0.5 (0.29-0.96)	0.04
CHF	23.9% (240)	19.5% (67)	1.3 (0.66-2.53)	0.46
CABG	13.9% (110)	4.0% (12)	3.9 (0.21-73.28)	0.37
Stroke	21.4% (123)	15.4% (78)	1.5 (0.70-3.16)	0.30
Hypertension	65.9% (726)	73.8% (335)	0.7 (0.52-0.92)	0.01
Hyperlipidemia	25.2% (561)	51.7% (341)	0.3 (0.24-0.42)	<0.001
Renal insufficiency	13.4% (555)	37.1% (367)	0.3 (0.19-0.36)	<0.001
COPD	21.2% (448)	17.2% (252)	1.3 (0.87-1.92)	0.2
Hypercoagulable state	5.8% (67)	6.0% (31)	1.0 (0.16-5.89)	0.98
PVD	50.8% (172)	42.4% (240)	1.4 (0.95-2.08)	0.09

Continuous data are presented as means; categorical data are given as percentages.

OR: odds ratio, CI: confidence interval, CAD: coronary artery disease, MI: myocardial infarction, CHF: congestive heart failure, CABG: coronary artery bypass grafting, COPD: chronic obstructive pulmonary disease, PVD: peripheral vascular disease.

Of the 776 patients (mean age 68.1 years) who underwent endovascular surgery, most 684 patients were treated from 2006 to 2015; 92 underwent treatment from 1996 to 2005. Overall technical success rates were 95.1% (95.6% in the 2006-2015 period and 92.1% in the 1996-2005 period), with 1.3 vessels per patient revascularized (1.3 in the 2006-2015 period and 1.4 in the 1996-2005 period). Overall mean follow-up was 25 months (25 in the 2006-2015 period and 27 between 1996 and 2005). Symptoms improved in 86.9% of the cases (87.8% in the 2006-2015 period and 81.5% in the 1996-2005 period). Overall complication and mortality rates were 13% and 4%, respectively (14.1% and 4.2% in 2006-2015 and 4.3% and 3.1% in 1996-2005). Analysis of complications based on 12 studies found that vascular sequelae (e.g., access site problems, pseudoaneurysms, and thromboses) accounted for —40% of total complications reported. Renal (12%), cardiac (9%), respiratory (8%), and neurological (8%) complications and bowel infarct/gangrene (8%) were also seen.

Examining the differences between open and endovascular treatments for CMI between 2006 and 2015 (Table 3), the odds of symptom improvement were 2.4 times higher for open surgery compared to endovascular repair.

On the other hand, the odds of complications for patients undergoing open surgery for CMI were 3.2 times higher than endovascular interventions.

The odds ratio for perioperative mortality for open versus endovascular was 1.09 (95% CI 0.7 to 1.8, p=0.75); however, this was not statistically significant. Moreover, the odds of vessel patency were 3.4 times greater in the open group (95% CI 2.0 to 6.0, p<0.001) at 1 year, 3.7 times greater (95% CI 2.2 to 6.0, p<0.001) at 2 years, and 3.8 times greater (95% CI 2.5 to 5.8, p<0.001) at 5 years.

The likelihood of having symptom recurrence at mean follow-up was 9.1 times higher for endovascular versus open treatment (95% CI to 14.3, p<0.001).

Assisted primary patency at 5 years was 6.4 times higher after open surgery than after endovascular surgery (95% CI 1.3 to 30.1, p=0.02).The rates for freedom from symptoms at 1, 2, and 5 years after treatment were also significantly higher for open compared to endovascular treatment.

For open and endovascular surgeries between 1996 and 2005, the results for symptom improvement, complications, and mortality (Table 3) were similar to those of the 2006 to 2015 timeframe.

The outcomes for patency, assisted primary patency, symptom recurrence, and freedom from symptoms were not significantly different for open versus endovascular operations performed in the 1996 to 2005 time period; however, this is likely due to very low numbers of patients available for analysis. The comparison of open surgery outcomes in the 2 time periods found more symptomatic improvement following surgery in the earlier decade compared to the latter **(Table 4).**

There were fewer complications, but a higher mortality. No statistically significant differences were seen for patency or freedom from symptoms at 5 years.

Among the endovascular procedures, those performed in the 1995-2005 period had a significantly lower postoperative complication rate and greater freedom from symptoms at 2 years.

However, it must be kept in mind that the comparison of each treatment mode between the 2 time periods was limited by the number of patients.

Table 3: comparison of open and endovascular surgery for CMI by decade

2006-2015	Open (n)	ndovascular (n)	OR (95%CI)	P
Number of patients	714	684	—	—
Mean vessels revascularized	1.6	1.3	—	—
Retrograde bypass	28.5%	—	—	—
Technical success	—	95.6%	—	—
Mean follow-up, mo	34.9	24.9	—	—
Symptom improvement	94.4%(578)	87.8% (594)	2.4(1.53 -3.63)	<0.001
Complications	34.7%(714)	14.1% (684)	3.2(2.48-4.20)	<0.001
Mortality	4.5%(714)	4.1% (684)	1.1(0.65-1.82)	0.75
Secondary procedure required Patency	7.5% (488)	31.0% (210)	0.2(0.12-0.28)	<0.001
6 months	83.0% (41)	68.0% (19)	2.3(0.65-8.12)	0.2
1 year	90.8%(185)	74.2% (399)	3.4(1.99-5.95)	<0.001
2 years	89.7%(252)	70.4% (222)	3.7(2.22-6.01)	<0.001
3 years	100.0%(35)	79.6% (92)	0.2*(0.12-0.29)	<0.001
5 years	80.4%(337)	52.2% (136)	3.76(2.45-5.79)	<0.001
At mean follow-up	91.4%(270)	78.5% (192)	2.92(1.69-5.05)	<0.001
Assisted primary patency				
1 year	96.0% (49)	85.7% (306)	3.99(0.92-17.28)	0.06
5 year	96.0% (47)	79.0% (82)	6.38(1.35-30.14)	0.02
Symptom recurrence				
1 year	22.4% (49)	21.7% (121)	1.04(0.47-2.31)	0.92
At mean follow-up	6.6% (439)	39.5% (189)	0.11(0.07-0.17)	<0.001
Freedom from symptoms				
1 year	89.3%(285)	68.2% (181)	3.9(2.39-6.35)	<0.001
2 years	71.0% (58)	53.0% (104)	2.18(1.10-4.32)	0.03
5 years	88.2%(324)	62.8% (164)	4.42(2.79-7.03)	<0.001
At mean follow-up	75.7%(111)	61.3% (128)	1.97(1.12-3.45)	0.02
1996-2005				
Number of patients	449	92	—	—
Mean vessels revascularized	1.9	1.4	—	—
Retrograde bypass	27.9%	—	—	—
Technical success	—	92.1%	—	—
Mean follow-up, mo	57.9	27.5	—	—
Symptom improvement	99.6%(396)	81.5% (92)	54.0(10.77-270.29)	<0.001
Complications	28.6%(338)	4.3% (92)	8.9(3.16-24.86)	<0.001
Mortality	7.4% (449)	3.1% (92)	2.5(0.72-8.43)	0.15
Patency at 3 years	78.0%(173)	89.0% (19)	0.4(0.10-1.93)	0.28
Patency at mean follow-up	86.3%(219)	82.6% (35)	1.3(0.51-3.45)	0.56
Symptom recurrence at mean follow-up Freedom from symptoms at mean	6.7%(132)	15.2% (41)	0.4(0.14-1.20)	0.1
Follow-up	96.0% (42)	100.0% (12)	0.04*(-0.02 to 0.1)	0.19

OR: odds ratio, CI: confidence interval. * Absolute difference.

Table 4: comparison of outcomes in the 2 time eriods by treatment method

Open	2006-2015	1996-2005	OR (95%CI)	P
Symptom improvement	94.4% (578)	99.6% (396)	14.0(2.93-66.81)	0.001
Complications	34.7% (714)	28.6% (338)	0.7(0.57-1.00)	0.05
Mortality	4.5% (714)	7.4% (449)	|1.7(1.02-2.79)	0.04
Patency				
3 years	100.0% (35)	78.0% (173)	-0.22*(-0.28 to-0.16)	<0.001
5 years	80.4% (337)	78.0% (24)	0.9(0.32-2.35)	0.77
At mean follow-up	91.4% (270)	86.3% (219)	0.6(0.33-1.05)	0.07
Symptom recurrence at follow-up	6.6% (439)	6.7% (132)	1.0(0.47-2.24)	0.95
Freedom from symptoms				
1 year	89.3% (285)	96.0% (74)	2.9(0.85-9.74)	0.09
5 years	88.2% (324)	83.1% (24)	0.7(0.21-2.02)	0.46
At mean follow-up	75.7% (111)	96.0% (42)	7.7(1.55-38.28)	0.01
Endovascular				
Symptom improvement	87.8% (594)	81.5% (92)	0.6(0.34-1.09)	0.1
Complications	14.1% (684)	4.3% (92)	0.3(0.10-0.77)	0.01
Mortality	4.1% (684)	3.1% (92)	0.7(0.22-2.55)	0.64
Patency				
1 year	74.2% (399)	74.0% (12)	1.0(0.27-3.66)	0.99
2 years	70.4% (222)	83.7% (38)	2.2(0.87-5.35)	0.1
3 years	79.6% (92)	89.0% (19)	2.1(0.45-9.51)	0.35
At mean follow-up	78.5% (192)	82.6% (35)	1.3(0.51-3.32)	0.59
Assisted primary patency at 1 year	85.7% (306)	83.0% (12)	0.8(0.17-3.79)	0.005
Symptom recurrence at mean follow-up	39.5% (189)	15.2% (41)	0.3(0.11-0.68)	0.79
Freedom from symptoms				
2 years	53.0% (104)	88.0% (23)	6.6(1.76-24.43)	0.005
At mean follow-up	61.3% (128)	100.0% (12)	0.39*(0.30-0.47)	<0.001

OR: odds ratio, CI: confidence interval. * Absolute difference.

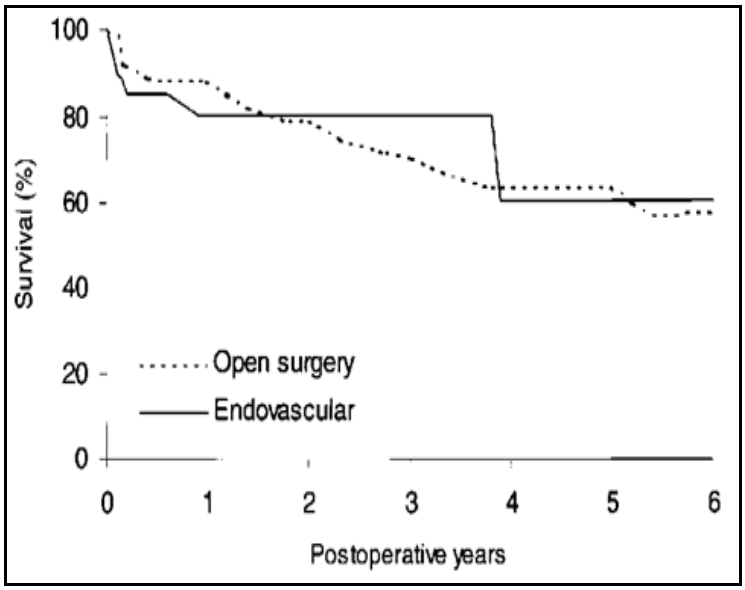

Figure 1: cumulative overall survival comparing open surgery treatment group with endovascular treatment group.

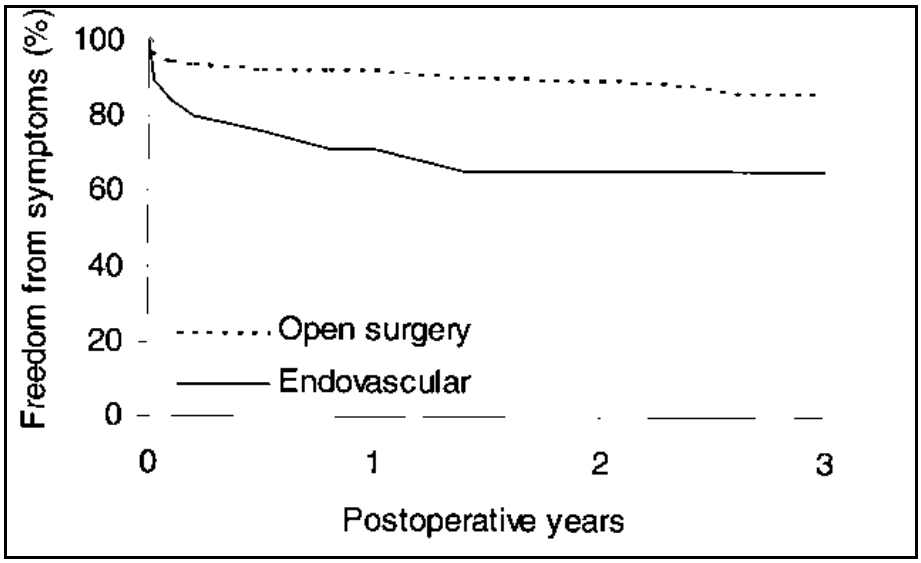

Figure 2: cumulative freedom from recurrent symptoms comparing open surgery treatment group with endovascular treatment group.

LIMITATIONS

This was a retrospective study analyzing previous studies, most of which were retrospective in design. Selection biases probably existed in the choice of procedures in the initial studies. While, clinical risk (demographic and comorbidities) was compared between open and endovascular surgeries, extent of disease and type of reconstruction (antegrade versus retrograde bypass, angioplasty versus stent, etc.) could not be compared as most studies did not report outcomes separately. While patency was defined as radio-graphic in most studies, the radiographic criteria varied.

CONCLUSION

Chronic mesenteric ischemia is a condition characterized by postprandial abdominal pain, which is ascribed to intestinal hypoperfusion. Patients were frequently malnourished and develop significant weight loss due to sitophobia. Traditionally, open surgery has been the treatment of choice; however, endovascular surgery was gaining wider acceptance. Based on the data, open surgeries surpass endovascular procedures in terms of symptom amelioration and long-term vessel patency, along with less significant symptomatic recurrence. Patients were undergoing open procedures do, however, had a higher rate of complications. Nonetheless, there was no statistically significant difference in mortality rates between the two approaches.

To date, there were no controlled trials showing the advantage of open surgery over the endovascular approach for CMI. Given the paucity of symptomatic patients, controlled studies are impractical. The preferred surgical technique used in treating this condition depends on the surgeon and the anatomy and physiology of each patient.

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