

Original Research Article

Predictors of mortality in acute mesenteric vascular ischemia with bowel gangrene

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Received: 06 September 2016

Accepted: 03 October 2016

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ABSTRACT

Background: Acute mesenteric vascular event can be thrombotic, embolic, vasospastic, or venous thrombosis. These patients present with nonspecific signs disproportionate to symptoms making early diagnosis difficult. Mortality remains high (30-100%). This prompted us to undertake this study to find predictors of mortality in these patients.

Methods: This was prospective non-study carried out at our tertiary referral hospital over defined period of 22 months during which all patients operated for acute mesenteric ischemic bowel gangrene were included. Variable data regarding demographics, clinical and biochemical parameters, operative findings and their association with mortality was recorded in predesigned case sheets. Chi-square test was applied to determine significance.

Results: Advanced age, presence of co-morbid conditions, delayed (>24 hours) presentation, hypotension, tachypnea, hypoxia, more than two system failures, more than three feet length of resected gangrenous bowel, < 100 cms of remnant viable bowel, need for second look surgery, complications of surgery and more than one mesenteric arterial involvement are negative predictors of mortality. Whereas laboratory parameters like haemoglobin, leucocyte count, serum creatinine and metabolic acidosis have no statistically significant correlation to mortality. Similarly presence of perforation of gangrenous intestine, ileocaecal resection, amount of contamination have no effect on mortality rate.

Conclusions: One of the reasons for persistent high mortality of this disease is its occurrence in higher age group and frequent association with comorbidities. Difficulties in diagnosis leads to delayed treatments; adding to mortality burden. Mesenteric angiography is underutilised diagnostic tool. Endovascular revascularisation procedures are not widely available and many patients are unsuitable due to clinical condition and risk of reperfusion injury. In presence of peritoneal signs and suspicion of disease urgent exploratory laparotomy is the gold standard.

Keywords: Acute mesenteric ischemia, Bowel gangrene, Mesenteric angiography, Mortality

INTRODUCTION

Patients with intestinal gangrene due to acute mesenteric vascular event/ischemia necessitating emergent surgery is one of the most commonly encountered surgical emergency at our tertiary care teaching hospital. This forms an important differential diagnosis of patients presenting to our emergency surgical department with 'acute abdomen' being third in order of frequency only after pancreatitis and gastrointestinal perforations. Acute mesenteric event could be embolic, thrombotic,

vasospastic or can be due to venous thrombosis.¹⁻³ Risk factors for embolic events are atrial fibrillation, rheumatic valvular heart disease, prosthetic valves, infective endocarditis. And those for thrombotic events which are more common are generalised atherosclerosis, hyperlipidaemia, diabetes mellitus and hypertension.⁴ Patients present with abdominal distention, vomiting with or without hematemesis and melena. They have signs of SIRS like tachycardia, tachypnea, hypotension, metabolic acidosis, leucocytosis etc. Often these patients pose a diagnostic challenge due to predominance of symptoms

and paucity of specific signs. High index of suspicion and aggressive investigation policy including contrast enhanced CT scan which has high sensitivity and specificity, is the key to achieve early diagnosis and execute prompt surgical treatment to limit morbidity and mortality in these patients.^{5,6} In spite of all attempts towards early diagnosis and treatment mortality in patients with acute mesenteric vascular ischemia leading to intestinal gangrene remains high.^{4,7,8} This high mortality rate prompted us to undertake this study to identify prognostic indicators of mortality in these patients to provide guidance for deciding management strategies.

The aim was to determine significant clinico-pathological prognostic factors which are determinants of mortality in patients with acute mesenteric vascular ischemia.

METHODS

Prospective observational non-interventional single centre study was done at department of general surgery at a tertiary care referral centre and teaching hospital. The study was done for 22 months. All patients of acute mesenteric vascular ischemia presenting primarily or being referred to our emergency surgical department over the study period (March 2012 to December 2014) were included which amounted to sample size of 64.

Quantitative data from all patients included was entered into Microsoft Excel sheets of Windows 2010 operating systems to generate a master chart. Outcome event was mortality. The results of variables were analysed using the Chi-square test of statistical significance. All statistical tests were interpreted at 95% confidence interval at 5% significance level. P-values less than 0.05 being considered statistically significant.

Inclusion criteria

Patients with acute or acute on chronic mesenteric vascular ischemia resulting in bowel gangrene who are

- Of either of the sex
- Above 18 years of age
- Presented primarily to us or referred from elsewhere but operated by us
- Diagnosed preoperatively or intraoperatively
- Diagnosed at autopsy for those who died prior to definitive surgery
- Willing to participate in the study by signing valid informed consent form.

Exclusion criteria

- Patients with bowel gangrene due to causes other than vascular events like arterial thrombosis, embolism, non-occlusive spasm or venous thrombosis

- Patients with bowel gangrene due to traumatic mesenteric tears
- Patients with bowel gangrene due to iatrogenic injury to mesenteric vessels
- Patients with chronic mesenteric vascular ischemia compensated by collateral circulation who do not progress to have bowel gangrene
- Patients younger than 18 years
- Patients unwilling to participate
- Pregnant and lactating females.

Methods

After due approval from institutional ethics committee the recruitment of patients started.

All the patients with bowel gangrene due to acute mesenteric vascular ischemia who satisfied inclusion criteria were included in the study. Informed valid consent was obtained by all participants after explaining in depth study purpose, procedures, risk involved etc. in their own language.

Study procedures included detailed history and clinical examination of patients and recording of parameters / variables in case record forms. Blood investigations and radiological imaging like x-rays, USG and CT scans were performed as per routine practice. Findings of these tests entered in the case record form as well. All patients received broad spectrum antibiotic and anaerobic cover. Necessary resuscitative measures like rehydration with crystalloid infusion, supplemental oxygen, correction of metabolic acidosis by bicarbonate and restoration of organ perfusion by correction of hypotension, correction of coagulation deficiencies and anaemia were carried out as per standardised protocols in preoperative preparation of patient. After adequate optimisation of physiology, patients underwent exploratory laparotomy through midline incision under general anaesthesia. All patients were operated by on call consultant assisted by surgical resident doctors. Surgical procedures were carried out depending upon the site and extent of bowel gangrene, residual bowel perfusion and oedema and patient's hemodynamic status. Surgical procedures included resection of gangrenous nonviable bowel followed either by anastomosis or diversion procedures like stoma.

Some patients required re-look or second-look surgery for resection of additional length of bowel which evolved into gangrene after primary surgery, a phenomenon well known in patients with mesenteric ischemia. In such patients length of gangrenous bowel was recorded as addition of length of bowel resected at both the surgeries and residual bowel length was calculated after last surgery. In patients undergoing diversion stomas length of residual small intestine was taken as distance of stoma from duodeno-jejunal flexure as distal length was not available for absorption of nutrients. All this data was also entered in case record forms and analysed statistically to derive conclusions.

Studied variables**Demographic parameters**

- Age
- Sex
- Addictions
- Co-morbidities like diabetes, hypertension, IHD, asthma, COPD etc
- Simultaneous presence of more than 2 co-morbid conditions.

Clinical parameters

- Stage of presentation
Early: < 24 hours of onset of symptoms
Late: > 24 hours of onset of symptoms
- Tachycardia: < 120 / min and > 120/ min
- Respiratory rate: < 26/min and > 26/min
- Hypotension: < 90 mm of Hg and > 90 mm of Hg
- Refractory hypotension :
< 90 mm of Hg after 2 lit of intravenous crystalloid infusion.
> 90 mm of Hg after 2 lit of intravenous crystalloid infusion

Laboratory parameters

- Leucocytosis: < 20,000/cmm and > 20,000/cmm
- Haemoglobin: < 8 gm% and > 8 gm %
- Metabolic acidosis: HCO_3^- > 18 and < 18
- Hypoxia PaO_2 : < 60 and > 60
- Serum creatinine: < 3.0 and > 3.0
- More than two system failures: yes or no

Operative finding

- Length of gangrenous bowel: < 3 feet and > 3 feet
- Length of remnant small intestine beyond DJ flexure: < 100 cms and > 100 cms
- Ileocaecal junction resected: Yes or No
- Perforation of gangrenous bowel present: Yes or No
- Amount of peritoneal contamination: < 1000 ml and > 1000 ml
- Two or more mesenteric vessels blocked: Yes or No
- Need for second look surgery
- Complications of surgery
- Postoperative period of mechanical ventilation : 0-2 days or > 2 days.

RESULTS

Overall mortality rate in our series of patients with ischemic bowel disease was 46.87%. Out of total sample size of 64, there were 30 (46.87%) patients below 60 years of age of whom 8 (26.66%) died. Rest 34 (53.12%) patients were above 60 years of age of which 22 (64.7%) died and this difference in mortality; higher in age group above 60 was statistically significant (Table 1).

Out of 42 (65.62%) males in study population 19 (45.23%) died whereas of the total 22 (34.37%) women in the study death rate was 50% (11 females). But this difference was statistically non-significant. Out of 64 patients, 35 (54.68%) had addictions in whom mortality rate was 51.42% and in 29 patients which make (45.31%) who did not have any addiction, death rate was 41.37%. This difference was not found to be statistically significant (Table 1).

Table 1: Comparison of demographic parameters and mortality.

Variables	No. of patients N = 64 (%)	Mortality N = 30 (%)	Chi square value	P value
Age (years)				
18 – 60	30 (46.87)	08 (26.66)	6.533	p < 0.05*
61 and above	34 (53.12)	22 (64.7)		
Sex / gender				
Males	42 (65.62)	19 (45.23)	2.133	p > 0.05
Females	22 (34.37)	11 (50)		
Addictions				
Present	35 (54.68)	18 (51.42)	1.200	p > 0.05
Absent	29 (45.31)	12 (41.37)		
Co-morbid conditions				
Absent	06 (9.37)	02 (33.33)	22.53	p < 0.05*
Present	58 (90.62)	28 (48.27)		
More than 2 Co- morbid conditions				
Present	32 (50)	21 (65.62)	4.8	P < 0.05*
Absent	26 (40.62)	09 (34.61)		

* p < 0.05 is statistically significant.

Majority that is 58(90.62%) of the patients had one or more of the comorbid conditions like diabetes, hypertension, ischemic heart disease, asthma, COPD etc. Of this group of patients 28 (48.27%) died whereas in the other group of patients free of any comorbid condition mortality was 2 out of 6(9.37%) and the rate was (33.33%). This difference was statistically significant.

In the comparison of mortality in the group of patients with less than 2 and more than two concomitant comorbidities the death rate 34.61% (9 out of 32 patients) which was lesser compared to 65.62% (21 out of 32 patients) respectively and the difference was statistically significant (Table 1).

Mortality rate was higher (95.65%) in 23 (35.93%) patients who presented late compared to 19.51% death rate in 41 (64.06%) patients presenting early and this difference was statistically significant (Table 2). 31 (51.56%) patients had tachycardia of more than 120/min of whom 20 (64.51%) died as compared to 10(30.3%) patients dying in the other group of 33 (51.56%) patients with pulse rate less than 120/min. Thus mortality was more in patients with tachycardia > 120/min though this difference could not attain statistical significance. In subgroup of patients with systolic BP > 90 mm Hg mortality rate was 9 out 34 that is 26.47% and that in other group of patients with systolic BP < 90 was 21 out of 30 patients, that is (70%) which was higher and was statistically significant.

Table 2: Comparison of clinical parameters and mortality.

Parameters	No. of patient N = 64 (%)	Mortality N = 30 (%)	Chi square value	p value
Stage of peritonitis/ delay (in presentation)				
Early < 24 hours	41 (64.06)	8 (19.51)	6.533	< 0.05*
Late > 24 hours	23 (35.93)	22 (95.65)		
Tachycardia				
< 120 beats/ min	33 (51.56)	10 (30.30)	3.333	> 0.05
> 120 beats/min	31 (48.43)	20 (64.51)		
Hypotension				
Systolic BP > 90 mm Hg	34 (53.12)	9 (26.47)	4.8	< 0.05*
Systolic BP < 90 mm Hg	30 (46.87)	21 (70)		
Tachypnea (respiratory rate)				
< 26 /min	48 (75)	21 (43.75)	4.8	< 0.05*
> 26 /min	16 (25)	9 (56.25)		
Refractory hypotension (systolic BP after 2 lit. of IV crystalloid infusion)				
> 90 mm Hg	53 (82.81)	21 (39.62)	4.8	p < 0.05*
< 90 mm Hg	11 (17.18)	9 (81.81)		

Total no. of patients; 64 p value < 0.05 is significant.

11 (17.18%) patients had refractory hypotension of whom 9 patients that is (81.81%) died which was higher than 39.62% (21 out of 53 patients) dying who did not have refractory hypotension and this difference was proven to be statistically significant. 56.25% of the patients with respiratory rate of >26/min died compared to 43.75% (lesser) in patients with respiratory rate of less than 26/min. This difference was statistically significant (Table 2).

Mortality rate was 43.48% and 52% in the patient with Haemoglobin of more than and less than 8 gm% respectively but this difference was statistically insignificant. Mortality was 48.14% and 45.94% in patient subgroups with leucocytosis of less than and more

than 20000/cmm respectively which was statistically insignificant. Mortality rate was 46.66% in patients who had serum creatinine of less than 2 as against 47.05% in those with creatinine more than 2 which statistically insignificant.

All the 24 patients who had PaO₂ lesser than 60 died (100%) compared to lesser proportion (15%) in the group with PaO₂ greater than 60 and this difference was statistically significant. 29.26% of the patients with HCO₃ more than 18 died compared to 78.23% in those with HCO₃ less than 18; but this difference was statistically insignificant. In subgroup of patients with more than 2 system failures mortality was 62.5% compared to 20.83% in the other and this difference was statistically significant (Table 3).

Table 3: Comparison of laboratory parameters and mortality.

Parameters	No. of patients N = 64 (%)	Mortality N = 30 (%)	Chi square value	p value
Haemoglobin				
> 8 gm%	39 (60.93)	17 (43.48)	0.532	p > 0.05
< 8 gm%	25 (39.06)	13 (52)		
Leucocytosis				
< 20,000/cmm	27 (42.18)	13 (48.14)	0.532	p > 0.05
> 20,000/cmm	37 (57.81)	17 (45.94)		
Serum creatinine				
< 2.0 mg%	30 (46.87)	14 (46.66)	1.332	p > 0.05
> 2.0 mg%	34 (53.13)	16 (47.05)		
Hypoxia				
PaO ₂ > 60	40 (62.5)	6 (15)	10.8	p < 0.05*
PaO ₂ < 60	24 (37.5)	24 (100)		
Metabolic acidosis				
HCO ₃ ⁻ > 18	41 (64.06)	12 (29.26)	1.2	p > 0.05
HCO ₃ ⁻ < 18	23 (35.93)	18 (78.23)		
More than 2 system failures*				
Yes	40 (62.5)	25 (62.5)	13.332	p < 0.05*
No	24 (37.5)	5 (20.83)		

Total no. of patients: 64 significant p value < 0.05; *System failures is considered when serum creatinine is >2.0 mg%; PaO₂ <60 mm hg or Systolic BP < 90 mm Hg.

Table 4: Comparison of operative findings and mortality:

Parameters	No. of patients N = 64 (%)	Mortality N = 30 (%)	Chi square value	p value
Length of intestinal gangrene				
< 3 feet	21 (32.81)	08 (38.09)	6.533	< 0.05*
> 3 feet	43 (67.18)	22 (51.16)		
Length of remnant small intestine beyond DJ flexure				
< 100 cms	19 (29.68)	06 (31.57)	10.8	< 0.05*
> 100 cms	45 (70.31)	24 (53.33)		
Ileocaecal junction resected				
Yes	39 (60.93)	20 (51.28)	3.333	> 0.05
No	25 (39.06)	10 (40)		
Ischemic intestinal perforation				
Absent	30 (46.87)	15 (50)	0.000	> 0.05
Present	34 (53.13)	15 (44.11)		
Amount of peritoneal contamination				
< 1000 ml	40 (62.5)	19 (47.5)	2.133	> 0.05
> 1000 ml	24 (37.5)	11 (45.83)		
Need for second look surgery				
Yes	09 (14.06)	07 (77.77)	8.533	< 0.05*
No	55 (85.93)	23 (41.81)		
Complications of surgery				
Yes	10 (15.62)	06 (60)	10.8	< 0.05*
No	54 (84.37)	24 (44.44)		
No. of days of mechanical ventilation required postoperatively				
0 -2 days	40 (62.5)	10 (25)	3.332	> 0.05
> 2 days	24 (37.5)	20 (83.33)		
No. of Mesenteric arteries involved				
Single	51 (79.68)	21 (41.17)	4.8	< 0.05*
Two or all three	13 (20.31)	09 (69.23)		

Total no. of patients studied; 64 p value < 0.05 is considered significant.

Mortality in patients with peritoneal contamination less than 1000 ml was 47.5% and that with contamination more than 1000 ml was 45.83% which was insignificant statistically. 7 out of 9 patients (77.77%) who needed second look surgery expired compared to 23 out of 55 of those (41.51%) who did not; and this was significant statistically. 60% of the patients who developed complications of the surgery expired compared to 44.44% who did not. This difference was statistically significant. Mortality rate in patients requiring postoperative mechanical ventilation more than 2 days was (83.33%) higher than those requiring the same for less than 2 days (25%). But this was not statistically significant difference. 51(79.68%) patients had single arterial disease of which 21(41.17%) died and of the 18(20.31%) patients who had two or all three mesenteric arteries involved 9(69.23%) died which was statistically significant difference (Table 4).

DISCUSSION

Mortality rate of acute mesenteric ischemia ranges from 30-100% in the scientific literature. In our study we found it to be 46.87%.^{3,9} This disease usually affects patients in higher age group who have multiple comorbid conditions⁴ and both advanced age and presence of comorbid conditions, especially more than one simultaneously are the significant risk factors adversely affecting mortality in our study which is consistent with most of the other studies.^{4,6,7,10} Both these factors are synergistic but independent determinants of mortality. Gender and presence or absence of addictions have no influence as per our study on mortality rates.

Another significant factor deciding mortality was delay in presentation to emergency department after beginning of symptoms which ultimately decides delay of definitive surgical intervention.^{1,11} Kassahun et al reported survival rate of 50% in patients diagnosed within first 24 hours and less than 30% in those presenting after 24 hours of symptoms.¹² Majority of the times the delay in presentation to our tertiary referral centre was due to delayed referral from other hospitals due to diagnostic dilemma. Thus early admission and early diagnosis⁴ and treatment before gangrene sets in or progresses is vital for favourable outcome. But same might be difficult to achieve as some of the complications of acute mesenteric ischemia like ileus, peritonitis, gastrointestinal haemorrhage, pancreatitis may mask the signs and delay diagnosis.¹³

Though CT angiography has very good; sensitivity to detect mesenteric ischemia invasive angiography is the gold standard for detecting early ischemia.⁵ It also has important therapeutic roll of revascularisation by embolectomy or catheter guided thrombolytic agent, anticoagulants or papaverin administration to prevent or limit the extent of gangrene. But in practice there are limitations to use these techniques as they are not

available easily and many patients may not be suitable for them. Bradbury et al suggested that in presence of signs of peritonitis mere suspicion of mesenteric vascular ischemia should be enough to lead to decision of emergent laparotomy without any further delay in imaging.¹⁴ Moreover delayed revascularisation poses risk of reperfusion injury.

In our study we found that clinical parameters like hypotension tachypnea, refractory hypotension and hypoxia were strong negative prognostic factors and they all independently were mortality predictors. Whereas tachycardia did not have significant correlation to mortality rate. Presence of more than 2 system failures was also a significant predictor of mortality in our study.¹¹ But laboratory values like haemoglobin, leucocyte count, serum creatinine and bicarbonate levels had no roll as per our study in mortality prediction. We could not study the correlation of serum lactate levels as facility was not available at our centre though it is significant factor reported in study by Kougias P et al.¹ D-dimer as a marker of thrombotic activity has also been proposed by Altinyollar H et al based on experimental animal models for early diagnosis of mesenteric ischemia.¹⁵

Length of gangrenous intestine and length of remnant small intestine both were found to be significant factors deciding mortality (negative and positive predictor respectively). Inclusion of right colon in resection was negative prognostic factor according to reports by Merida A et al though our results did not confirm to that.¹⁰

Presence of perforation of gangrenous intestine and the amount of peritoneal contamination did not have any mortality predictive value in our study results. More than one mesenteric artery involvement resulted in comparatively higher mortality; thus proving it's predictive value for mortality which could be merely due to the fact that more the no. of arteries involved wider would be the extent of gangrene and resection required and also the collateral circulation would be ineffective in maintain intestinal viability. Complications of surgery like pneumonia, deep venous thrombosis, anastomotic dehiscence, intraperitoneal abscesses etc. had negative predictive value for mortality. Period of postoperative mechanical ventilation had no mortality prediction value as per our study.

Thus to sum up mortality in acute mesenteric ischemia is high and has largely remained unchanged.^{7,8} Looking at above predictors, it is utmost important to diagnose and treat these patients early before system failures set in. Diagnostic and therapeutic selective mesenteric angiographic interventions have a great potential in reducing mortality rates in selected patient population.¹⁰ Surgeon should have high index of suspicion and low threshold for exploratory laparotomy in suspected cases with peritoneal irritation signs.¹⁴ Many patients land up

having short bowel syndrome with resultant nutritional, immunological complications and dependence on parenteral nutrition which is challenging to manage.^{13,16}

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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Cite this article as: Dhamnaskar SS, Sawarkar PC, Mandal S, Vijaykumaran P. Predictors of mortality in acute mesenteric vascular ischemia with bowel gangrene. *Int Surg J* 2016;3:1996-2002.