

Diaphragm disease in emergency surgery

Abstract

Background/Aims Diaphragm disease of the small bowel has been described in the literature over the last three decades. The pathognomonic characteristic of multiple circumferential stenosis is noted on gross examination of the bowel. It is a severe form of non-steroidal anti-inflammatory drug-induced enteropathy, often presenting as acute small bowel obstruction. A systematic review was performed to identify risk factors and patient outcomes in histologically-proven diaphragm disease of the small intestine in patients undergoing emergency operation for small bowel obstruction.

Methods A comprehensive search was performed between January 1975 and March 2019 using relevant MeSH terms. Studies were chosen based on predefined inclusion criteria. Diaphragm disease of the small intestine was defined as macroscopically detected thin diaphragm-like mucosal folding inside the lumen of the bowel. The parameters assessed included patient characteristics, duration of use of non-steroidal anti-inflammatory drugs, type of emergency surgery performed, complications, recurrence, presentation and diagnosis of diaphragm disease.

Results A total of 21 studies were analysed which included 17 case reports, one case series, and three retrospective comparative studies. Overall 29 patients with diaphragm disease of the small bowel were reported following emergency laparotomy for small bowel obstruction. Use of non-steroidal anti-inflammatory drugs was noted in all cases with an average duration of 3–5 years. All patients presented acutely with features of small bowel obstruction and had emergency laparotomy, except one who underwent laparoscopic resection. In the comparative studies patients were more likely to be female and to have been taking non-steroidal anti-inflammatory drugs for more than 7 years.

Conclusions This is a rare disease, difficult to diagnose and often confirmed by the intra-operative macroscopic appearance of circumferential stenosis of the bowel. Risk factors for developing small bowel diaphragm disease include long-term use of non-steroidal anti-inflammatory drugs, and female gender. Patients with this disease are at increased risk of developing acute small bowel obstruction, so early identification is important.

Key words: Diaphragm disease; Emergency surgery; Non-steroidal anti-inflammatory drug-induced enteropathy; Small bowel obstruction

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Introduction

Patients who have been taking non-steroidal anti-inflammatory drugs for analgesia over a long period are at a higher risk of developing non-steroidal anti-inflammatory drug-induced enteropathy, one manifestation of which is diaphragm disease of the small bowel. This condition is difficult to diagnose on presentation and definitive diagnosis relies on the histopathology of the resected specimen showing features of mucosal infolding in the lumen of the bowel forming a diaphragm and causing obstruction.

First described by Lang et al (1988) diaphragm disease of the small bowel is thought to be caused by a combination of inflammatory response, fibrosis and mucosal remodelling within the lumen of the small bowel which has been exposed to long-term non-steroidal anti-inflammatory drugs. This is a rare benign condition with pathognomonic histological characteristics. Long-term ongoing vague abdominal symptoms followed by acute presentation with florid small bowel obstruction is usual for the disease. A systematic review was performed with respect to the presentation with bowel obstruction and treatment with emergency surgery.

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Materials and methods

Data sources

A comprehensive search for all articles published between 1 January 1975 and 1 March 2019 was performed using MEDLINE, Embase, CINAHL, Ovid and Cochrane databases. A combination of the following terms was used for the search: ‘Diaphragm disease’, ‘NSAIDs enteropathy’, ‘Small bowel obstruction’, ‘Small bowel resection’, ‘NSAID-induced complications’. Both plain text and MeSH terms were used in the search to maximise results.

Study selection

All studies that reported diaphragm disease were included. Abstracts presented in conferences, reviews, technical papers and non-English papers where an English translation was not obtainable were excluded. The diagnosis of diaphragm disease was based on the histopathology of the resected small bowel specimen.

Data extraction

Data were extracted and assessed independently by both authors. In case of any disagreement, the in-house statistician was asked to review the study to reach a consensus. The PRISMA guidelines were followed (Figure 1). After combining the above terms, the abstract of each study was analysed. The full texts of the studies identified by the above selection criteria were obtained and carefully scrutinised, and the references of these studies were cross-checked for any other possible articles.

Statistical analysis

The mean patient characteristics were synthesised by calculating raw weighted means. Incidence was described in percentages. In the meta-analysis, the Mantel–Haenszel statistical method with a random effects model was selected for dichotomous data while

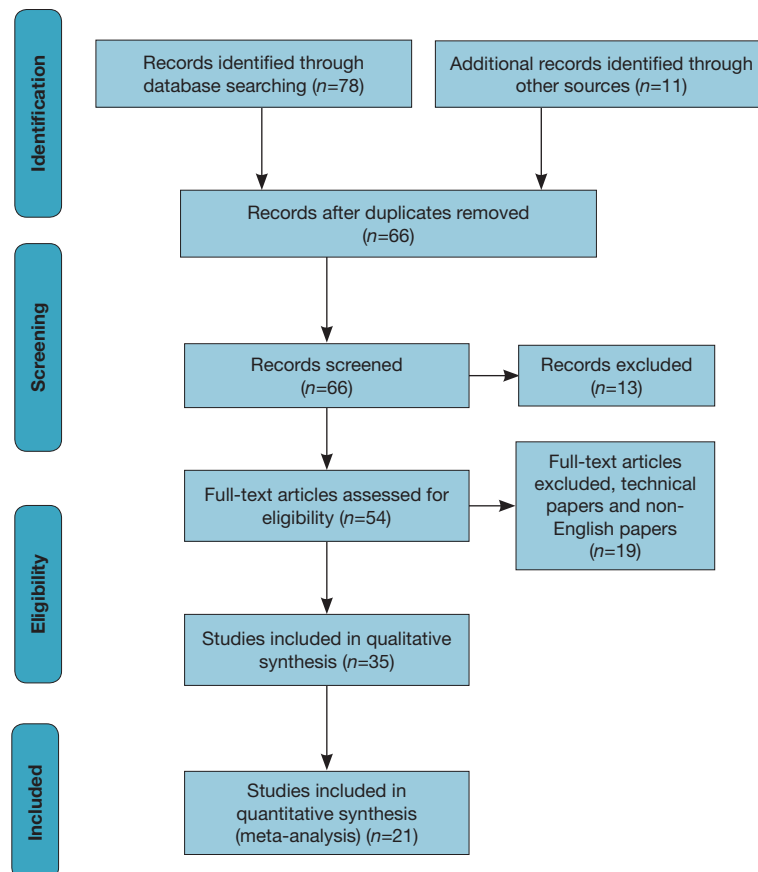


Figure 1. PRISMA flowchart.

inverse variance method with a random effects model was selected for continuous data. These models account for the variation of sample size and heterogeneity of the different studies. Effect was estimated using odds ratios for dichotomous values and mean difference for continuous data; 95% confidence intervals were measured wherever possible. Where standard deviation values were not available, imputed values for standard deviation were used. These values were tested in a sensitivity analysis. All *P* values are two-sided and considered statistically significant at a value of less than 0.05. Heterogeneity across the trials was assessed using Cochrane's *Q* statistics (χ^2) ($P < 0.1$) and I^2 statistics. This measures the proportion of overall variation attributable to inter-study heterogeneity. A high I^2 estimate indicates the presence of high heterogeneity. The publication bias was assessed with funnel plots.

Results

A total of 21 studies met the inclusion criteria (Figure 1). There were 17 case reports, one case series, and three retrospective comparative studies (Table 1). Not all studies commented on all known pre-existing factors for diaphragm disease of the small bowel, for example duration of drug history; therefore, selection and reporting bias may have been present.

Pooled analysis

There were 29 cases of diaphragm disease of the small bowel, the majority of which involved the ileum (83%), with 17% involving the jejunum. All the cases presented with small bowel obstruction and diagnosis was made retrospectively from the histology in all cases. The most common operation performed was laparotomy and small bowel resection, one patient (3%) had laparoscopic resection, one patient (3%) had additional stricturoplasty and one patient (3%) had a right hemicolectomy. Six cases did not report the patient demographics (age, sex). A total of 29 patients were identified with a median age of 66 years, and the median duration of non-steroidal anti-inflammatory drug usage in these patients was 7 years (not reported in three cases).

Meta-analysis

Pooling these studies, seven patients with diaphragm disease of the small bowel presenting with bowel obstruction were compared to an equal number of patients presenting with small bowel obstruction from other causes. There was no difference in the mean age and sex between the two groups. The length of stay and recovery time was shorter in the group diagnosed with diaphragm disease.

Discussion

Acute surgical admission and abdominal surgery throws up a plethora of different diagnoses. Increased use of non-steroidal anti-inflammatory drugs has seen a rise in the number of cases of surgical pathologies caused by these drugs. As diaphragm disease presents as a small bowel obstruction it is important to elicit a history of non-steroidal anti-inflammatory drug use in patients with obstructive symptoms. A variety of imaging techniques can be used to help with diagnosis (including computed tomography scans, magnetic resonance imaging, enteroclysis, capsule endoscopy), but many patients with an acute abdomen require urgent laparotomy, although laparoscopic assessment is preferred if this is technically feasible. Chernoleskiy et al (2010) describe a laparoscopic approach in their case report, which is probably a better option to consider in patients presenting with chronic symptoms. A small number of studies describe the intraoperative diagnostic dilemma; there can be vague features of terminal ileal thickening that mimic inflammatory bowel disease, hence reports of right hemicolectomy being performed in the cases described by Kwo and Tremaine (1995). Stricturoplasty was used successfully by Speed et al (1994) when there was a preoperative suspicion of intraluminal small bowel pathology.

The pathogenesis of the disease is uncertain. The most common pathologies noted are enteropathy as a result of enterocyte injury, fibrosis, subcellular injury and mucosal barrier

Table 1. Study details

Study	No of patients	Age (years)	Gender (M:F)	Duration of NSAID use (years)	Site of disease	Surgery	Mortality
Neoptolemos and Locke (1983)	1	73	F	3	Ileum	Laparotomy and resection	0
Saverymuttu et al (1986)	1	53	F	8	Ileum	Laparotomy and resection	0
Sukumar (1987)	1	75	F	2	Ileum	Laparotomy and resection	0
Lang et al (1988)	7	70 (median)	4:3	5 (median)	Ileum	Laparotomy and resection	1
Fellows et al (1992)	1	69	F	5	Jejunum	Laparotomy and resection	0
McCune et al (1992)	1	62	F	12	Ileum	Laparotomy and resection	0
Matsuhashi et al (1992)	1	30	F	3	Ileum	Laparotomy and resection	0
Speed et al (1994)	1	42	F	10	Ileum	Laparotomy, resection and stricturoplasty	0
Kwo and Tremaine (1995)	1	35	F	2	Ileum	Laparotomy and right hemicolectomy	0
McGonigal et al (1997)	1	78	F	3	Ileum	Laparotomy and resection	0
O'Bichere and Campbell (1999)	1	–	M	–	Ileum	Laparotomy and resection	0
Crowther and Mathews (2000)	1	67	M	–	Jejunum	Laparotomy and resection	0
de Sanctis et al (2001)	1	76	F	–	Ileum	Laparotomy and resection	0
Santolaria et al (2001)	1	54	M	–	Jejunum and ileum	Laparotomy and resection	0
Onwudike et al (2002)	1	75	M	5	Ileum	Laparotomy and resection	0
Zhao et al (2005)	1	75	F	20	Jejunum	Laparotomy and resection	0
Moffat et al (2006)	1	54	F	2	Ileum	Laparotomy and resection	0
Velchuru et al (2006)	2	69 (median)	1:1	–	Ileum	Laparotomy and resection	0
Lapner and Stephen (2007)	1	52	F	6	Ileum	Laparotomy and resection	0
Chernolesskiy et al (2010)	1	52	M	8	Jejunum	Laparoscopic resection	0
Pilgrim et al (2011)	2	66 (median)	1:1	3 (median)	Ileum	Laparotomy and resection	0

All studies were retrospective and all cases presented with small bowel obstruction. Continuous data are reported as mean values. NSAID = non-steroidal anti-inflammatory drug.

breakdown, resulting in an inflammatory response leading to circumferential ulceration (Zhao et al, 2005; Velchuru et al, 2006; Chernoleskiy et al, 2010). Ulceration caused by cyclo-oxygenase 1 (COX-1) inhibition leading to micro-ischaemia is believed to be the initial step in the formation of the ‘diaphragms’ described as circumferential stenotic lesions (Zhao et al, 2005). The disease process is restricted to the mucosa; the other layers of the bowels are not affected. The most common location of the disease in the small bowel is the ileum. Detailed review of the studies does not demonstrate any differences in histological characteristics in patients on COX-1 inhibitors compared to those of patients taking other non-steroidal anti-inflammatory drugs. Microscopic images reveal mucosal ulceration at the apex of the diaphragms, thickening of the muscularis mucosae with a disorganised arrangement of the muscular bundles and fibrosis of the lamina propria, similar to the description of Lang et al (1988).

Surgery remains the cornerstone of management of these patients, who often are elderly, taking long-term non-steroidal anti-inflammatory drugs and have multiple other comorbidities. Once the offending small bowel is resected there have been no reports of recurrence. There is value in trying to prevent this disease developing by restricting the use of non-steroidal anti-inflammatory drugs. This article has highlighted this rare disease, its presentation and associated risk factors, emphasising the need for thorough evaluation of the risks and benefits of non-steroidal anti-inflammatory drugs and their long-term possible side effects.

Conclusions

Diaphragm disease of the small intestine is a rare form of disease, difficult to diagnose and often noted and confirmed by the intraoperative macroscopic appearance of circumferential stenosis of the bowel. It is a morbid and potentially fatal complication of long-term use of non-steroidal anti-inflammatory drugs. Increased awareness of the condition and careful use of non-steroidal anti-inflammatory agents will help earlier diagnosis. Women and patients on long-term non-steroidal anti-inflammatory drugs are at a high risk of developing diaphragm disease of the small bowel. Patients on non-steroidal anti-inflammatory drugs with ongoing chronic vague abdominal symptoms should be assessed for diaphragm disease as a part of excluding non-steroidal anti-inflammatory drug-induced enteropathy and prompt treatment should be initiated.

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Conflicts of interest

The authors declare no conflicts of interest.

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Key points

- Diaphragm disease is a rare but clinically important cause of small bowel obstruction.
- Early diagnosis of the condition and urgent surgical intervention leads to a better patient outcome.
- Often encountered in patients on long-term non-steroidal anti-inflammatory drugs, with characteristic circumferential stenosis, surgical excision is the treatment of choice for diaphragm disease.
- This systematic review highlights the associated factors, commonest presenting features and effective treatment modalities in clinical practice.

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