Sunday, 1 Dec. 2019

MASTERCLASS

09.00
When the appendix plays nasty: intraoperative surprises, immediate solutions, and long-term treatment options
Justin Davies, Cambridge, UK

09.40
All the secrets of the pelvic floor - common disorders and proven solutions
Julie Cornish, Cardiff, UK

10.20
taTME in 2020 – when the dust settles: current and innovative indications, implementation, and practical advices
Roel Hompes, Amsterdam, NL

11.30
Complete mesocolic excision: indications, surgical approaches, and pitfalls
Paris Tekkis, London, UK

12.10
The views of an Editor and the wisdom of an Expert: contemporary publications with the potential to change and improve practice
Neil Mortensen, Oxford, UK

14.00
To ostomize or not and when? The value and downside of a diverting stoma versus virtual ileostomy versus no stoma
Gabriela Möslein, Wuppertal, DE

14.40
Extended lymph node dissection: indications, surgical anatomy, and technical approaches
Peter Sagar, Leeds, UK

15.20
Is the longer the new better - how to safely extend the interval after neoadjuvant chemoradiotherapy prior to surgery for rectal cancer
Ronan O'Connell, Dublin, IE

16:30
The colorectal anastomosis: time-proven wisdom, innovative configurations, and salvage techniques
André d'Hoore, Leuven BE

17.10
All you need to know about stomas but never dared to ask
Willem Bemelman, Amsterdam, NL

17.50
The EBSQ Coloproctology Examination
Michel Adamina, Winterthur, CH

18.00
Wrap-up
Michel Adamina, Winterthur, CH

Monday, 2 Dec. 2019

SCIENTIFIC PROGRAMME

09.45
Opening and welcome
Jochen Lange, St.Gallen, CH

10.00
Pathophysiology and non-operative management of symptomatic uncomplicated diverticular disease
Robin Spiller, Nottingham, UK

10.30
Surgery of acute diverticulitis – evidence, eminence and real life
Willem Bemelman, Amsterdam, NL

11.00
Management of atypical diverticulitis
Dieter Hahnloser, Lausanne, CH

11.30
Hartmann reversal: open, laparoscopic or transanal?
Roel Hompes, Amsterdam, NL

13.30
The surgeon personality – influence on decision making, risk-taking and outcomes
Desmond Winter, Dublin, IE

14.00
SATELLITE SYMPOSIUM Medtronic

15.00
Clinical applications of image-guided cancer surgery
Cornelis van de Velde, Leiden, NL

16.00
Volvulus of the colon – a treatment algorithm
Peter Sagar, Leeds, UK

16.30
Hereditary colorectal cancer syndromes: tailored surgical treatment
Gabriela Möslein, Wuppertal, DE

17.00
Lars Pahlman and Herand Abcarian (2015)
Herand Abcarian, Chicago, US

17.20
Lars Påhlman Lecture
Steven Wexner, Weston, US

Tuesday, 3 Dec. 2019

09.00
Robotic-assisted versus conventional laparoscopic surgery for rectal cancer
Amjad Parvaiz, Poole, UK

09.30
Robotic multivisceral resection
Paris Tekkis, London, UK

10.00
SATELLITE SYMPOSIUM Karl Storz

11.30
Neoadjuvant chemotherapy for advanced colon cancer: clinical and pathological Results
Dion Morton, Birmingham, UK
Philip Quirke, Leeds, UK

12.30
Cytoreductive surgery and hyperthermic intraoperative chemotherapy for intestinal and ovarial cancers: lessons learned from 2 decades of clinical trials
Vic Verwaal, Aarhus, DK

14.30
Mechanical bowel obstruction: rush to the OR or stent and dine
Neil Mortensen, Oxford, UK

15.00
Controversies in IBD surgery
André d'Hoore, Leuven, BE

16.00
How to deal with IBD and dysplasia
Janindra Warusavitarne, London, UK

16.30
Perianal Crohn – avoiding delay and best surgical practice
Justin Davies, Cambridge, UK

17.00
Perianal Crohn – stem cells therapy and current medical approach
Gerhard Rogler, Zürich, CH

Wednesday, 4 Dec. 2019

09.00
Is anastomotic leak an infectious disease
Ronan O'Connell, Dublin, IE

09.30
Is it time to invest in robotic surgery?
Antonino Spinelli, Milan, IT

10.00
SATELLITE SYMPOSIUM Intuitive

11.00
New developments in robotic systems
Alberto Arezzo, Torino, IT

12.00
Posterior component separation for abdominal wall reconstruction: evolution from open to minimal invasive using the robotic platform
Filip Muysoms, Gent, BE

14.00
Coloproctology 4.0 – the networked surgeon
Richard Brady, Newcastle upon Tyne, UK

14.30
SATELLITE SYMPOSIUM Olympus

15.30
The elderly colorectal patient – functional outcomes and patient reported outcomes
Isacco Montroni, Faenza, IT

16.30
The microbiome and colorectal cancer
Philip Quirke, Leeds, UK

17.00
Surgical management of rectal endometriosis
Eric Rullier, Bordeaux, FR

17.30
EAES Presidential Lecture 3D printing for the general surgeon
Andrea Pietrabissa, Pavia, IT

Thursday, 5 Dec. 2019

09.00
Management of locoregionally advanced colon cancer
Torbjörn Holm, Stockholm, SE

09.30
ROUNDTABLE
Herand Abcarian, Chicago, US
Bill Heald, Basingstoke, UK

10.30
Artificial intelligence in colorectal surgery
Michele Diana, Strasbourg, FR

11.30
The mesentery in colonic diseases
Calvin Coffey, Luimneach, IE

12.00
Technical pearls and typical mistakes in minimal invasive colectomy
Antonio Lacy, Barcelona, ES

12.30
Choosing the right anastomotic technique in colon surgery
Roberto Persiani, Rom, IT

13.00
Precision surgery: past, present and future
Brendan Moran, Basingstoke, UK

13.30
Poster award
Michel Adamina, Winterthur, CH

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Management of colonic complications of type IV Ehlers–Danlos syndrome: a systematic review and evidence-based management strategy

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Abstract

Aim Type IV Ehlers Danlos Syndrome (EDS) is a connective tissue disorder affecting approximately 1 per 100,000-200,000 people. Life expectancy is reduced secondary to spontaneous vascular rupture or colonic perforation. Surgery carries significant morbidity and mortality. While strategies to manage colonic perforation include primary repair with or without a defunctioning stoma, Hartmann's procedure, total abdominal colectomy with end ileostomy and ileorectal anastomosis, evidence is contradictory and has not previously been evaluated in order to form a treatment strategy. We aim to review the published literature and identify outcome data relating to operative management of colonic perforation in type IV EDS.

Methods Pubmed, EM-BASE, Cochrane library and Google Scholar were searched with the following details: Ehlers Danlos Syndrome AND colonic surgery. The main outcome measure was re-perforation rates following colonic surgery on patients with type IV EDS. If

the nature of surgery and follow up were reported, data were recorded in a SPSS database according to PRISMA guidelines.

Results One hundred and nine operations have been described in 51 patients in 44 case series. There were 26 visceral re-perforations, 2 affecting the small intestine and 24 colonic. Survival analysis favoured total abdominal colectomy compared with operations where the colon was left *in situ*.

Conclusions Total abdominal colectomy with end ileostomy or ileorectal anastomosis are the safest strategies after colonic perforation in type IV EDS. Anastomotic leak rates are high. End colostomy is high risk for colonic re-perforation and anastomotic leak rates are extremely high. Restoration of colonic continuity should be avoided.

Keywords Type IV Ehlers Danlos syndrome, Colonic perforation

Introduction

Type IV Ehlers–Danlos syndrome (EDS) is a connective tissue disorder due to abnormal synthesis of procollagen III; it has a prevalence of approximately 1 per 100 000–200 000 [1]. Life expectancy is significantly reduced (median 45–50 years), and most patients frequently die due to spontaneous vascular rupture or colonic perforation. In 25% of cases the first complication in patients with EDS occurs by the age of 20, and patients have an 80% risk of

EDS-related complications by the age of 40 [2]. The mortality associated with hollow visceral and arterial rupture is 20% and 45%, respectively [2]. Although the diagnosis may be overlooked at initial presentation, facial characteristics and/or an individual or family history of easy bruising, excessive joint laxity, vascular, uterine or colonic rupture and spontaneous pneumothorax may raise suspicion [2,3]. The genetic abnormality responsible for EDS is a mutation of the *COL3A1* gene C2q31 (OMIM 130 050) [4] and follows an autosomal dominant pattern of inheritance, with significant heterogeneity in phenotypic expression [2–7].

Type IV EDS is sufficiently common that many surgeons will encounter a manifestation of the condition at

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some point in their careers, usually as a result of managing one of its complications. Patients with colonic complications may present with classical signs of abdominal pain and peritonism, and quite frequently bleeding per rectum [5–7]. The most common presentation of type IV EDS is with colonic perforation, and in 80% of cases the perforation occurs in the sigmoid colon. Rates of spontaneous colonic perforation in type IV EDS are unclear but have been suggested to be approximately 25% [2]. Faecal impaction and intramural haematoma formation may lead to perforation as a result of poor tensile strength in the colonic wall due to defective collagen, although routine pathological examination of the bowel wall in the resected segment usually fails to identify any primary abnormality [7].

Surgery in this group of patients is technically challenging due to extremely poor tissue quality, and it carries very significant morbidity and mortality. Repeat perforation rates of up to 55% following segmental resection have been described, and a colostomy does not appear to obviate this risk [2,8].

A number of strategies to manage patients with suspected or confirmed EDS and colonic perforation have been described in the literature. These include primary repair [9–11], primary repair and defunctioning stoma [5,6,9,11–15], Hartmann's procedure [9,14–31] and total abdominal colectomy (TAC) with either an end-ileostomy or ileorectal anastomosis (IRA) [8,32–36]. While total colectomy and IRA may prevent further colonic perforation, the leak rate of IRA in such cases has been reported to be as high as 50% [35]. The optimum treatment for patients with a colonic perforation due to EDS is therefore unclear at present and the relative infrequency of this condition, even in specialist centres, results in a small number of cases being encountered, making it difficult to develop a firm evidence-based approach to management.

Since no clear evidence base currently exists with specific relation to the management of the colon in EDS, the aim of this systematic review was to attempt to identify and critically integrate the available literature with our own experience of the management of patients with EDS in two national specialist centres in order to develop a rational management strategy based upon the best currently available evidence.

Method

A systematic review of published material relating to colonic involvement in EDS was undertaken. The following databases were searched: PubMed, Embase, Cochrane Library and Google Scholar. Searches were performed using the following search strategy: (Ehlers

Danlos syndrome) AND (colon OR colonic) AND (surgery OR surgical procedures OR perforation). The PRISMA guidelines (http://www.prisma-statement.org/) were adhered to throughout. One reviewer (DS) independently screened and reviewed all records identified through database searching and additional records identified using other sources. Studies were included if they related to patients with type IV EDS who required elective or emergency surgery for colonic manifestations of their disease. Both review articles and individual case reports were identified. No meta-analyses or Level I/II evidence were identified during the search. Data were extracted from papers if it was possible to establish the nature of surgery undertaken and details of follow-up. Further perforation of the colon was defined by the presence of extraluminal bowel contents or air at laparotomy distinct from a breakdown in the anastomosis. Anastomotic leak was censored separately from re-perforation where it was clear from the data that a leak had occurred operatively. No mathematical models to assess bias were applicable to the data because only Level III evidence was available in the published literature.

Data extraction and statistical analysis

Principal summary measures tabulated in those patients with EDS and colonic perforation concerned the nature of the operation performed, the sequelae of that operation in terms of all reported complications, with particular emphasis on repeat visceral perforation, the need for further surgery and overall survival. Particular attention was paid to the duration of follow-up. Data were collected in an electronic database (SPSS Statistics for Windows, v.19.0; IBM Corp., Armonk, New York, USA) Survival analysis, using re-perforation as the key primary outcome, was undertaken using Kaplan–Meier plots. For comparative analysis of unmatched data, the chi-square or Fisher's exact tests were used. $P < 0.05$ was taken as the level of statistical significance.

Results

A total of 43 case reports describing 102 operations in 48 patients (Fig. 1) [5,8–49] were identified by electronic literature searching and cross-referencing. An additional three patients undergoing seven surgical procedures were identified from the case records of the two national specialist intestinal failure units at Salford and St Mark's Hospitals, UK. The total dataset therefore comprised 51 patients (26 male) with a median (range) age of 23 (5.0–66.0) years, undergoing 109 surgical procedures.

The initial operation was an emergency procedure in 50 of the 51 (97.9%) patients. Almost all of these

procedures (49/50, 98%) were undertaken for spontaneous colonic perforation, and the remaining procedure was for rupture of the inferior mesenteric artery, which necessitated resection of the left colon. The single initial elective operation was undertaken for colonic ectasia. Thereafter there were 58 subsequent operations performed either electively or as an emergency (Table 1).

There were 26 further visceral perforations in those patients initially presenting with colonic complications of EDS during a median follow-up period of 12 (0–180) months: 24 of them related to the residual colon and two were small bowel perforations. Of the two small bowel perforations one occurred in the first postoperative week secondary to a leaking colonic anastomosis. The other spontaneous small bowel perforation occurred at 2 months post-IRA.

Further perforation of the colon as defined by the presence of extraluminal bowel contents or air at laparotomy distinct from a breakdown in the anastomosis occurred a median (range) of 24 (0–120.0) months after the first operative procedure. There was a significant difference in the re-perforation rate between the group of patients who had restoration of colonic continuity and those who were left defunctioned with a colostomy ($\chi^2 = 7.234$, $P = 0.007$). Kaplan–Meier survival analysis demonstrated a significant advantage in favour of TAC with respect to visceral re-perforation (log rank $P = 0.031$, $\chi^2 = 4.632$, 95% CI 67–110; Fig. 2).

Both IRA (2/14, 14%) and colo-colonic anastomosis (3/18, 17%) were associated with a significant incidence

Table 1 Surgical intervention and re-perforation data.

	No re-perforation	Re-perforation
Hartmann	25	8
Repair and defunction	16	1
TAC and IRA	13	1
TAC and ileostomy	7	0
Unknown	1	4
Drain	0	1
Exteriorize	8	1
Resection and join	1	2
Repair	2	0
Reversal Hartmann	7	8
Intestinal failure reconstruction	3	0
Total	83	26

IRA, ileorectal anastomosis; TAC, total abdominal colectomy.

of reported clinical anastomotic leakage, but the difference between the two procedures was not statistically significant ($P = 0.624$, Fisher's exact test). There was, however, a significantly greater visceral re-perforation rate after colo-colic anastomosis, compared with IRA (10/18, 55% *vs* 1/14, 7% respectively, $P = 0.005$, Fisher's exact test).

Both elective and emergency surgery were associated with significant mortality and morbidity. There were five deaths in the emergency operative group and seven in the elective group (Table 2). Surgery was associated with a high incidence of postoperative complications, including: intra-abdominal bleeding, wound dehiscence, adhesions in four patients, small bowel injury in four patients and vascular complications in five patients, including false aneurysms of the hepatic, renal, iliac and sigmoid arteries [5,6,8,16,22,25,37]. A rupture of the inferior epigastric artery led to necrotizing fasciitis in one patient [14]. Two patients developed intestinal failure as a result of operative small bowel injury [16,42]. One patient had adhesive bowel obstruction 6 months postoperatively, leading to jejunal perforation [44].

Discussion

The optimum strategy for the management of colonic complications in patients with type IV EDS would not only be evidence-based but also encompass both elective and emergency treatment. This is unlikely to ever be achievable. The frequency with which even specialist centres encounter cases of EDS is relatively low, and adequately powered randomized trials of different methods of managing colonic perforation in EDS, either acutely or with respect to later intestinal reconstruction,
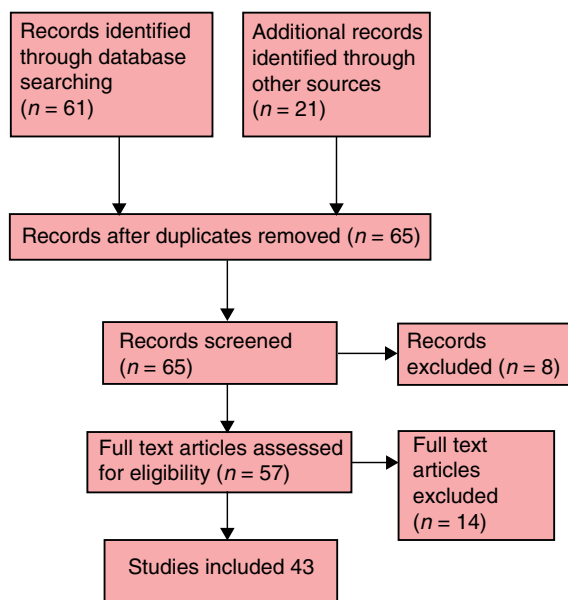

Figure 1 PRISMA flow diagram for data retrieval.

Risk of recurrent spontaneous visceral perforation in Ehlers Danlos Syndrome Type IV
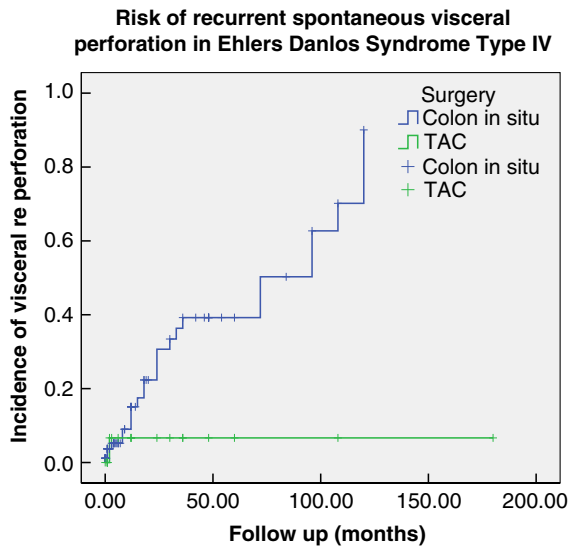

Figure 2 Survival analysis of patients with type IV EDS with regard to incidence of re-perforation and type of surgery performed. A significantly higher risk of re-perforation was seen in those patients left with their colon *in situ* (log rank $P = 0.031$, $\chi^2 = 4.63$, 95% median CI 67–100).

are most unlikely to ever be undertaken. However, it is likely that all centres offering general abdominal and colorectal surgery will encounter patients with this rare condition.

It is noteworthy that, almost without exception, the patients with colonic manifestations of EDS in all published studies presented with spontaneous perforation, predominantly of the sigmoid colon. The diagnosis of EDS was not made at initial presentation in any of these patients but was only arrived at subsequently, because of the relatively young age of the patient, the family

history, subsequent clinical course or a combination of these factors. The findings of the present study are therefore most likely to be of relevance to patients who have already undergone emergency treatment for EDS, and in whom consideration is being given to the management of further spontaneous colonic perforation, or in planning elective surgery following colonic perforation.

The aim of the present study was to establish a comprehensive, balanced and unbiased evidence base for informing management strategy in such cases by including every published case of colonic perforation associated with EDS for which data on mode of treatment and detailed outcome data, including length of follow-up, were available. The results of the study therefore summarize the entire published experience of the management of patients with colonic perforation due to type IV EDS, and consequently have afforded us the opportunity to undertake a statistical analysis of the effect of some of the different treatment strategies upon outcome.

The present study indicates that intestinal re-perforation rates after segmental resection and anastomosis or repair are significantly higher than those after total colectomy, and suggests that the safest approach for a patient known to have EDS and who has recovered from a Hartmann's procedure to deal with the presenting colonic perforation is a total abdominal colectomy with either an end-ileostomy or an ileorectal anastomosis. Ileorectal anastomosis and end-ileostomy appear to be associated with a similar risk of further intestinal perforation after total colectomy, but an ileorectal anastomosis exposes patients to a relatively high risk of anastomotic leak. Given the particularly high morbidity and mortality likely to result from anastomotic leakage

Table 2 Perioperative deaths.

Reference	Operation	Emergency/elective	Cause of death
Aldridge [9]	Closure of perforation	Elective	Multiple organ failure
Schofield *et al.* [13]	Segmental resection	Emergency	Gastroaortic fistula
Sykes [30]	Total colectomy and ileorectal anastomosis	Elective	Multiple organ failure
Blaker *et al.* [17]	Closure colostomy	Elective	Multiple organ failure
Sentongo *et al.* [14]	Closure colostomy	Elective	Anastomotic leak
Collins *et al.* [39]	Closure colostomy	Elective	Anastomotic leak
Soonawala *et al.* [26]	Hartmann's procedure	Emergency	Retroperitoneal haemorrhage
McAleese [21]	Hartmann's procedure	Emergency	Myocardial infarction
Demirogullari *et al.* [18]	Total colectomy and ileorectal anastomosis	Emergency	Multiple organ failure
Schippers and Ditters [24]	Closure colostomy	Elective	Upper gastrointestinal haemorrhage
Silva *et al.* [48]	Hartmann's procedure	Emergency	Spontaneous rupture of left renal and iliac arteries
Fogel [31]	Hartmann's procedure	Emergency	Multiple organ failure

in this group of patients, a decision to undertake ileorectal anastomosis should be made only after detailed discussion with the patient with respect to the increased risk of potentially serious complications.

The present study also shows that, unlike in cancer or diverticular disease, restoration of colonic continuity in EDS is associated with a risk of further colonic perforation which is likely to be regarded as unacceptably high by both surgeons and patients. Over one-third of patients who had undergone an apparently successful reversal of Hartmann's procedure sustained a further colonic perforation over a follow-up period of up to 120 months. It is unclear whether this figure would be even higher if longer periods of follow-up were available for this patient population. While these data support a policy of completion colectomy after spontaneous colonic perforation in EDS, the role of prophylactic colectomy is less clear. While this has been advocated by some authors [34], there is no currently available evidence to suggest that such a strategy is likely to be of benefit and it seems most likely to be applicable to patients with an abnormally dilated colon.

While it is usually unclear at the time of perforation that the patient has EDS, there are several additional clinical clues that may raise suspicion of a connective tissue disorder. A characteristic facial appearance has been described [2,3], and there may be evidence of easy bruising, a previous history or repeated spontaneous pneumothorax and/or a family history of premature death from vascular rupture or colonic perforation, suggesting the diagnosis [2,3]. Operative findings are of technically challenging conditions, with unusually delicate tissues which are excessively prone to tearing and bleeding, and the bowel has been described as handling like tissue paper. A definitive diagnosis relies, however, on demonstrating decreased expression of type III collagen from fibroblasts obtained from skin biopsy and either exon deletion or single nucleotide polymorphism of the *COL3A1* gene [4]. If the diagnosis is confirmed by these investigations then discussion concerning further surgery should centre around completion colectomy and either end-ileostomy or IRA. All surgery carries significant morbidity and mortality; consequently consideration should be given regarding referral to specialist intestinal failure centres.

Once type IV EDS has been diagnosed, it is essential that assessment for further surgery also encompasses cardiovascular evaluation in the form of echocardiogram, aneurysm screening and access to vascular surgical, intensive care and nutritional support facilities in any centre planning to undertake reconstructive surgery. Specific intra-operative risks, such as the propensity for patients with EDS to bleed, cervical spine subluxation

during endotracheal intubation and the potential risk of arterial injury during surgery and central line insertion [7], should also be considered and discussed. Wound dehiscence, infections and incisional hernias are also common due to poor tissue quality. Colonic fistulas, stoma problems and severe intra-abdominal adhesions have also been described [5–7,48]. The last may follow a particularly complicated course and should be managed initially by aggressive decompression with a nasogastric tube because of the increased risk of small bowel perforation resulting from distension of the abnormally friable small intestine [44].

The validity of an analysis which is based on interpretation of case series and therefore subject to publication bias is a significant limitation of this review. The results must therefore be interpreted with some caution. However, one recent case series by Frank *et al.* [50] of 133 patients has also reported a high operative death rate (nine patients) and an increased risk of colonic perforation with type IV EDS. The authors also noted that reversal of Hartmann's procedure carries a high risk of perforation or anastomotic leakage, and El Masri has also cautioned specifically against reversal of Hartmann's due to a high risk of leak and further gastrointestinal complications [51]. These findings, together with our own data, make it very difficult to justify restoration of colonic continuity under these circumstances and suggest that subtotal colectomy should be regarded as the definitive operation for these patients.

Summary

The present study represents a novel attempt to bring together a sufficiently large dataset to enable logical conclusions to be drawn about the management of colonic perforation in patients with type IV EDS. Although no Level I or II evidence exists to undertake a meta-analysis, the data provide factual evidence in support of a policy of total abdominal colectomy with end-ileostomy or, if stoma averse, ileorectal anastomosis after initial presentation with colonic perforation in type IV EDS. In contrast, end-colostomy or restoration of colonic continuity carry a high risk of further colonic perforation.

Conflicts of interest

None declared.

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