



# Surgical morbidity is acceptable following a one or two stage mesentery-including surgery for Crohn's disease and comparable to mesentery-sparing surgery

Christina A. Fleming<sup>1#</sup>, Helen M. Mohan<sup>1#</sup>, Miranda Kiernan<sup>2#</sup>, Muhammad Fahad Ullah<sup>1</sup>, David Waldron<sup>1</sup>, Colin Peirce<sup>1,3</sup>, Dara Walsh<sup>4</sup>, Manus Moloney<sup>5</sup>, Maeve Skelly<sup>5</sup>, Paul Tibbitts<sup>3</sup>, J. Calvin Coffey<sup>1,2,3^</sup>

<sup>1</sup>Department of Surgery, University Hospital Limerick, Limerick, Ireland; <sup>2</sup>Centre for Interventions in Infection, Inflammation & Immunity [4i], University of Limerick, Limerick, Ireland; <sup>3</sup>University of Limerick Graduate Entry Medical School, Limerick, Ireland; <sup>4</sup>Department of Medical Illustration, University Hospital Limerick, Limerick, Ireland; <sup>5</sup>Department of Gastroenterology, University Hospital Limerick, Limerick, Ireland

**Contributions:** (I) Conception and design: JC Coffey, HM Mohan, CA Fleming, M Kiernan; (II) Administrative support: JC Coffey, HM Mohan, CA Fleming, M Kiernan, P Tibbitts, D Waldron, D Walsh; (III) Provision of study materials or patients: JC Coffey, HM Mohan, CA Fleming, M Kiernan, P Tibbitts, D Waldron, D Walsh; (IV) Collection and assembly of data: JC Coffey, HM Mohan, CA Fleming, M Kiernan, P Tibbitts, M Moloney, C Peirce, M Skelly, David Waldron, Dara Walsh; (V) Data analysis and interpretation: JC Coffey, HM Mohan, CA Fleming, M Kiernan, D Walsh; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

<sup>#</sup>These authors contributed equally to this work.

**Correspondence to:** Prof. J. Calvin Coffey, PhD, FRCSI. Department of Surgery, University Hospital Limerick, Dooradoyle, Limerick, Ireland. Email: calvin.coffey@ul.ie.

**Background:** It has recently been suggested that mesenteric-including (MI) resection for Crohn's disease (CD) is associated with reduced surgical recurrence. Whilst there is a perception that MI resection is associated with increased surgical morbidity there is a lack of data to support this. The aim of this study was to perform a retrospective comparison of 30-day morbidity following MI resection and conventional mesenteric-sparing (MS) resection for CD.

**Methods:** Three patient cohorts were studied and compared: (I) one-stage MI resection, (II) two-stage MI resection, (III) conventional MS resection. Two-stage resection included initial defunctioning ileostomy and subsequent MI resection at a later time. 30-day morbidity was classified using the Clavien-Dindo system and compared between groups. Complications studied included bleeding complications and perioperative blood transfusion requirements. Data were analyzed using univariate and multivariate analysis using SPSS26.0.

**Results:** A total of 117 patients were analyzed [n=30 MS control group, n=87 MI (n=76 one-stage, n=11 two-stage)]. Increases in 20-day morbidity or in Clavien-Dindo III complications were not observed in MI (48%, n=42) compared to MS (50%, n=15) resection (P=0.87). There were no 30-day mortalities. Bleeding complications were comparable as were perioperative blood transfusion requirements [MI 18% (n=16), MS 27% (n=8), P=0.33]. On multivariate analysis, MI resection was not associated with increased 30-day morbidity [odds ratio (OR) =0.75; 95% confidence interval (CI): 0.68–6.58; P=0.194] or Clavien-Dindo III complications (OR =1.816; 95% CI: 0.79–5.64; P=0.099). Of the eleven patients who underwent initial diversion, 10 (90.1%) underwent a successful staged MI resection with similar 30-day morbidity.

**Conclusions:** MI resection for CD was not associated with increased morbidity. For patients in whom an MI resection is not feasible at first surgery, a two-staged approach involving initial diversion followed by interval MI resection is a feasible strategy.

**Keywords:** Crohn's disease (CD); mesentery; morbidity; surgical outcomes

<sup>^</sup> ORCID: 0000-0003-0007-8206.

Received: 09 July 2022; Accepted: 26 December 2022. Published online: 15 March 2023.

doi: 10.21037/map-22-3

View this article at: <https://dx.doi.org/10.21037/map-22-3>

## Introduction

Crohn's disease (CD) is an inflammatory disease that can affect any part of the gastrointestinal tract (1-5). Most patients will require surgery at least once and of those who do undergo surgery, a substantial proportion require later reoperation for a Crohn's related indication (6). Whilst endoscopic recurrence can occur early during the first year following surgery, the requirement for re-operative surgery (i.e., surgical recurrence) is usually maximal during the first two years postoperatively, and increases slightly thereafter (7). Traditionally, surgery for CD emphasizes a conservative sparing of the intestine (8). This concept has also been applied to the extent of mesenteric resection and the mesentery is usually preserved and retained by detaching the mesentery at the junction with the intestine. This differs from cancer surgery, where complete mesocolic resection or total mesorectal excision are advocated to reduce local recurrence. Emerging data now support a role for the mesentery in CD and for resection of the mesentery (3-6).

A previous study from our group demonstrated that mesentery-including (MI) surgery for CD results in decreased surgical recurrence rates (9-12). A separate study by de Groof *et al.* demonstrated that inclusion of the mesorectum [a separate region of the mesenteric continuum (1,3,6)] is also associated with improved outcomes in patients undergoing proctectomy for CD affecting the rectum (13). These findings have prompted randomized controlled trials to further characterize the relationship between inclusion of the mesentery and postoperative recurrence, in patients requiring ileocolic resection for CD (e.g., The MESOCOLIC Trial, Clinical Trials.gov, NCT03769922) (14). Current European guidelines do not reference mesenteric resection in CD (15). While American guidelines discuss different benefits relating to the extent of mesenteric resection, a recommendation on the optimum extent of mesenteric resection is not made (16).

Resections for CD carry a significant risk of postoperative complications (17). Infectious complications are common, as patients may be debilitated from chronic disease and medications pre-operatively (18). Previous studies have shown that those with perforated CD are more likely to experience prolonged hospitalisation and permanent ileostomy formation (18). Combination immunosuppression and

previous resection have been linked to a higher rate of intra-abdominal postoperative sepsis (18). Kamel *et al.* recently found that patients on biological agents preoperatively had similar short term outcomes to those who were not (19).

There is a perception that MI resection in CD may be a high risk surgical strategy associated with increased surgical morbidity, in particular increased risk of significant bleeding and vascular injury. The theory underpinning this concept is that the mesentery in CD is involved in the disease process and as a result is thickened, inflamed and can bleed briskly on division (8). However, there is a paucity of data to support the perception of increased surgical morbidity with MI in CD. While randomised controlled trials (RCTs) are currently in progress, this study aimed to report on 30-day morbidity following MI resection for CD. We present the following article in accordance with the STROBE reporting checklist (available at <https://map.amegroups.com/article/view/10.21037/map-22-3/rc>).

## Methods

A retrospective comparative cohort analysis was performed on a prospectively maintained institutional database of consecutive patients undergoing mesentery-including surgery for CD from 2010–2020. The aim of this study was to report 30-day morbidity following surgery for CD in patients undergoing mesentery-including (MI) resection and to compare this in a cohort of patients who underwent mesenteric-sparing (MS) surgery. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Ethical approval was prospectively obtained from the University of Limerick Hospital Group ethics committee (Ref 57/15) and individual consent for this retrospective analysis was waived.

### *Study population and study design*

Patients were diagnosed with CD in keeping with European Crohn's and Colitis Organization (ECCO) criteria and clinical management guided by ECCO guidelines (20). Disease activity was classified using the Vienna classification (21). Three patient cohorts were reported on: (I) one-stage MI resection, (II) two-stage MI

resection, (III) conventional MS resection. All CD patients who underwent consecutive MI resections, irrespective of disease location (small bowel, ileocolic, colonic), from August 2010 to December 2020 at University Hospital Limerick were included. Indications for surgery included symptomatic stricturing disease, fistulizing CD or symptomatic CD refractory to medical therapy. Patients aged >18 years of age were included.

In a small cohort of patient, surgical planes could not be identified and thus an MI resection could not be conducted. In these scenarios the authors utilized a two-stage approach whereby at initial surgery defunctioning ileostomy was fashioned (first stage) and a subsequent interval attempt at MI resection performed when disease activity was quiescent (second stage). The authors report on the success rates and safety of this approach; 30-day morbidity in patients undergoing MI resection (one-stage and two-stage) was compared with that of a historic cohort of patients who underwent primary MS resection for ileocolic CD (1).

### *Clinical management and surgical technique*

All patients diagnosed with CD were managed by the multidisciplinary team [gastroenterology, IBD clinical nurse specialist (CNS), dietician, IBD surgeon]. All patients underwent preoperative optimisation. This included nutritional optimization, correction of anemia and rationalization of immunosuppressive medication. Further perioperative risk reduction strategies included antibiotic prophylaxis at the time of surgery and venous thromboembolism (VTE) prophylaxis including the use of: prophylactic dose low molecular weight heparin (LMWH), thrombo-embolus deterrent (TED) stockings and full length sequential compression devices (SCDs) commenced intra-operatively and until mobility established.

The principles of mesentery-including surgery for ileocolic MI resection have been previously reported (1,22). In brief, the mesentery was fully mobilized and partially excised. The mobilization process was considered complete, if the mesentery was fully detached back to the level of the root region. The root region is the region of mesentery at the head of the pancreas, containing the superior mesenteric artery and vein. The root region was not dissected though. The mesentery was fully detached and the ileal division made just proximal to the mesenteric transition zone i.e., the zone where the mesentery changes from normal to abnormal. From this level, the mesentery was divided towards, but not including, the root region. The mesenteric

division was then continued away from the root region to the colon, which was divided at a level where both colon and adjoining mesentery were normal in appearance. The technique of hemostatic mesenteric division involved the use of overlapping Kocher clamps and 0-vicryl suture ligation. Similar principles of MI resection were utilized for small bowel and colonic CD resection. In minimally invasive cases, mesenteric division was performed extracorporeally in the same standard manner. In mesentery-sparing resection, the mesentery was divided near flush with the mesenteric margin of the intestine.

### *Study endpoints*

Surgical morbidity was classified using the Clavien-Dindo grading system as follows: grade I, any deviation from normal post-operative course not requiring surgical endoscopic or radiological intervention; grade II, complications requiring drug treatments; grade III, complications requiring surgical, endoscopic or radiological intervention; grade IV, life-threatening complications, grade V, death of the patient. The primary endpoint was to analyze the impact of MI resection on overall 30-day morbidity and severe morbidity defined as perioperative morbidity classified as Clavien-Dindo III and above. All patients were reviewed in person at six weeks post-operatively by the clinical team to ensure that all 30-day morbidity was captured. Bleeding complications including intra-operative major vascular injury, re-operation for bleeding complications and requirement for perioperative blood transfusion, were compared. Detailed clinical and pathological data were reported for each cohort including age, gender, smoking status, duration of disease and pre-operative medication.

### *Statistical analysis*

Data were analyzed using the statistical package SPSS, version 26 (SPSS software, Chicago, IL, USA) and graphs generated using GraphPad PRISM, version 8.4.2. Continuous variables were summarized using mean and standard deviation (SD) and categorical variables, including 30-day morbidity, type of morbidity and classification (Clavien-Dindo) reported using frequency (n) and percentages. Statistical analysis of 30-day morbidity, bleeding complications and transfusion requirement between MI and MS resection was performed using chi-squared test ( $P < 0.05$ ).

Two phases of binary logistic regression were performed to analyze the relationship between MI resection and 30-day morbidity (first analysis) and severe 30-day morbidity defined as Clavien-Dindo III (second analysis). The following variables were included in the univariable analysis: age (A1/A2 by Vienna classification), smoking status (yes/no) CD behavior (stricturing/fistulating or complicated), mesentery including resection (yes/no), pre-operative use of steroids or anti-TNF therapy (yes/no). Subsequent multivariable analysis was performed using variables that achieved  $P < 0.25$  on univariable analysis using a stepwise backward method. Odds of 30-day morbidity and Clavien-Dindo III were reported as odds of morbidity occurring i.e., odds ratio (OR) with 95% confidence intervals (CIs) also reported. Statistical significance was considered as  $P < 0.05$ .

## Results

### *Patient demographics and clinical characteristics*

One hundred and seventeen patients were included [mesentery including,  $n=87$  ( $n=76$  one-stage,  $n=11$  two-stage) and mesentery sparing,  $n=30$ ] as summarized in *Figure 1*. Mean age at the time of surgery was 37 years in both MS and MI one-stage and 41 years in MI two-stage and an even gender balance was observed in all groups (*Table 1*). Forty-eight point three percent ( $n=14$ ) of MS patients were current smokers at the time of surgery with 40.8% ( $n=31$ ) in the MI one-stage and 33% ( $n=3$ ) in MI two-stage group. The most common site of disease was ileocolic and B2 (stricturing) phenotype was the most common in MS [70% ( $n=21$ )] and MI one-stage groups [76.3% ( $n=58$ )] while B3 (penetrating) was the most common phenotype in the MI two-stage group [54.5% ( $n=6$ )]. All MS resections were performed laparoscopically while, all MI two-stage were open resections and MI one-stage resections were performed either open [71% ( $n=54$ )], laparoscopically [19.7% ( $n=15$ )] or robotically [9.2% ( $n=7$ )].

### *Surgical morbidity*

AS outline in *Table 2*, thirty day morbidity was reported in 48% ( $n=42$ ) of all patients who underwent MI resection (one- and two-stage) and in 50% ( $n=15$ ) of the MS resection group ( $P=0.87$ ). Morbidity is summarized in *Figure 2*. Patients who underwent MI resection more frequently experienced Clavien-Dindo II morbidity compared to those in the MS group [MS 60% ( $n=9$ ), MI 81% ( $n=34$ ),  $P=0.11$ ]. More Clavien-Dindo III complications were reported in MS

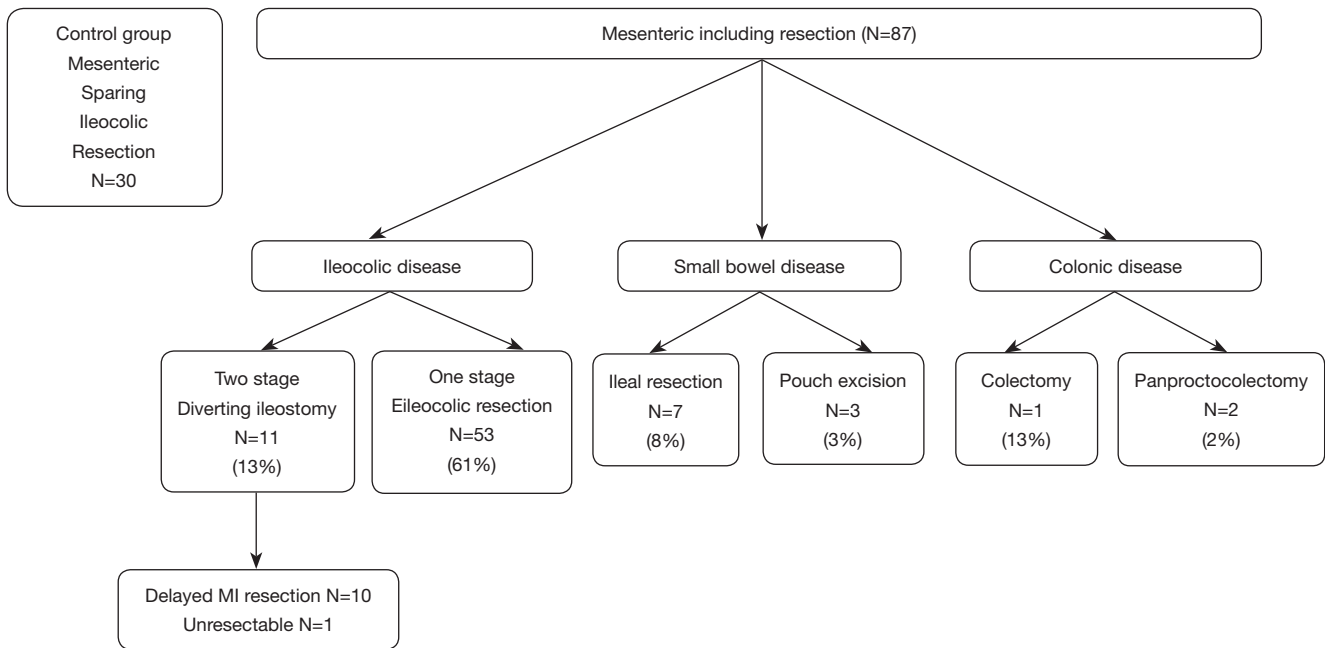
resection group [MS 27% ( $n=4$ ), MI 7% ( $n=3$ ),  $P=0.13$ ] and similar Clavien-Dindo IV rates were between groups [MS 7% ( $n=1$ ), MI 5% ( $n=2$ ),  $P=0.78$ ]. No 30-day mortalities were reported.

Subgroup analysis did not identify a significant difference in type of 30-day morbidity between MS and MI resection groups. Anastomotic leak rates were twice as high in MS surgery but this did not reach significance ( $P=0.28$ ). Conversely, surgical site infection rates were higher in the MI group [25.3% ( $n=22$ )] compared to MS [16.7% ( $n=5$ )] but again this did not reach significance ( $P=0.33$ ). VTE rates were comparable [MS 3.3% ( $n=1$ ), MI 3.4% ( $n=3$ ),  $P=0.98$ ] and the highest VTE rate was observed in those who underwent MI colonic resection (7.7%,  $n=1$ ). The majority of post-operative complications were managed conservatively. One patient in each group required radiologically guided drainage of a collection and re-operative rates were 10% ( $n=3$ ) following MS resection and 2.3% ( $n=2$ ) following MI resection ( $P=0.072$ ). Two MS resection patients required revision of abdominal wound and one MI resection patient required laparotomy, washout and proximal diversion following an anastomotic leak.

On multivariate analysis (*Table 3*), MI resection was not associated with increased 30-day morbidity (OR =0.75; 95% CI: 0.68–6.58;  $P=0.194$ ) or Clavien-Dindo III complications (OR =1.82; 95% CI: 0.79–5.64;  $P=0.099$ ). Current smoking status was the only factor associated with increased overall 30-day morbidity [OR =1.17; 95% CI: 0.59–17.72;  $P=0.027$ ]. While smoking status was associated with severe (Clavien-Dindo III) complications on univariate analysis (OR =2.17; 95% CI: 0.49–9.01;  $P=0.030$ ) this association was not significant on multivariate analysis (OR =1.92; 95% CI: 1.10–6.99;  $P=0.054$ ). Age, CD phenotype and pre-operative steroid or anti-TNF use were not significantly associated with either outcome in this analysis.

### *Bleeding complications and transfusion requirement*

No intra-operative major vascular injuries were reported. Post-operative intra-abdominal bleeding or hematoma formation was reported in 6.7% ( $n=2$ ) of MS resection patients and 1.1% ( $n=1$ ) of MI resection patients (one-stage). One patient required re-operation for bleeding following MS ileocolic resection and no patients required return to theatre for management of hemorrhagic complications following MI resection. Perioperative blood transfusion



**Figure 1** Flow chart of selection of included patients. MI, mesenteric-including.

**Table 1** Demographic and clinicopathological characteristics of included cohorts

| Demographics, disease phenotype, group characteristics | Conventional (mesentery-sparing, n=30) | One stage (mesentery-included, n=76) | Two stage (mesentery-included, n=11) |
|--|--|--------------------------------------|--------------------------------------|
| Age (years), mean ± SD                                 | 37.7±13.7                              | 37.3±11.66                           | 41±11                                |
| Gender (male:female)                                   | 14:16                                  | 33:43                                | 5:6                                  |
| Active smoking, n (%)                                  | 14 (48.3)                              | 31 (40.8)                            | 3 [27]                               |
| Duration of disease (months), mean ± SD                | 75±17                                  | 72±16                                | 156±13                               |
| Vienna classification, n (%)                           |  |                                      |                                      |
| Age at diagnosis                                       |  |                                      |                                      |
| A1   | 27 (90.0)                              | 56 (73.7)                            | 9 (82.0)                             |
| A2   | 3 (10.0)                               | 20 (26.3)                            | 2 (18.0)                             |
| Location   |  |                                      |                                      |
| L1   | 3 (10.0)                               | 10 (13.2)                            | 0                                    |
| L2   | 0                                      | 13 (17.1)                            | 0                                    |
| L3   | 27 (90.0)                              | 53 (69.7)                            | 11 (100.0)                           |
| L4   | 0                                      | 0                                    | 0                                    |

**Table 1** (continued)

Table 1 (continued)

| Demographics, disease phenotype, group characteristics | Conventional (mesentery-sparing, n=30) | One stage (mesentery-included, n=76) | Two stage (mesentery-included, n=11) |
|--|--|--------------------------------------|--------------------------------------|
| Disease phenotype                                      |  |                                      |                                      |
| B1   | 9 (30.0)                               | 7 (9.2)                              | 0                                    |
| B2   | 21 (70.0)                              | 58 (76.3)                            | 5 (45.5)                             |
| B3   | 0                                      | 11 (14.5)                            | 6 (54.5)                             |
| Medication pre-op, n (%)                               |  |                                      |                                      |
| Steroid  | 13 (55.2)                              | 37 (48.7)                            | 9 (81.8)                             |
| Anti-TNF   | 5 (17.2)                               | 19 (25.0)                            | 8 (72.7)                             |
| Other  | 20 (69.0)                              | 52 (68.0)                            | 9 (82.0)                             |
| None   | 5 (17.2)                               | 12 (15.8)                            | 0                                    |
| Location of disease, n (%)                             |  |                                      |                                      |
| Ileocolic  | 27 (90.0)                              | 53 (69.7)                            | 11 (100.0)                           |
| Small bowel  | 3 (10.0)                               | 10 (13.2)                            | 0                                    |
| Colonic  | 0                                      | 13 (17.1)                            | 0                                    |
| Operation, n (%)                                       |  |                                      |                                      |
| Ileocolic resection                                    | 27 (90.0)                              | 53 (69.7)                            | 10 (90.1)                            |
| Small bowel resection                                  | 3 (10.0)                               | 10 (13.2)                            | 0                                    |
| Colonic resection                                      | 0                                      | 13 (17.1)                            | 0                                    |
| Surgical technique, n (%)                              |  |                                      |                                      |
| Laparoscopic   | 30 (100.0)                             | 15 (19.7)                            | 0                                    |
| Open   | 0                                      | 54 (71.0)                            | 10 (90.1)                            |
| Robotic  | 0                                      | 7 (9.2)                              | 0                                    |
| 30D readmission, n (%)                                 | 3 (10)                                 | 4 (5.3)                              | 1 (9.1)                              |
| 30D morbidity, n (%)                                   | 15 (50)                                | 37 (48.7)                            | 5 (45.5)                             |
| 30D mortality, n (%)                                   | 0                                      | 0                                    | 0                                    |

SD, standard deviation; A, age; L, location; B, disease behaviour; TNF, tumour necrosis factor; 30D, 30-day.

requirement is summarized in *Figure 2*. Transfusion was required in 27% (n=8) patients following MS resection and 18.8% (n=16) following MI resection (P=0.33). There was no significant difference in transfusion requirement in patients following one- or two-stage MI resection (both 18%) and following ileocolic (23%), small bowel (10%) or colonic (23%) MI resection. The lowest rates of transfusion

requirement were observed following small bowel resection.

### *Two-staged mesenteric resection*

In eleven patients surgical planes were not apparent on initial laparotomy. This was due to advanced CD. All eleven underwent defunctioning loop ileostomy formation. All



**Table 2** Surgical morbidity at 30-day post-operatively

| Demographics, disease phenotype, group characteristics | Mesentery sparing (n=30) | Mesentery including (all, n=87) | One stage (mesentery including, n=76) | Ileocolic resection (n=53) | Small bowel resection (n=10) | Colonic resection (n=13) | Two stage (mesentery included, n=11) |
|--|--------------------------|---------------------------------|---------------------------------------|----------------------------|------------------------------|--------------------------|--------------------------------------|
| Post-op complication, n (%)                            |                          |                                 |                                       |                            |                              |                          |                                      |
| 30-day morbidity                                       | 15 (50.0)                | 42 (48.3); P=0.870              | 37 (48.7)                             | 27 (50.0)                  | 5 (50.0)                     | 5 (38.5)                 | 5 (45.0)                             |
| Anastomotic leak (surgical)                            | 3 (10.0)                 | 4 (4.6); P=0.282                | 3 (3.9)                               | 2 (3.8)                    | 1 (10.0)                     | 0                        | 1 (9.1)                              |
| Surgical site infection (including dehiscence)         | 5 (16.7)                 | 22 (25.3); P=0.334              | 19 (25.0)                             | 11 (20.1)                  | 3 (30.0)                     | 4 (30.8)                 | 3 (27.3)                             |
| Intra-abdominal sepsis                                 | 1 (3.3)                  | 4 (4.6); P=0.768                | 3 (3.9)                               | 2 (3.8)                    | 0                            | 1 (7.7)                  | 1 (9.1)                              |
| Intra-abdominal bleeding or haematoma                  | 2 (6.7)                  | 1 (1.1); P=0.099                | 1 (1.3)                               | 1 (1.9)                    | 0                            | 0                        | 0                                    |
| Fistula  | 1 (3.3)                  | 2 (2.3); P=0.757                | 2 (2.6)                               | 1 (1.9)                    | 1 (10.0)                     |                          | 0                                    |
| Urinary tract infection                                | 1 (3.3)                  | 4 (4.6); P=0.768                | 4 (5.3)                               | 1 (1.9)                    | 1 (10.0)                     | 2 (15.4)                 | 0                                    |
| Respiratory tract infection                            | 1 (3.3)                  | 2 (2.3); P=0.757                | 2 (2.6)                               | 1 (1.9)                    | 0                            | 1 (7.7)                  | 0                                    |
| VTE  | 1 (3.3)                  | 3 (3.4); P=0.976                | 3 (3.9)                               | 2 (3.8)                    | 0                            | 1 (7.7)                  | 0                                    |
| Mortality  | 0                        | 0; –                            | 0                                     | 0                          | 0                            | 0                        | 0                                    |
| Management of 30-day morbidity                         |                          |                                 |                                       |                            |                              |                          |                                      |
| Drainage of collection                                 | 1 (3.3)                  | 1 (1.1); P=0.426                | 1 (1.3)                               | 0                          | 0                            | 0                        | 0                                    |
| Re-operation (total)                                   | 3 (10.0)                 | 2 (2.3); P=0.072                | 1 (1.3)                               | 1 (1.9)                    | 0                            | 0                        | 1 (9.1)                              |
| Revision of abdominal wound                            | 2 (6.7)                  | 0; –                            | 0                                     | 0                          | 0                            | 0                        | 0                                    |
| Laparotomy and washout                                 | 0                        | 1 (1.1); –                      | 1 (1.3)                               | 1 (1.9)                    | 0                            | 0                        | 0                                    |
| Re-operation for bleeding                              | 1 (3.3)                  | 0; –                            | 0                                     | 0                          | 0                            | 0                        | 0                                    |
| Blood transfusion requirement                          |                          |                                 |                                       |                            |                              |                          |                                      |
| Anaemia (requiring blood transfusion)                  | 8 (27.0)                 | 16 (18.4); P=0.333              | 14 (18.0)                             | 12 (23.0)                  | 1 (10.0)                     | 3 (23.0)                 | 2 (18.0)                             |

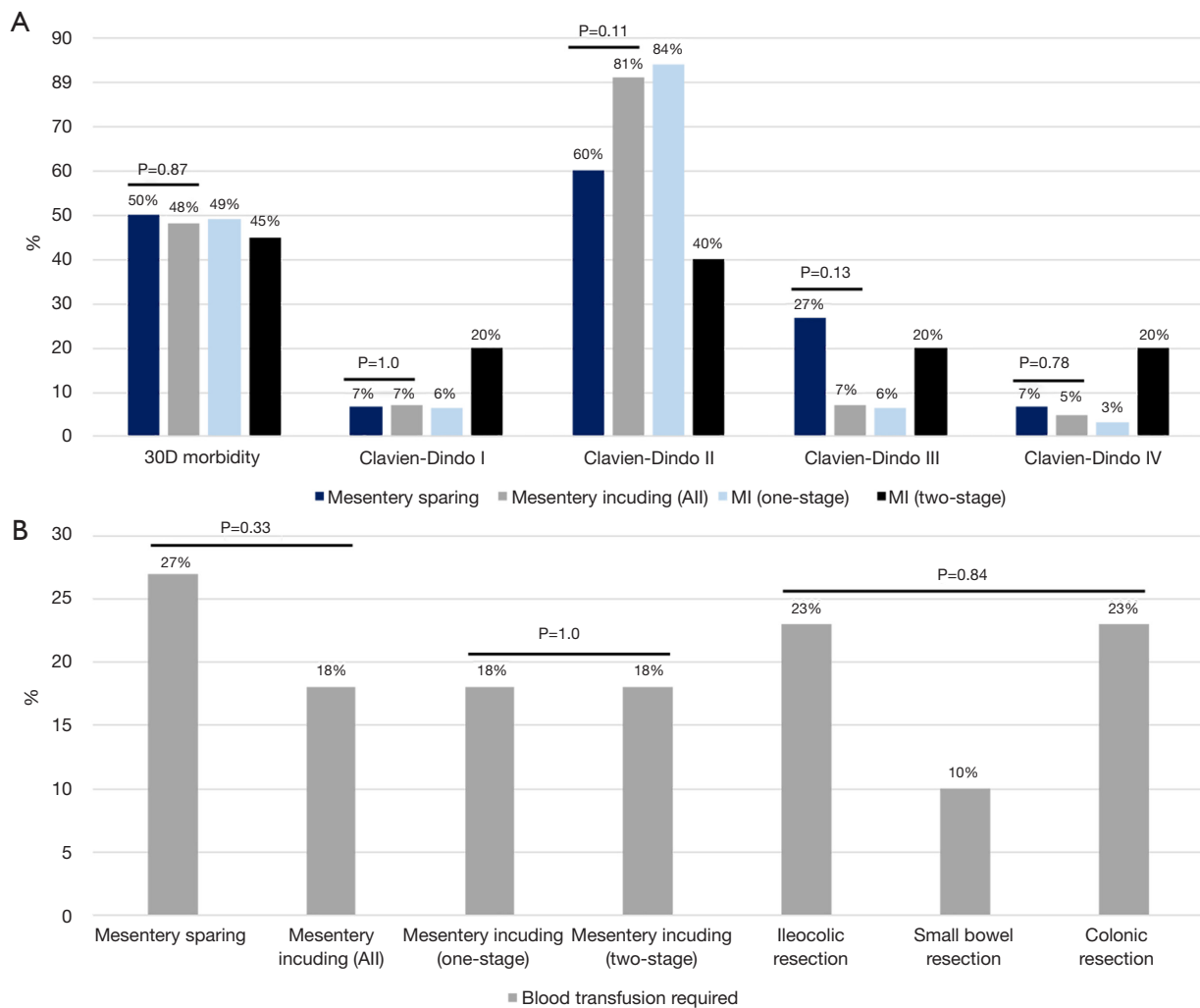
P values calculated using chi-squared test. \*, 30-day morbidity following interval MI ileocolic resection. VTE, venous thromboembolism; MI, mesentery-including.

eleven fully recovered post-operatively and discharged home without requirement for further surgical intervention. Following a period of approximately 6 months, 10 of these patients (90.1%) proceeded to successful interval MI ileocolic resection. Six had restoration of intestinal continuity at the second operation. Four had the loop ileostomy reversed at a later stage; 30-day morbidity was comparable in one-stage (49%, n=37) and two-stage (45%, n=5) MI resection. One patient was diagnosed with a small

bowel adenocarcinoma following staged MI resection performed four months after initial diversion. This patient was discussed at gastrointestinal oncology multidisciplinary team (MDT) and received adjuvant chemotherapy.

## Discussion

Emerging data suggest that inclusion of the mesentery in surgery for CD, is associated with improved long-term



**Figure 2** Bar charts summarising distribution of categories of complications and complication rates. (A) Comparison of complications by Clavien-Dindo classification system across all groups. (B) Perioperative blood transfusion requirement following ileocolic resection (up to seven days post-operatively). 30D, 30-day; MI, mesentery including.

outcomes. The question thus arises as to the short term outcomes (i.e., complications) associated with inclusion of the mesentery. In this analysis, MI resection for CD was not associated with increased 30-day morbidity or severe morbidity (Clavien-Dindo III) and complication rates were similar to quoted international ranges (23,24). Furthermore, MI resection was not associated with increased major vascular injury, bleeding complications or blood transfusion. In select patients with extensive CD a pragmatic two-stage approach involving initial defunctioning ileostomy and subsequent successful MI resection was possible in 90% of cases.

In previous conventional practice, the mesentery was not included in standard surgical approaches for CD as it was speculated that it may be associated with increased rates of complications. In addition, 'standard' CD resection was already associated with significant morbidity (24). The authors have previously reported that MI resection for ileocolic CD was associated with reduced surgical recurrence rates (1). Similar benefits may be associated with inclusion of the mesentery during proctectomy for CD (13). Increasing recognition of the complex role of the mesentery in both the etiology and disease activity of CD underpins



**Table 3** Risk factors for developing 30-day morbidity and for developing severe 30-day morbidity

| Risk factors  | Univariate analysis |            |       | Multivariate analysis |            |       |
|---|---------------------|------------|-------|-----------------------|------------|-------|
|   | OR                  | 95% CI     | P     | OR                    | 95% CI     | P     |
| Risk factors for developing (all cause) 30 day-morbidity                |                     |            |       |                       |            |       |
| Age   | 0.53                | 0.18–1.56  | 0.25  | 0.58                  | 1.01–1.12  | 0.453 |
| Smoking   | 2.50                | 0.88–7.37  | 0.058 | 1.17                  | 0.59–17.72 | 0.027 |
| CD behaviour (fistulating/stricturing)                                  | 1.80                | 0.65–5.08  | 0.259 | –                     | –          | –     |
| Mesenteric resection  | 0.82                | 0.66–4.32  | 0.221 | 0.75                  | 0.68–6.58  | 0.194 |
| Pre-op steroids/antiTNF   | 1.89                | 0.64–5.50  | 0.247 | 1.23                  | 0.75–15.65 | 0.113 |
| Risk factors for developing severe (Clavien-Dindo III) 30-day morbidity |                     |            |       |                       |            |       |
| Age   | 1.15                | 0.40–8.11  | 0.222 | 1.08                  | 0.31–2.82  | 0.347 |
| Smoking   | 2.17                | 0.49–9.01  | 0.030 | 1.92                  | 1.10–6.99  | 0.054 |
| CD behaviour (fistulating/stricturing)                                  | 1.01                | 0.99–1.01  | 0.840 | –                     | –          | –     |
| Mesenteric resection  | 0.98                | 0.78–4.56  | 0.180 | 1.82                  | 0.79–5.64  | 0.099 |
| Pre-op steroids/antiTNF   | 2.15                | 0.40–11.42 | 0.231 | 1.53                  | 0.06–2.55  | 0.097 |

OR, odds ratio; 95% CI, 95% confidence interval; P, P value, significant at <0.05; CD, Crohns' disease; Pre-op, pre-operative; TNF, tumour necrosis factor.

the concept of inclusion of the mesentery as part of surgery for CD (3,25). While there is a perception that MI resection in CD may be a high risk surgical strategy associated with increased surgical morbidity, in particular increased risk of significant bleeding and vascular injury, this was not supported by the findings of the present study.

Importantly, dissection of the mesenteric root region was not performed. The idea of dissection through this region is often muted as the main concern regarding inclusion of the mesentery in surgery for CD. In cases of ileocolic disease the mesentery was fully mobilized to the level of the root region to facilitate delivery of the intestine and easy access to the mesentery for its division. The proximal intestinal division was placed immediately proximal to the mesenteric transition zone (i.e., the zone where the mesentery changes from normal to abnormal) (1,22). The distal intestinal division was placed in the small bowel or colon (where appropriate) at the first level at which both mesentery and bowel were macroscopically normal in appearance.

In this study, faecal diversion was employed as the first step as part of a staged MI resection in patients with severe complicated CD requiring urgent surgery. In these cases, normal surgical planes could not be identified and diversion was associated with disease regression to the point that a mesenteric resection was possible at the subsequent

operation. The staged strategy was successful in 90% of cases. The benefits of a staged approach must be offset against the potential risks. One patient was diagnosed with a small bowel adenocarcinoma of the terminal ileum. The incidence of adenocarcinoma of the small intestine is generally low, with an incidence 50-fold lower than colorectal carcinoma in general (26). While CD is a risk factor for development of small bowel adenocarcinoma, the risk remains low at about 4%, even in high risk patients with CD. It is difficult to detect with screening and screening is not currently recommended (27). Whilst loop ileostomy formation and deferral of resection might be criticized in this regard, a similar risk also arises with stricturoplasty, or bypass, where the intestine is also retained. It is also worth considering the impact of faecal diversion on disease activity and microbial diversity (2,28-30).

Limitations of this study include the retrospective analysis of data collected. Information on baseline haematological results, minor intra-operative vascular complications and exact timing of blood transfusion were not recorded and thus could not be reported on. Whilst there were some differences in clinicopathological characteristics between groups such as heterogeneity is a feature of clinical practice. The MESOCOLIC Trial (Clinical Trials.gov, NCT03769922), is a randomized,

multicenter trial that will determine and compare outcomes in patients undergoing either mesenteric resection of conventional resection for ileocolic CD (14). Of note however, the safety of MI surgery is also supported by other non-RCT based research (1,31).

## Conclusions

In conclusion, in this cohort analysis operative morbidity was similar for patients undergoing either a conventional resection (in which the mesentery was retained) or surgery in which the mesentery was included, for CD. A staged resection involving defunctioning loop ileostomy and later resection is a feasible option for patients in whom inclusion of the mesentery cannot be achieved at initial operation.

## Acknowledgments

The study team thank the inflammatory bowel disease multidisciplinary team at University Hospital Limerick for supporting this study. The findings of this manuscript were presented at the Irish Association of Coloproctology Annual Meeting, Dublin, May 2019.

*Funding:* None.

## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at <https://map.amegroups.com/article/view/10.21037/map-22-3/rc>

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://map.amegroups.com/article/view/10.21037/map-22-3/coif>). JCC serves as the Editor-in-Chief of *Mesentery and Peritoneum*. The other authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are 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. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Ethical approval was prospectively obtained from the University of Limerick Hospital Group ethics committee (Ref 57/15) and individual consent for this retrospective analysis was waived. .

*Open Access Statement:* This is an Open Access article

distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

## References

1. Coffey CJ, Kiernan MG, Sahebally SM, et al. Inclusion of the Mesentery in Ileocolic Resection for Crohn's Disease is Associated With Reduced Surgical Recurrence. *J Crohns Colitis* 2018;12:1139-50.
2. Kiernan MG, Coffey JC, McDermott K, et al. The Human Mesenteric Lymph Node Microbiome Differentiates Between Crohn's Disease and Ulcerative Colitis. *J Crohns Colitis* 2019;13:58-66.
3. Coffey JC, O'Leary DP. The mesentery: structure, function, and role in disease. *Lancet Gastroenterol Hepatol* 2016;1:238-47.
4. Fumery M, Pariente B, Sarter H, et al. Long-term outcome of pediatric-onset Crohn's disease: A population-based cohort study. *Dig Liver Dis* 2019;51:496-502.
5. Rivera ED, Coffey JC, Walsh D, et al. The Mesentery, Systemic Inflammation, and Crohn's Disease. *Inflamm Bowel Dis* 2019;25:226-34.
6. Connelly TM, Malik Z, Sehgal R, et al. Should surgical intervention become a primary treatment modality in Crohn's disease?—A review of the role of surgery and emerging surgical techniques. *Mesentery Peritoneum* 2018;2:2.
7. Fornaro R, Caratto E, Caratto M, et al. Post-operative recurrence in Crohn's disease. Critical analysis of potential risk factors. An update. *Surgeon* 2015;13:330-47.
8. Shaffer VO, Wexner SD. Surgical management of Crohn's disease. *Langenbecks Arch Surg* 2013;398:13-27.
9. Coffey JC, O'Leary DP, Kiernan MG, et al. The mesentery in Crohn's disease: friend or foe? *Curr Opin Gastroenterol* 2016;32:267-73.
10. Sehgal R, Connelly TM, Mohan HM, et al. The importance of the mesentery in emergency general surgery: ignore the mesentery at your peril. *Mesentery Peritoneum* 2018;2:4.
11. Coffey JC, O'leary DP. Defining the mesentery as an organ and what this means for understanding its roles in digestive disorders. *Expert Rev Gastroenterol Hepatol*

- 2017;11:703-5.
12. Mao R, Kurada S, Gordon IO, et al. The Mesenteric Fat and Intestinal Muscle Interface: Creeping Fat Influencing Stricture Formation in Crohn's Disease. *Inflamm Bowel Dis* 2019;25:421-6.
  13. de Groof EJ, van der Meer JHM, Tanis PJ, et al. Persistent Mesorectal Inflammatory Activity is Associated With Complications After Proctectomy in Crohn's Disease. *J Crohns Colitis* 2019;13:285-93.
  14. Li Y, Mohan H, Lan N, et al. Mesenteric excision surgery or conservative limited resection in Crohn's disease: study protocol for an international, multicenter, randomized controlled trial. *Trials* 2020;21:210.
  15. Bemelman WA, Warusavitarne J, Sampietro GM, et al. ECCO-ESCP Consensus on Surgery for Crohn's Disease. *J Crohns Colitis* 2018;12:1-16.
  16. Lightner AL, Vogel JD, Carmichael JC, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Surgical Management of Crohn's Disease. *Dis Colon Rectum* 2020;63:1028-52.
  17. Bellolio F, Cohen Z, Macrae HM, et al. Outcomes following surgery for perforating Crohn's disease. *Br J Surg* 2013;100:1344-8.
  18. McKenna NP, Habermann EB, Glasgow AE, et al. Intra-abdominal Sepsis After Ileocolic Resection in Crohn's Disease: The Role of Combination Immunosuppression. *Dis Colon Rectum* 2018;61:1393-402.
  19. Kamel AY, Ayoub F, Banerjee D, et al. Effects of Preoperative Use of Biologic Agents on Operative Outcomes in Crohn's Disease Patients. *Am Surg* 2018;84:1526-30.
  20. Gomollón F, Dignass A, Annese V, et al. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 1: Diagnosis and Medical Management. *J Crohns Colitis* 2017;11:3-25.
  21. Louis E, Collard A, Oger AF, et al. Behaviour of Crohn's disease according to the Vienna classification: changing pattern over the course of the disease. *Gut* 2001;49:777-82.
  22. Coffey JC, Sehgal R, Walsh D. *Mesenteric Principles of Gastrointestinal Surgery, Basic and Applied Science*. 1st edition. Boca Raton, FL, USA: CRC Press, 2017.
  23. Buskens CJ, Bemelman WA. Inclusion of the Mesentery in Ileocolic Resection for Crohn's Disease is Associated with Reduced Surgical Recurrence: Editorial by Coffey et al. *J Crohns Colitis* 2018;12:1137-8.
  24. de Buck van Overstraeten A, Eshuis EJ, Vermeire S, et al. Short- and medium-term outcomes following primary ileocaecal resection for Crohn's disease in two specialist centres. *Br J Surg* 2017;104:1713-22.
  25. Buskens CJ, de Groof EJ, Bemelman WA, et al. The role of the mesentery in Crohn's disease. *Lancet Gastroenterol Hepatol* 2017;2:245-6.
  26. de Bree E, Rovers KP, Stamatiou D, et al. The evolving management of small bowel adenocarcinoma. *Acta Oncol* 2018;57:712-22.
  27. Simon M, Cosnes J, Gornet JM, et al. Endoscopic Detection of Small Bowel Dysplasia and Adenocarcinoma in Crohn's Disease: A Prospective Cohort-Study in High-Risk Patients. *J Crohns Colitis* 2017;11:47-52.
  28. Magro DO, Santos A, Guadagnini D, et al. Remission in Crohn's disease is accompanied by alterations in the gut microbiota and mucins production. *Sci Rep* 2019;9:13263.
  29. Beamish EL, Johnson J, Shaw EJ, et al. Loop ileostomy-mediated fecal stream diversion is associated with microbial dysbiosis. *Gut Microbes* 2017;8:467-78.
  30. Watanabe Y, Mizushima T, Okumura R, et al. Fecal Stream Diversion Changes Intestinal Environment, Modulates Mucosal Barrier, and Attenuates Inflammatory Cells in Crohn's Disease. *Dig Dis Sci* 2022;67:2143-57.
  31. Holubar SD, Gunter RL, Click BH, et al. Mesenteric Excision and Exclusion for Ileocolic Crohn's Disease: Feasibility and Safety of an Innovative, Combined Surgical Approach With Extended Mesenteric Excision and Kono-S Anastomosis. *Dis Colon Rectum* 2022;65:e5-13.

doi: 10.21037/map-22-3

**Cite this article as:** Fleming CA, Mohan HM, Kiernan M, Fahad Ullah M, Waldron D, Peirce C, Walsh D, Moloney M, Skelly M, Tibbitts P, Coffey JC. Surgical morbidity is acceptable following a one or two stage mesentery-including surgery for Crohn's disease and comparable to mesentery-sparing surgery. *Mesentery Peritoneum* 2023;7:1.