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# Adhesion formation after surgery for locally advanced colonic cancer in the COLOPEC trial

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The COLOPEC trial collaborators are co-authors of this study and are listed under the heading Collaborators.

## Introduction

Small bowel obstruction, infertility, and chronic abdominal pain are generally mentioned as the main clinical consequences of adhesion formation after abdominal surgery<sup>1,2</sup>. Difficulties experienced during reoperation are less pronounced consequences, but seem to have a huge impact. A large retrospective cohort study<sup>3</sup> revealed that adhesiolysis was significantly associated with risk of sepsis (odds ratio (OR) 5.12), intra-abdominal complications (OR 3.46), and wound infection (OR 2.45). There is very limited literature on intraoperative assessment of adhesions and modifiable risk factors, especially in patients with locally advanced colonic cancer<sup>4,5</sup>. Laparoscopic surgery seems to reduce the burden of adhesions, but is considered a relative contraindication in T4 disease<sup>6</sup>. The aim of this study was to compare the presence and severity of adhesions after laparoscopic or open resection of locally advanced colonic cancer at 18-month re-exploration of the abdomen in the COLOPEC randomized trial, which was designed to assess adjuvant hyperthermic intraperitoneal chemotherapy<sup>7</sup>.

## Methods

Detailed methods of this study are provided in [Appendix S1](#). Outcomes of the present study were presence and severity (classified from 0 to 10 according to Dowson and colleagues<sup>6</sup>) of adhesions at 18 months. Severe adhesions were defined as those with a Dowson score exceeding 6. The Zühlke score classifies adhesions as: 1, filmy adhesions; 2, stronger adhesions requiring sharp dissection; 3, dense vascularized adhesions requiring sharp dissection; and 4, extreme dense vascularized adhesions with high risk of organ damage during dissection<sup>8</sup>.

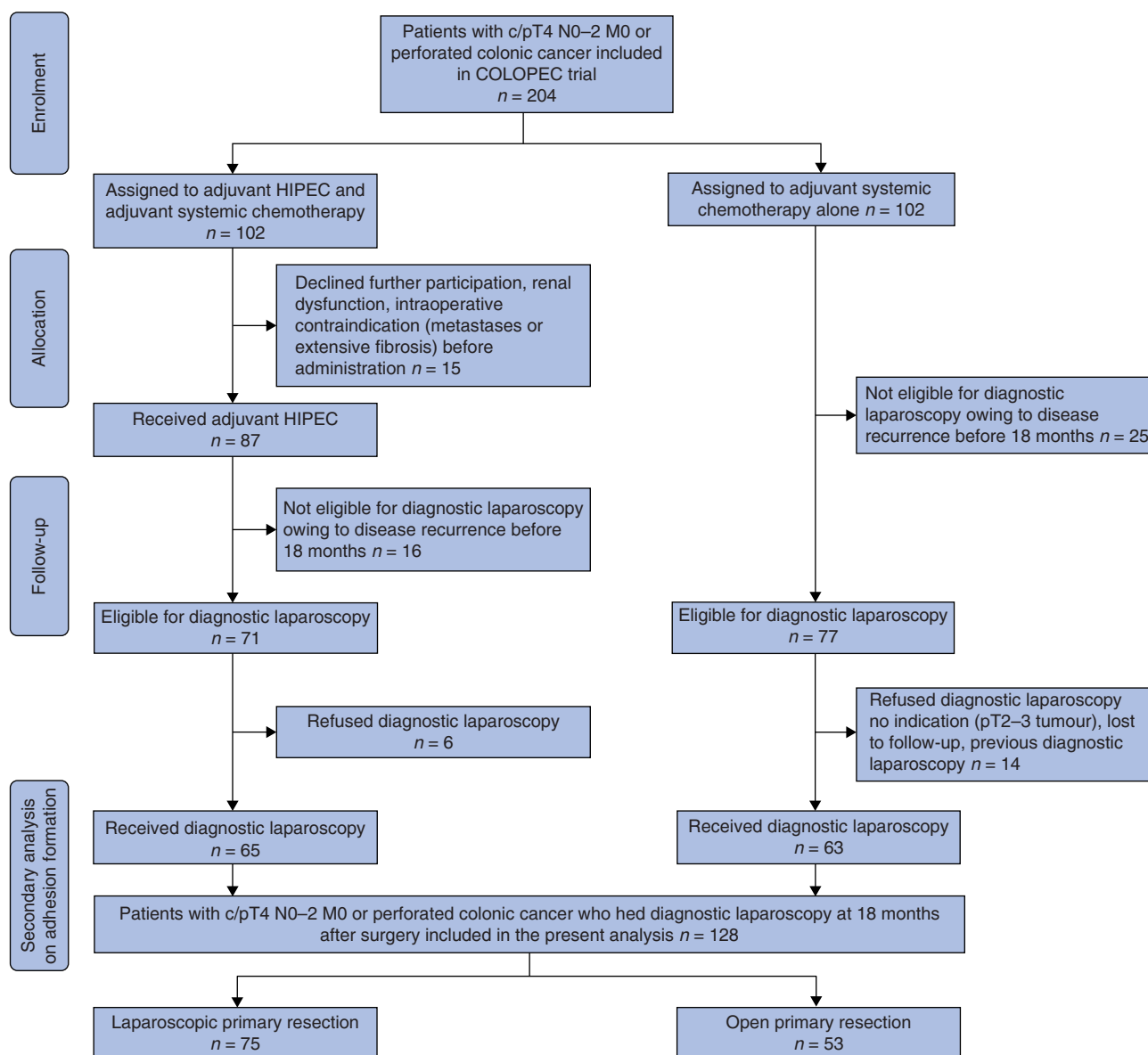
## Results

[Figure 1](#) shows patient enrolment, allocation, and follow-up in the COLOPEC trial and how the inclusion of patients in the present analysis was derived. In short, 204 patients with resectable primary c/pT4 N0–2 M0 or perforated colonic tumours were randomized and evaluated by laparoscopy at 18 months. The primary tumour resection was laparoscopic in 75, open in 43, and converted in 10 patients ([Table 1](#)). Adhesions were present in 36 patients (48 per cent) in the laparoscopic group and 46 (89 per cent) in the open group ([Table 2](#)). Adhesions after open primary resection were more often extensive (42 versus 11 per cent), more often had a Zühlke score of 3 or higher (51 versus 14 per cent), and had a significantly higher mean Dowson adhesion severity score (5.3 versus 2.4). Serosal tears occurred during adhesiolysis in five patients after open primary resection, but not after initial laparoscopic resection.

Previous abdominal surgery, multivisceral resection, and perforation were included in a multivariable model as confounders for adhesion formation. Open surgery was associated with the presence (OR 6.33, 95 per cent c.i. 2.24 to 17.89) ([Table S1](#)) and severity (OR 4.37, 1.84 to 10.41) of adhesions ([Table S2](#)).

## Discussion

Few studies have evaluated adhesions after open and laparoscopic abdominal surgery by re-exploration<sup>4–6,9</sup>, and were limited by sample size, varying indication, or an insufficient time interval to re-exploration. The clinical relevance of the present findings relate to metachronous metastases requiring abdominal re-exploration. The use of laparoscopy for locally advanced colorectal cancer surgery is accepted<sup>10</sup> and with that will come fewer adhesional issues. The present trial did not randomize between



**Fig. 1** CONSORT study flow diagram

HIPEC, hyperthermic intraperitoneal chemotherapy.

surgical approaches and there existed allocation bias as a result (a higher proportion of patients with perforation, pT4b tumours, and multivisceral resections in the open group). The approach may have been influenced by these factors, which may themselves have influenced adhesion risks. The study supports the view that the formation and severity of adhesions is reduced by laparoscopic surgery for locally advanced colonic cancer.

## Collaborators

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**Table 1** Baseline characteristics of all patients who underwent re-exploration at 18 months in the COLOPEC trial, stratified by surgical approach for primary tumour resection

|   | Available data | Laparoscopic primary resection (n = 75) | Open primary resection (n = 53) |
|---|----------------|---|---------------------------------|
| <b>Men</b>  | 128 (100)      | 44 (59)                                 | 26 (49)                         |
| <b>Age (years)*</b>                               | 128 (100)      | 61 (53–69)                              | 60 (47–73)                      |
| <b>ASA fitness grade</b>                          |                |   |                                 |
| I   | 128 (100)      | 31 (41)                                 | 16 (30)                         |
| II  |                | 42 (56)                                 | 34 (64)                         |
| III   |                | 2 (3)                                   | 3 (6)                           |
| <b>Previous abdominal surgery</b>                 | 127 (99.2)     | 26 (35)                                 | 16 (31)                         |
| Cholecystectomy                                   |                | 3 (4)                                   | 1 (2)                           |
| Appendicectomy                                    |                | 8 (11)                                  | 3 (6)                           |
| Hysterectomy                                      |                | 3 (4)                                   | 1 (2)                           |
| Colorectal resection                              |                | 4 (5)                                   | 2 (4)                           |
| Small bowel resection                             |                | 1 (1)                                   | 0 (0)                           |
| Gastric perforation                               |                | 1 (1)                                   | 0 (0)                           |
| Other abdominal procedures                        |                | 10 (13)                                 | 9 (17)                          |
| <b>Primary tumour (resection) characteristics</b> |                |   |                                 |
| Pathological T category                           |                |   |                                 |
| pT2   | 128 (100)      | 0 (0)                                   | 2 (4)                           |
| pT3   |                | 6 (8)                                   | 10 (19)                         |
| pT4a  |                | 64 (85)                                 | 24 (45)                         |
| pT4b  |                | 5 (7)                                   | 17 (32)                         |
| Perforation                                       | 128 (100)      | 10 (13)                                 | 16 (30)                         |
| Emergency   | 128 (100)      | 8 (11)                                  | 12 (23)                         |
| Conversion  | 128 (100)      | 0 (0)                                   | 10 (19)                         |
| Multivisceral resection                           | 128 (100)      | 16 (21)                                 | 31 (59)                         |
| Procedure type                                    |                |   |                                 |
| (Extended) right hemicolectomy                    | 128 (100)      | 27 (36)                                 | 21 (40)                         |
| (Extended) left hemicolectomy                     |                | 11 (15)                                 | 7 (13)                          |
| Sigmoid resection                                 |                | 22 (29)                                 | 18 (33)                         |
| Subtotal colectomy                                |                | 1 (1)                                   | 1 (2)                           |
| Anterior resection                                |                | 14 (19)                                 | 6 (11)                          |
| <b>Postoperative course</b>                       |                |   |                                 |
| Surgical complications                            | 128 (100)      | 20 (27)                                 | 20 (38)                         |
| Anastomotic leakage                               |                | 1 (1)                                   | 1 (2)                           |
| Abscess   |                | 1 (1)                                   | 0 (0)                           |
| Wound infection                                   |                | 1 (1)                                   | 3 (6)                           |
| Postoperative ileus                               |                | 5 (7)                                   | 4 (8)                           |
| Fascial dehiscence                                |                | 0 (0)                                   | 0 (0)                           |
| CD grade $\geq$ II complications                  | 128 (100)      | 15 (20)                                 | 17 (32)                         |
| Surgical reintervention                           | 126 (98.4)     | 4 (5)                                   | 1 (2)                           |
| Laparotomy  |                | 2 (3)                                   | 1 (2)                           |
| Laparoscopy                                       |                | 2 (3)                                   | 0 (0)                           |
| With creation of ileostomy                        |                | 1 (1)                                   | 0 (0)                           |
| With creation of colostomy                        |                | 0 (0)                                   | 0 (0)                           |
| Adjuvant HIPEC without CRS                        | 128 (100)      | 38 (51)                                 | 25 (47)                         |
| Successful laparoscopic adjuvant HIPEC            | 63 (100)       | 33 (87)                                 | 11 (44)                         |
| Converted laparoscopic adjuvant HIPEC             |                | 1 (3)                                   | 2 (8)                           |
| Open adjuvant HIPEC                               |                | 4 (11)                                  | 12 (48)                         |

Values in parentheses are percentages unless indicated otherwise; \*values are median (i.q.r.). CD, Clavien–Dindo; HIPEC, hyperthermic intraperitoneal chemotherapy; CRS, cytoreductive surgery.

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**Table 2 Adhesions during re-explorations at 18 months in the COLOPEC trial, stratified by surgical approach for primary tumour resection**

|  | Available data | Laparoscopic primary resection<br>(n = 75) | Open primary resection<br>(n = 53) | P¶       |
|--|----------------|--|------------------------------------|----------|
| <b>Any adhesions</b>                                 | 127 (99.2)     | 36 (48)                                    | 46 (89)                            | < 0.001  |
| <b>Subjective assessment of extent of adhesions</b>  | 81 (98.8)      |  |                                    | 0.001    |
| Limited  |                | 29 (81)                                    | 18 (40)                            |          |
| Moderate   |                | 3 (8)                                      | 8 (18)                             |          |
| Extensive  |                | 4 (11)                                     | 19 (42)                            |          |
| <b>Difficulties with abdominal entry</b>             | 127 (99.2)     | 3 (4)                                      | 8 (15)                             | 0.025    |
| <b>Highest Zühlke score†</b>                         | 116 (90.6)     |  |                                    | < 0.001  |
| 0  |                | 39 (53)                                    | 7 (16)                             |          |
| 1  |                | 9 (12)                                     | 3 (7)                              |          |
| 2  |                | 15 (21)                                    | 11 (26)                            |          |
| 3  |                | 6 (8)                                      | 16 (37)                            |          |
| 4  |                | 4 (5)                                      | 6 (14)                             |          |
| <b>Anatomical site</b>                               | 74 (90.2)      |  |                                    |          |
| 1: access wound                                      |                | 30 (86)                                    | 37 (95)                            | 0.245    |
| 2: site of pathology                                 |                | 15 (43)                                    | 7 (18)                             | 0.019    |
| 3: other distant sites‡                              |                | 15 (43)                                    | 18 (46)                            | 0.776    |
| <b>Total no. of anatomical sites</b>                 | 119 (92.9)     |  |                                    | < 0.001  |
| 1  |                | 18 (24)                                    | 23 (51)                            |          |
| 2  |                | 9 (12)                                     | 9 (20)                             |          |
| 3  |                | 8 (11)                                     | 7 (15)                             |          |
| <b>Small bowel involvement</b>                       | 74 (90.2)      | 11 (15)                                    | 24 (53)                            | < 0.001  |
| <b>Dowson adhesion severity score (range 0–10)*§</b> | 116 (90.6)     | 2.4 (3.0)                                  | 5.3 (3.0)                          | < 0.001# |
| <b>Adhesiolysis</b>                                  | 82 (100)       | 18 (50)                                    | 24 (52)                            | 0.845    |
| Duration (min)*                                      | 32 (39.0)      | 14.43 (24.69)                              | 19.89 (23.64)                      | 0.530#   |
| Estimated area (cm <sup>2</sup> )*                   | 61 (74.4)      | 31.46 (56.51)                              | 102 (146.39)                       | 0.023#   |
| Highest difficulty score (range 0–5)*                | 46 (56.1)      | 0.94 (1.11)                                | 1.79 (1.79)                        | 0.056#   |
| <b>Complications</b>                                 |                |  |                                    |          |
| Serosal tear   | 125 (97.7)     | 0 (0)                                      | 5 (10)                             | 0.010    |
| Inadvertent enterotomy                               | 128 (100)      | 0 (0)                                      | 1 (2)                              | 0.414    |
| <b>Re-exploration at 18 months</b>                   | 128 (100)      |  |                                    |          |
| Laparoscopic   |                | 75 (100)                                   | 53 (100)                           | –        |
| Converted laparoscopic                               |                | 2 (3)                                      | 6 (11)                             | 0.046    |

Values in parentheses are percentages unless indicated otherwise; \*values are mean (s.d.). †Zühlke score: 1, filmy adhesions; 2, stronger adhesions requiring sharp dissection; 3, dense vascularized adhesions requiring sharp dissection; 4, extreme dense vascularized adhesions with high risk of organ damage during dissection. ‡Including abdominal wall outside access wound, perihepatic left subphrenic region, pelvis, omentum, mesentery. §Adapted from Dowson et al.<sup>6</sup>; worst severity score (0–3 points) + overall extent of adhesions in peritoneal cavity (0–3 points) + number of sites (0–3 points) + involvement of small bowel (0–1 point). ¶ $\chi^2$  test, except #Student's t-test.

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E.S.Z. and D.D.W. contributed equally to this work. This study was endorsed by the Dutch Colorectal Cancer Group and the Dutch Peritoneal Oncology Group.

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**Disclosure.** The authors declare no conflict of interest.

## Supplementary material

Supplementary material is available at BJS online.

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