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Staging accuracy, treatment pathways, and outcomes of minimally invasive surgery in clinical T4 colorectal cancer: how reliable is the T4 label?

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Abstract

Background: Clinical T4 (cT4) staging of colorectal cancer is imprecise, yet the label often precludes minimally invasive surgery (MIS). We assessed cT4 staging accuracy and the outcomes of selective MIS for cT4 colon cancer.

Methods: We reviewed patients resected for non-metastatic cT4 colorectal cancer at one center (2011–2022) and described their treatment pathways. MIS and open surgery were compared in elective colon resections using inverse probability of treatment weighting. The primary endpoint was recurrence-free survival (RFS); secondary endpoints were overall survival (OS), peritoneal metastasis, R0 resection, and 30-day morbidity.

Results: Of 383 patients (colon, 297; rectum, 86), 42.1% of colon cancers presented acutely, and 11.4% required emergency open resection. Among those without neoadjuvant therapy, only 55.6% had pathologic T4 disease. Of 263 elective colon resections, 178 were minimally invasive and 85 open, the latter favored for cT4b tumors and elevated carcinoembryonic antigen. After weighting, MIS was not associated with inferior RFS (hazard ratio [HR], 0.66; 95% confidence interval [CI], 0.42–1.04) or OS (HR, 0.69; 95% CI, 0.41–1.15). R0 rates were comparable (96.1% vs 95.3%), and 30-day complications were less frequent after MIS (−17.4 percentage points; 95% CI, −29.5 to −3.4). Peritoneal metastasis was uncommon (12 events; 5.5% vs 4.0% at 5 years), an exploratory estimate too imprecise to establish equivalence.

Conclusions: Because nearly half of cT4 tumors are overstaged, the label alone should not preclude MIS. Selected on the surgeon's appraisal of disease extent, MIS was associated with lower morbidity without a detectable survival penalty, although residual confounding remains possible.

Keywords: Colonic neoplasms, Neoplasm staging, Diagnostic accuracy, Minimally invasive surgical procedures, Laparoscopy, Peritoneal neoplasms, Propensity score

Background

Clinical T4 (cT4) colorectal cancer, defined by tumor penetration of the visceral peritoneum (cT4a) or invasion of adjacent organs or structures (cT4b), represents the most locally advanced form of non-metastatic disease. These tumors carry a higher risk of incomplete resection and peritoneal recurrence, and a poorer prognosis, than tumors of lower T categories [1, 2]. Because the clinical T category determines much of the subsequent management, a cT4 designation sets in motion the most intensive treatment available for localized disease.

How that treatment unfolds depends on tumor location. The rectum lies within the bony pelvis, where the circumferential resection margin is at risk; rectal cancer is therefore staged with pelvic magnetic resonance imaging (MRI), and locally advanced tumors generally receive preoperative chemoradiotherapy or total neoadjuvant therapy before total mesorectal excision or, when adjacent pelvic organs are involved, multivisceral resection [3]. The colon, by contrast, is largely intraperitoneal and mobile, and cT4 colon cancer is usually managed with upfront en bloc resection followed by adjuvant chemotherapy [4]. Neoadjuvant chemotherapy selected on radiologic stage has shown promise in a randomized trial [5] but has not yet displaced upfront surgery. Colon cancer also presents more often as an emergency: obstruction is present at diagnosis in 10%–18% of patients, emergency resection carries higher morbidity and mortality and worse long-term outcomes than elective surgery, and self-expandable metallic stents can bridge patients to elective resection, although their use depends on tumor location [6]. In either site, a cT4 label favors en bloc multivisceral resection and, frequently, an open rather than a minimally invasive operation.

All of these decisions rest on a clinical stage that is often wrong. Computed tomography (CT) has limited accuracy for the local staging of colon cancer [7], and imaging cannot reliably distinguish true invasion of the serosa or an adjacent organ from peritumoral

inflammation or adhesion. In the upfront-surgery arm of the FOxTROT trial, local radiologists correctly identified only 41% of T4 tumors, even though T3–4 disease as a group was recognized with a positive predictive value of 95% [8]. Across four experienced radiology teams, agreement on the clinical T category was inadequate, and CT detected only 33% of pathologic T4 tumors [9]. Published rates of pathologic confirmation range from fewer than half of cT4 tumors [10] to about three-quarters in a small series with suspected organ invasion [11]. Overstaging predominates, so many patients are treated for disease more extensive than they actually have.

The choice of operative approach shows the consequences most clearly. Minimally invasive surgery (MIS) is widely adopted for resectable colorectal cancer, and in randomized trials laparoscopic resection achieved long-term survival similar to that of open surgery in stage II–III colon cancer [12] and similar locoregional recurrence and survival in rectal cancer [13]. Patients with T4 tumors, however, were underrepresented or excluded, and MIS for T4 disease remains controversial. Meta-analyses and propensity score–matched series have reported comparable R0 resection rates and survival after laparoscopic and open resection of T4 colon cancer [14–17], population-based data have favored MIS [18, 19], and series that selected patients on clinical rather than pathologic stage have concluded that suspected T4 disease is not in itself a contraindication to laparoscopy [11, 20]. These comparisons nonetheless remain vulnerable to selection bias, because open surgery is reserved for the most advanced tumors, and most were restricted to pathologic T4 disease, a group that cannot be identified when the approach is chosen. Several retrospective studies and a recent meta-analysis have also reported more peritoneal recurrence after MIS for T4 colon cancer [21–23], raising the possibility, not yet established, that pneumoperitoneum or tumor manipulation promotes peritoneal dissemination.

If a substantial proportion of cT4 tumors are overstaged, the label alone may be an insufficient reason to withhold MIS. We therefore hypothesized that MIS, applied selectively on the basis of the surgeon's assessment of disease extent, would not be associated with worse outcomes than open surgery. To test this hypothesis, we first determined how often cT4 disease was confirmed pathologically and whether preoperative characteristics could identify overstaged tumors. We then described the treatment pathways of patients with cT4 colorectal cancer and, because rectal cancer follows a distinct staging and treatment sequence, compared MIS with open surgery in elective resections of cT4 colon cancer, with recurrence-free survival as the primary outcome.

Methods

Study design and patients

We retrospectively reviewed an institutional database of patients who underwent resection for primary cT4 colorectal cancer at a single tertiary center between January 2011 and December 2022. Operations from January 2023 onward were not included, so that every patient had at least 18 months of potential follow-up before the data cut-off in June 2024. The study was approved by the institutional review board (approval no. VC26RISI0243), which waived the requirement for informed consent.

Clinical T stage was assigned before surgery according to the American Joint Committee on Cancer (AJCC) 8th edition, using contrast-enhanced CT for colon tumors and pelvic MRI for rectal tumors. Eligibility was based solely on information available before surgery, because the pathologic depth of invasion is unknown when the operative approach is chosen. Of 646 patients in the database, 83 operated on in 2023–2025 were not included, and 180 were excluded because of clinical M1 disease (n = 167), undetermined M stage (Mx, n = 6), anal squamous cell carcinoma (n = 2), ostomy creation without resection (n = 1), or a synchronous cancer in another organ (n = 4), leaving 383 patients (Fig. 1). Four other patients

with a synchronous cancer in another organ underwent elective resection for cT4 colon cancer; they were retained, and the primary analysis was repeated without them.

Study cohorts

The 383 patients formed the full cT4 cohort, which was used to assess staging accuracy and to describe clinical presentation and treatment. Operative approaches were compared only in the elective colon cohort (n = 263). Emergency resections (n = 34, all for colon cancer) were excluded from this comparison because all were performed with an open approach, leaving no comparable group. Rectal cancers (n = 86) were described separately, because their staging and treatment differ from those of colon cancer and only 8 were resected with an open approach.

Surgical expertise and technique

All operations were performed by three colorectal surgeons, each with more than 10 years of experience in minimally invasive colorectal surgery, at an institution that treats approximately 200–230 colorectal cancer cases annually. The operative technique was standardized and identical for laparoscopic and open procedures: D3 lymph node dissection; complete mesocolic excision for right hemicolectomy; high ligation of the inferior mesenteric artery with splenic flexure mobilization for left-sided and rectal resections; and specimen extraction through a midline incision after right or left hemicolectomy and through a Pfannenstiel incision after anterior or low anterior resection. A wound protector was used in every case, and any adjacent organ or structure suspected to be involved was resected en bloc, regardless of approach. The institutional goal for every operation was a textbook outcome, a composite measure in which all desired short-term outcomes of a colorectal cancer resection, including a radical resection and an uncomplicated recovery, are achieved [24].

Choice of operative approach

During the study period, no standardized algorithm or mandatory multidisciplinary tumor board review guided the choice of approach for locally advanced colon cancer. The operating surgeon selected the approach on the basis of preoperative imaging, suspected invasion of adjacent organs, and the patient's clinical condition. Laparoscopy was the standard minimally invasive technique; robotic surgery was used only for rectal cancer (n = 4), so all minimally invasive colon resections were laparoscopic. Patients were analyzed according to the intended approach (intention to treat), with conversions to open surgery retained in the MIS group. Because the individual surgeon was not recorded in the database, period of surgery served as a proxy for institutional experience and changes in practice.

Definitions

Emergency surgery was an unplanned resection during the index admission for perforation, obstruction, or another acute complication that precluded elective preparation. Obstruction was defined as obstructive symptoms (abdominal pain, distension, nausea, or vomiting) with an obstructing tumor and proximal colonic dilatation on abdominopelvic CT [6]. It was classified by its management before resection: decompression with a self-expandable metallic stent or a diverting stoma, or resection without prior decompression, performed either as an emergency or electively once symptoms had settled with conservative treatment. Perforation was free or contained perforation at the tumor site, identified before or during surgery. Right-sided tumors extended from the cecum to the mid-transverse colon and left-sided tumors from the distal transverse colon to the rectosigmoid junction; rectal cancer was a tumor within 15 cm of the anal verge. Pathologic stage followed the AJCC 8th edition, and pathologic T4 (pT4) disease was subclassified as pT4a (penetration of the visceral peritoneum) or pT4b (invasion of adjacent organs or structures). Combined organ resection was en bloc resection of any adjacent organ or structure. Complications within 30 days of

surgery were recorded; because the database did not grade them, those requiring reoperation or radiologic or endoscopic intervention were classified as Clavien–Dindo grade III or higher.

Outcomes

Staging accuracy was measured as the proportion of cT4 tumors confirmed as pT4. It was assessed in patients who had not received neoadjuvant therapy, in whom the pathologic T category reflects the untreated tumor.

For the comparison of operative approaches, the primary outcome was recurrence-free survival (RFS), measured from surgery to the first recurrence or death from any cause. Secondary outcomes were overall survival (OS), measured from surgery to death from any cause; the cumulative incidence of peritoneal metastasis, dated to its detection; R0 resection; any 30-day complication; and complications of Clavien–Dindo grade III or higher. All patients in the elective colon cohort had complete dates of surgery and last contact, and those without an event were censored at last contact. Cancer-specific survival was not analyzed because the cause of death could not be determined reliably.

Statistical analysis

Continuous variables are reported as median (interquartile range) and compared with the Mann–Whitney U test; categorical variables are reported as number (percentage) and compared with the chi-square or Fisher's exact test. Median follow-up was estimated with the reverse Kaplan–Meier method. Because the study was not designed as a formal non-inferiority comparison, results are presented as estimates with 95% confidence intervals (CI), and interpretation focuses on the range of effects compatible with the data. All tests were two-sided, with $P < 0.05$ considered significant.

Staging accuracy. In patients with colon cancer who had not received neoadjuvant therapy, preoperative factors associated with pathologic confirmation were identified by univariable and multivariable logistic regression and reported as odds ratios (OR). Candidate

184 factors were age, sex, clinical T category, initial carcinoembryonic antigen (CEA) level (≥5 vs
185 <5 ng/mL, with missing values classified as <5 ng/mL), clinical node status, tumor sidedness,
186 and presentation (emergency resection, or obstruction or perforation managed electively).
187 Period of surgery was omitted because clinical T4 was not subclassified before 2016 and was
188 therefore collinear with period; operative approach was omitted because it was itself chosen
189 partly on the basis of suspected invasion. The ability of the model to separate confirmed from
190 overstaged tumors was summarized with the area under the receiver operating characteristic
191 curve (AUC).

192 *Balancing the treatment groups.* In the elective colon cohort, the probability of receiving
193 MIS (the propensity score) was estimated by logistic regression from preoperative factors
194 likely to influence both the choice of approach and prognosis: age, sex, body mass index,
195 American Society of Anesthesiologists class (I–II vs III–IV), initial CEA level (log-
196 transformed), obstruction status (none, decompressed by stent or stoma, or resected without
197 decompression), perforation, clinical T category (cT4a, cT4b, or cT4 not otherwise specified),
198 clinical node status, tumor sidedness, and period of surgery (2011–2015, 2016–2020, or
199 2021–2022). Factors determined during or after surgery, such as combined organ resection,
200 pathologic stage, and adjuvant chemotherapy, were deliberately excluded, because they are
201 consequences of the approach rather than reasons for choosing it. Each patient was then
202 weighted by the inverse of the probability of the approach actually received, using stabilized
203 inverse probability of treatment weighting (IPTW) [25]; weights were truncated at the 1st and
204 99th percentiles (range, 0.42–2.30). The weighted groups were considered balanced when
205 every covariate had an absolute standardized mean difference (SMD) below 0.10 (Additional
206 file 1: Table S1), and the overlap of propensity scores between groups is shown in Additional
207 file 1: Fig. S1. To show how surgeons chose the approach, the same model is also reported as
208 ORs for open surgery (Additional file 1: Table S2). Missing values (initial CEA, n = 1;

sidedness, n = 5) were handled by median imputation and a separate missing category, respectively.

Outcome analyses. Survival was estimated with the Kaplan–Meier method and compared with the log-rank test, both without and with weighting. Hazard ratios (HR) were estimated with Cox proportional hazards models, and the proportional hazards assumption was checked with scaled Schoenfeld residuals. To express results on a clinically intuitive scale, differences in 5-year survival and in restricted mean survival time up to 5 years were also calculated. The cumulative incidence of peritoneal metastasis was estimated with death as a competing event, and subdistribution hazard ratios (sHR) were estimated with the Fine–Gray model [26]; because only 12 peritoneal metastases occurred, this model included the approach alone, and the outcome was treated as exploratory. R0 resection and complication rates were compared as weighted risk differences. Confidence intervals and P values for weighted estimates were obtained by bootstrapping with 2,000 resamples, re-estimating the propensity score in each resample so that uncertainty in the weights was taken into account.

Sensitivity and subgroup analyses. The robustness of the primary result was examined with weighted Cox models using robust variance, in three ways. First, the weighting method was varied: overlap weights, untruncated weights, and a doubly robust model that also adjusted for all propensity score covariates. Second, the analysis population was varied: conversions were analyzed as open surgery (per protocol); patients with perforation or neoadjuvant chemotherapy, with less than 5 years of potential follow-up, or with a synchronous cancer in another organ were excluded in separate analyses; and the analysis was restricted to patients in whom the two approaches were more comparable, namely those without cT4b disease, those with cT4a disease, and those within the region of common propensity score support. Third, the model was additionally adjusted for adjuvant chemotherapy. All elective colorectal resections (n = 349) were also analyzed together, with

stratification by tumor site and a test for interaction between approach and site. The E-value was calculated to indicate how strongly an unmeasured confounder would have to be associated with both approach and outcome to explain away the observed association [27]. Patients with pathologically confirmed T4 disease were analyzed as an exploratory subgroup, with the propensity score re-estimated and pT4b added as a covariate, and outcomes of pT4a and pT4b disease were compared irrespective of approach. Sensitivity and subgroup analyses were not adjusted for multiple comparisons. Analyses were performed in Python 3.13 (Python Software Foundation, Wilmington, DE, USA) with lifelines 0.30, statsmodels 0.15, and SciPy 1.18.

Results

Study population and clinical presentation

Of the 646 patients in the database, 383 were included: 297 with colon cancer and 86 with rectal cancer (Fig. 1).

Among the 297 patients with cT4 colon cancer, 125 (42.1%) presented acutely, and 34 (11.4%) required emergency resection: 14 for perforation, 14 for obstruction, and 6 for another acute complication (Table 1). All emergency resections were open. Compared with patients treated with MIS, those treated with open surgery more often presented acutely (56.3% vs 32.6%; $P < 0.001$), particularly with perforation (16.8% vs 2.2%; $P < 0.001$), had higher initial CEA levels, and more often had cT4b disease (19.3% vs 9.6%).

Accuracy of clinical T4 staging

Of the 304 patients who had not received neoadjuvant therapy and had a recorded pathologic T category, 169 (55.6%) had pT4 disease (pT4a, 75; pT4b, 94), whereas 135 (44.4%) were overstaged, with pT3 tumors in 132 and pT2 tumors in 3 (Table 2). Confirmation rates were similar for colon (56.0%) and rectal cancer (5 of 11) and did not change significantly over time (61.1% in 2011–2015, 54.1% in 2016–2020, and 50.0% in

2021–2022; P = 0.403). The clinical T subcategory was a weak guide: 50.3% of cT4a and 63.4% of cT4b tumors were confirmed as pT4 (P = 0.091 across categories), and only 19 of the 41 tumors staged as cT4b (46.3%) were found to invade an adjacent organ (pT4b).

An initial CEA level of 5 ng/mL or higher was associated with a higher rate of confirmation (66.9% vs 46.1%; P < 0.001) and, in the multivariable model for colon cancer, was the only independent predictor (adjusted OR, 2.29; 95% CI, 1.38–3.79). Neither cT4b category (adjusted OR, 1.87; 95% CI, 0.87–4.02) nor electively managed obstruction or perforation independently predicted confirmation, and the model separated confirmed from overstaged tumors poorly (AUC, 0.68). Confirmation was also more frequent among patients treated with open surgery than among those treated with MIS (70.6% vs 45.9%), consistent with the selection of open surgery for tumors that appeared more advanced.

Colon and rectal cancer

Rectal cancers followed a different course (Table 3). Neoadjuvant therapy, predominantly long-course chemoradiotherapy, was given to 75 of 86 patients with rectal cancer (87.2%) but to only 3 of 297 patients with colon cancer. Rectal cancers more often required combined organ resection and had higher rates of radial margin involvement (19.8% vs 8.2%) and recurrence (44.2% vs 20.5%). Because only 8 rectal resections were open, rectal outcomes are reported descriptively.

Elective colon cohort

The comparative cohort comprised 263 patients who underwent elective resection for cT4 colon cancer: 178 by MIS, all laparoscopic, and 85 by open surgery (Table 4). The proportion treated by MIS rose from 60.0% in 2011–2015 to 70.5% in 2016–2020 and 72.7% in 2021–2022, and 9 MIS procedures (5.1%) were converted to open surgery. The groups were similar in age, sex, American Society of Anesthesiologists class, obstruction status, and period of surgery. Patients selected for open surgery, however, had higher initial CEA levels (median

7.8 vs 4.1 ng/mL; P = 0.001), more often had cT4b disease (21.2% vs 9.6%; P = 0.002), and had larger tumors (median 8.0 vs 6.5 cm; P < 0.001). In multivariable analysis, cT4b category (OR, 3.33; 95% CI, 1.46–7.60) and a higher initial CEA level (OR per unit of log-transformed CEA, 1.39; 95% CI, 1.07–1.81) were independently associated with the choice of open surgery (Additional file 1: Table S2).

The pathologic findings were consistent with this selection. Compared with the MIS group, the open group more often required combined organ resection (47.1% vs 15.2%; P < 0.001), most frequently of the urinary tract (15.3% vs 7.9%) or small bowel (12.9% vs 0.6%), and more often had pT4 disease (81.0% vs 46.1%) and pT4b disease (52.4% vs 22.5%). Adjuvant chemotherapy was given at similar rates (MIS, 52.8%; open, 54.1%).

Before weighting, the largest imbalances were in initial CEA level (SMD, −0.39), body mass index (0.35), cT4b category (−0.33), and perforation (−0.23). After weighting, every covariate was balanced (maximum absolute SMD, 0.057; Additional file 1: Table S1), with stabilized weights ranging from 0.42 to 2.30. The propensity scores of the two groups overlapped across most of their range, and only 8 patients lay outside the region of common support (Additional file 1: Fig. S1).

Surgical outcomes

R0 resection rates were similar after MIS and open surgery (96.1% vs 95.3%; weighted, 96.0% vs 96.7%; Table 5). MIS was associated with less estimated blood loss (median 80 vs 100 mL; P < 0.001) and fewer intraoperative transfusions (2.2% vs 14.1%; P < 0.001), without a significant difference in operating time (median 205 vs 199 minutes; P = 0.054). Thirty-day complications occurred in 20.2% of patients after MIS and 35.3% after open surgery (weighted difference, −17.4 percentage points; 95% CI, −29.5 to −3.4), whereas major complications (Clavien–Dindo grade III or higher) did not differ significantly (weighted, 4.2% vs 6.6%; difference, −2.4 percentage points; 95% CI, −9.6 to 4.2).

Recurrence-free and overall survival

Over a median follow-up of 61.8 months, 53 patients in the elective colon cohort developed recurrence (distant in 46, locoregional and distant in 4, and locoregional only in 3), and 67 died. Without adjustment, 5-year RFS was 74.7% (95% CI, 66.9–80.9) after MIS and 55.3% (95% CI, 43.4–65.8) after open surgery (log-rank P = 0.004; HR, 0.54; 95% CI, 0.35–0.83), and 5-year OS was 79.7% (95% CI, 72.0–85.5) and 70.1% (95% CI, 57.9–79.4), respectively (log-rank P = 0.039; HR, 0.60; 95% CI, 0.37–0.98).

Weighting attenuated these differences, which were no longer statistically significant (Table 5, Fig. 2). Weighted 5-year RFS was 73.5% after MIS and 60.0% after open surgery (difference, 13.5 percentage points; 95% CI, 0.4–26.9; HR, 0.66; 95% CI, 0.42–1.04; P = 0.076), and the restricted mean RFS over 5 years differed by 5.5 months (95% CI, −0.6 to 11.7). Weighted 5-year OS was 79.7% and 73.4%, respectively (difference, 6.3 percentage points; 95% CI, −6.1 to 19.3; HR, 0.69; 95% CI, 0.41–1.15; P = 0.151). The proportional hazards assumption held (P = 0.62 for weighted RFS). The E-value for the RFS HR was 2.01: an unmeasured confounder would need to be associated with both the approach and the outcome by a risk ratio of at least 2.01 to fully explain the point estimate, whereas none would be needed to make the result compatible with no difference, because the CI included 1.

Peritoneal metastasis

Peritoneal metastasis developed in 12 patients in the elective colon cohort: 9 of 178 (5.1%) after MIS and 3 of 85 (3.5%) after open surgery. With death treated as a competing event, the weighted 5-year cumulative incidence was 5.5% and 4.0%, respectively (difference, 1.4 percentage points; 95% CI, −5.7 to 6.7; sHR, 1.35; 95% CI, 0.38–4.84; P = 0.647; Fig. 3). With so few events, these estimates are imprecise and compatible both with no difference and with a clinically important increase after MIS. No peritoneal metastasis occurred after any of the 34 emergency resections.

Sensitivity analyses

The primary result was consistent across sensitivity analyses, with HRs for RFS ranging from 0.59 to 0.73 (Additional file 1: Table S3); estimates were similar with overlap or untruncated weights, with a doubly robust model, with additional adjustment for adjuvant chemotherapy, when conversions were analyzed as open surgery, and when patients with a synchronous cancer in another organ were excluded. Restricting the analysis to patients in whom the approaches were more comparable yielded HRs for RFS of 0.66 (95% CI, 0.39–1.10) after excluding cT4b disease (n = 228), 0.59 (95% CI, 0.29–1.22) in cT4a disease (n = 147), and 0.64 (95% CI, 0.40–1.02) within the region of common propensity score support (n = 255). In the combined analysis of all 349 elective colorectal resections, stratified by tumor site, the HR for RFS was 0.69 (95% CI, 0.44–1.07), and the association did not differ between colon and rectal cancer (P for interaction, 0.98 for RFS and 0.85 for OS).

Pathologic T4 subgroup

Among the 150 patients in the elective colon cohort with pathologically confirmed T4 disease (MIS, 82; open, 68), the weighted HRs were 0.63 (95% CI, 0.37–1.17) for RFS and 0.76 (95% CI, 0.40–1.46) for OS (Additional file 1: Table S4). Peritoneal metastasis occurred in 7 patients after MIS and 3 after open surgery (weighted 5-year cumulative incidence, 8.8% vs 5.2%; difference, 3.6 percentage points; 95% CI, −5.9 to 12.9; sHR, 1.79; 95% CI, 0.48–6.65). Irrespective of approach, 5-year RFS was 49.4% for pT4a and 63.9% for pT4b disease (P = 0.186), and peritoneal metastasis occurred in 6 of 66 patients with pT4a disease (5-year cumulative incidence, 9.5%) and 4 of 84 with pT4b disease (5.1%).

Discussion

This study shows that clinical T4 staging is often inaccurate and that this inaccuracy bears directly on the choice of operative approach. Nearly half of the tumors staged as cT4 (44%) were not pT4, and no preoperative characteristic reliably identified them. A cT4 label

alone is therefore an insufficient reason to exclude MIS. The surgeons in this cohort did not rely on the label alone; they reserved open surgery for tumors that appeared to invade adjacent organs or were accompanied by higher CEA levels, and the pathology largely confirmed their judgment. Applied selectively in this way, MIS was associated with fewer postoperative complications, a similar R0 resection rate, and no worse recurrence-free or overall survival than open surgery.

The degree of overstaging in our cohort agrees with previous reports. CT has limited accuracy for the local staging of colon cancer [7]; in the FOxTROT trial, local radiologists correctly identified only 41% of T4 tumors [8], and agreement on the clinical T category was poor even among experienced radiology teams [9]. In a previous cT4 cohort, fewer than half of the tumors were pathologically T4 [10]. Several factors may explain this overstaging. On imaging, peritumoral inflammation, desmoplastic reaction, and adhesions to adjacent structures can mimic serosal penetration or organ invasion. The same confusion arises at operation: in published series of multivisceral resection for apparent organ invasion, histologic tumor infiltration was confirmed in only 44%–70% of patients [28, 29], comparable to the 46% of cT4b tumors confirmed as pT4b in our cohort. A paucity of visceral fat, which obscures tissue planes, has also been associated with inaccurate T staging on CT [30]. Finally, a tumor is the lead point in about half of adult intussusceptions [31]; when a colon cancer intussuscepts, the telescoped bowel forms a bulky mass that may appear to extend beyond the bowel wall despite a limited depth of invasion.

Because routinely available preoperative factors discriminated poorly between confirmed and overstaged tumors, this uncertainty cannot be resolved before surgery, and its consequences for multidisciplinary planning are considerable. Relying on a cT4 label alone would commit many patients with pT3 disease to open surgery, forfeiting the short-term benefits of MIS, and would expose a substantial proportion of patients without T4 disease to

neoadjuvant chemotherapy, since trials of neoadjuvant chemotherapy for colon cancer have selected patients on radiologic stage [5]. For this reason, the FOxTROT investigators have proposed radiologic T3–4 status as a group, rather than T4 status, as the selection criterion for neoadjuvant therapy [8]. We suggest that a cT4 classification should prompt multidisciplinary review and planning rather than determine the operative approach. Such review would include re-examination of the images by a dedicated radiologist, consideration of the CEA level, and preparation for en bloc resection or conversion if invasion is confirmed.

Staging was not the only determinant of treatment; clinical presentation and tumor location shaped the pathway before the operative approach was considered. Forty-two percent of patients with cT4 colon cancer presented acutely, and 11% required emergency resection, all by an open approach. In this setting, the approach is dictated by the patient's physiological condition and the need for source control, and outcomes are worse than after elective resection [6]; because no comparable MIS group existed, these patients were described but not compared. Tumor location determined how obstruction was managed. No stent was placed for the 23 obstructing tumors between the cecum and the hepatic flexure, in keeping with the practice of primary resection for right-sided obstruction [6], whereas 33 of 81 obstructing tumors of the transverse or left colon (41%) were decompressed with a stent as a bridge to surgery [6], and 21 of these 33 patients (64%) subsequently underwent MIS. Rectal cancer followed a distinct pathway, with local staging by MRI, neoadjuvant therapy in 87% of patients, and predominantly minimally invasive resection, and was therefore reported separately.

Among patients treated electively, the surgeons chose the approach according to the anticipated extent of disease rather than a categorical rule. Open surgery was favored for cT4b tumors and for tumors with higher CEA levels, and the pathology supported this judgment: compared with MIS resections, open resections had higher rates of pT4 disease (81% vs 46%)

and pT4b disease (52% vs 23%) and required combined organ resection about three times as often (47% vs 15%). MIS was thus used mainly for tumors that proved to be pT3 or pT4a, and it achieved an R0 resection rate of 96% with conversion in 5% of procedures. Conversion should be regarded as an intraoperative safeguard when tumor fixation or adjacent organ involvement threatens an en bloc R0 resection, rather than as a failure of the approach [32, 33]. CEA was associated both with the choice of open surgery and with pathologic confirmation of T4 disease, suggesting that it may usefully complement imaging when the approach is selected.

With this selective approach, MIS was associated with fewer 30-day complications, less blood loss, and fewer transfusions, without worse recurrence-free or overall survival. The large unadjusted survival advantage of MIS (HR, 0.54) was substantially attenuated after weighting (HR, 0.66), consistent with pooled and population-based evidence that much of the apparent survival benefit of MIS in T4 disease reflects case selection [14, 15, 18, 19]. The benefit supported by our data is therefore a short-term one, fewer complications without oncologic compromise, rather than longer survival. Moreover, because the surgical judgment that we regard as appropriate practice also determined who received MIS, the comparison cannot be interpreted causally. Unrecorded factors, such as the surgeon's assessment of technical difficulty, tumor fixation on imaging, and findings at initial laparoscopy, are likely to have favored MIS. Consistent results after restriction to patients without cT4b disease, to those with cT4a disease, and to the region of common propensity score support, together with an E-value of 2.01, offer some reassurance, but no analysis can fully account for unmeasured selection. The conclusion that our data support is therefore narrower: when experienced surgeons selected patients with cT4 colon cancer for MIS, outcomes were no worse than those of open surgery. The data do not show that MIS is appropriate for every cT4 tumor.

Peritoneal metastasis remains the principal oncologic concern with MIS for T4 colon cancer [21–23]. In our cohort, it occurred in 5.1% of patients after MIS and 3.5% after open surgery, and the difference was larger among patients with pathologically confirmed T4 disease (weighted 5-year incidence, 8.8% vs 5.2%). With only 12 events, these estimates are compatible both with no difference and with a clinically important increase after MIS; they are exploratory and do not establish equivalence for peritoneal recurrence. Peritoneal metastasis was more frequent after pT4a than after pT4b disease (9.5% vs 5.1%), consistent with the established role of visceral peritoneal penetration as a risk factor [2]. These observations argue for meticulous tumor handling, a low threshold for conversion when tumor integrity is at risk, and focused surveillance for peritoneal recurrence after resection of pT4a disease. Strategies to prevent peritoneal recurrence, such as hyperthermic intraperitoneal chemotherapy, have shown inconsistent results [34–37] and were beyond the scope of this study.

Limitations

This study has several limitations. First, it was a retrospective observational study in which the surgeon chose the operative approach without a standardized algorithm. Although all measured preoperative covariates were balanced after weighting, residual confounding by surgical judgment, technical complexity, and intraoperative findings cannot be excluded, and the survival results should be interpreted as associations rather than causal effects. Second, the individual operating surgeon could not be identified. Because all operations were performed with a standardized technique by three surgeons, each with more than 10 years of experience in minimally invasive colorectal surgery, variation in expertise was limited, but surgeon-level effects could not be analyzed. Third, the findings come from a single tertiary center with a mature laparoscopic practice, approximately 200–230 colorectal cancer cases a year, and no robotic colon surgery. They may not apply to lower-volume centers, to surgeons with less

experience in laparoscopic multivisceral resection, to robotic surgery, or to health care systems with different referral patterns, and they should not be taken to support MIS for cT4 disease outside experienced hands. Fourth, staging accuracy was assessed from the original radiology reports without central review, and CT protocols changed during the study period; the reported accuracy therefore reflects routine practice rather than expert reading. Fifth, peritoneal metastases were few, limiting the precision of this outcome, and peritoneal recurrence that developed after a first non-peritoneal recurrence may not have been captured. Sixth, the cause of death was not reliably recorded, precluding analysis of cancer-specific survival, and rectal cancer could only be described, because few rectal resections were open. Finally, the 12-year study period spanned changes in imaging, systemic therapy, and surgical practice; period of surgery was included in the propensity model, but residual temporal effects may persist.

Conclusions

Clinical T4 staging was often inaccurate: nearly half of cT4 tumors were not confirmed as pT4, and no preoperative factor reliably identified them. A cT4 label alone should therefore not exclude patients from MIS. In this experienced center, MIS applied selectively on the basis of the surgeon's assessment of disease extent was associated with fewer 30-day complications and no worse recurrence-free or overall survival than open surgery, although residual confounding cannot be excluded. Rather than dictating open surgery, a cT4 classification should prompt multidisciplinary review and an individualized choice of operative approach. Whether MIS affects the risk of peritoneal metastasis remains uncertain and should be evaluated in larger cohorts.

List of abbreviations

AJCC, American Joint Committee on Cancer; AUC, area under the receiver operating characteristic curve; CEA, carcinoembryonic antigen; CI, confidence interval; CT, computed

tomography; cT4, clinical T4; cT4a, clinical T4a (penetration of the visceral peritoneum); cT4b, clinical T4b (invasion of adjacent organs or structures); HR, hazard ratio; IPTW, inverse probability of treatment weighting; MIS, minimally invasive surgery; MRI, magnetic resonance imaging; OR, odds ratio; OS, overall survival; pT4, pathologic T4; RFS, recurrence-free survival; sHR, subdistribution hazard ratio; SMD, standardized mean difference

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of St. Vincent's Hospital, The Catholic University of Korea (approval no. VC26RISI0243), which waived the requirement for informed consent because of the retrospective design and the use of de-identified data. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available because they contain clinical information on individual patients, but de-identified data are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

NY conceived and designed the study, analyzed and interpreted the data, and drafted the manuscript. HMC and BHK contributed to the study design, provided patient data, and critically revised the manuscript. JYM and HKK collected and curated the data. All authors read and approved the final manuscript.

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670 **Figure legends**

671 **Fig. 1 Patient flow diagram.** Patients operated on from January 2023 onward were not
672 included to ensure at least 18 months of potential follow-up. The comparison of operative
673 approaches was restricted to elective resections of clinical T4 colon cancer; emergency
674 resections and rectal cancers were described separately. MIS, minimally invasive surgery.

Fig. 2 Weighted overall and recurrence-free survival after MIS versus open resection of clinical T4 colon cancer. Overall survival (A) and recurrence-free survival (B) after laparoscopic (MIS) versus open elective resection, weighted by stabilized inverse probability of treatment weights. Hazard ratios with bootstrap 95% confidence intervals and weighted log-rank P values are shown. Numbers at risk are unweighted. Recurrence-free survival counts recurrence or death from any cause as an event. MIS, minimally invasive surgery.

Fig. 3 Weighted cumulative incidence of peritoneal metastasis after MIS versus open resection. Cumulative incidence of peritoneal metastasis after laparoscopic (MIS) versus open elective resection of clinical T4 colon cancer, weighted by stabilized inverse probability of treatment weights, with death without peritoneal metastasis as a competing event. The subdistribution hazard ratio (sHR) is from a weighted Fine–Gray model. Two events in the open group occurred 9 days apart (14.7 and 15.0 months) and appear as a single step. Note the expanded y-axis scale (0–15%). MIS, minimally invasive surgery.

Additional file

Additional file 1 (.docx). Table S1. Covariate balance before and after weighting. Table S2. Preoperative factors associated with the choice of open surgery. Table S3. Sensitivity analyses. Table S4. Outcomes in patients with pathologically confirmed T4 disease, and comparison of pT4a and pT4b disease. Fig. S1. Distribution of propensity scores by operative approach.

Table 1. Characteristics of patients with clinical T4 colon cancer, including emergency resections, by surgical approach

Variable	Overall (n = 297)	MIS (n = 178)	Open (n = 119)	P
Demographics				
Age, years	68 [59–79]	66 [58–76]	70 [60–80]	0.143
Male sex	162 (54.5)	98 (55.1)	64 (53.8)	0.829
Body mass index, kg/m²	23.0 [20.8–25.4]	23.5 [21.2–25.6]	22.5 [20.1–24.0]	0.003
ASA class				0.197
I	95 (32.0)	60 (33.7)	35 (29.4)	
II	174 (58.6)	106 (59.6)	68 (57.1)	
III	27 (9.1)	12 (6.7)	15 (12.6)	
Current or former smoker	46 (15.5)	23 (12.9)	23 (19.3)	0.135
Diabetes mellitus	66 (22.2)	43 (24.2)	23 (19.3)	0.327
Period of surgery				0.272
2011–2015	87 (29.3)	48 (27.0)	39 (32.8)	
2016–2020	164 (55.2)	98 (55.1)	66 (55.5)	
2021–2022	46 (15.5)	32 (18.0)	14 (11.8)	
Presentation and preoperative staging				
Initial CEA, ng/mL	4.7 [2.4–11.5]	4.1 [2.3–9.4]	7.1 [2.9–12.9]	0.017
Obstruction and its management[a]				0.086
No obstruction	193 (65.0)	123 (69.1)	70 (58.8)	
Stent	33 (11.1)	21 (11.8)	12 (10.1)	
Diverting stoma	1 (0.3)	0 (0.0)	1 (0.8)	
Resection without decompression	70 (23.6)	34 (19.1)	36 (30.3)	
Perforation	24 (8.1)	4 (2.2)	20 (16.8)	<0.001
Emergency surgery	34 (11.4)	0 (0.0)	34 (28.6)	<0.001
For perforation	14 (4.7)	0 (0.0)	14 (11.8)	
For obstruction	14 (4.7)	0 (0.0)	14 (11.8)	
Other indication	6 (2.0)	0 (0.0)	6 (5.0)	
Acute presentation (obstruction, perforation, or emergency surgery)[b]	125 (42.1)	58 (32.6)	67 (56.3)	<0.001
Tumor sidedness[c]				0.171
Right	134 (45.1)	75 (42.1)	59 (49.6)	
Left	155 (52.2)	99 (55.6)	56 (47.1)	
Clinical T category				0.010
cT4a	168 (56.6)	112 (62.9)	56 (47.1)	
cT4b	40 (13.5)	17 (9.6)	23 (19.3)	
cT4 NOS	88 (29.6)	48 (27.0)	40 (33.6)	
Clinical node positive	272 (91.6)	164 (92.1)	108 (90.8)	0.675
Clinical TNM stage				0.675
II	25 (8.4)	14 (7.9)	11 (9.2)	
III	272 (91.6)	164 (92.1)	108 (90.8)	
Neoadjuvant chemotherapy	3 (1.0)	1 (0.6)	2 (1.7)	0.566
Operative characteristics				
Laparoscopic	178/178 (100.0)	178/178 (100.0)	—	
Robotic	0/178 (0.0)	0/178 (0.0)	—	
Conversion to open	9/178 (5.1)	9/178 (5.1)	—	
Operation time, min	200 [170–233]	205 [175–240]	193 [162–220]	0.014
Estimated blood loss, mL	100 [50–150]	80 [50–100]	100 [80–200]	<0.001
Intraoperative transfusion	23 (7.7)	4 (2.2)	19 (16.0)	<0.001
Diverting ostomy	24 (8.1)	9 (5.1)	15 (12.6)	0.019
Combined organ resection[d]	73 (24.6)	27 (15.2)	46 (38.7)	<0.001
Urinary tract (bladder, ureter, kidney)	29 (9.8)	14 (7.9)	15 (12.6)	
Small bowel	13 (4.4)	1 (0.6)	12 (10.1)	

Variable	Overall (n = 297)	MIS (n = 178)	Open (n = 119)	P
Peritoneum, omentum, or abdominal wall	16 (5.4)	7 (3.9)	9 (7.6)	
Uterus or adnexa	11 (3.7)	3 (1.7)	8 (6.7)	
Stomach or duodenum	5 (1.7)	1 (0.6)	4 (3.4)	
Liver or gallbladder	4 (1.3)	1 (0.6)	3 (2.5)	
Other (para-aortic nodes, vas deferens, etc.)	10 (3.4)	4 (2.2)	6 (5.0)	
R0 resection	286 (96.3)	171 (96.1)	115 (96.6)	1.000
Postoperative course				
30-day complication	82 (27.6)	36 (20.2)	46 (38.7)	<0.001
Clavien–Dindo grade ≥ III[e]	17 (5.7)	8 (4.5)	9 (7.6)	0.265
Anastomotic leakage	1 (0.3)	1 (0.6)	0 (0.0)	1.000
Reoperation	5 (1.7)	2 (1.1)	3 (2.5)	0.393
Adjuvant chemotherapy[f]	157 (52.9)	94 (52.8)	63 (52.9)	0.982
Pathology				
Tumor size, cm	7.0 [5.0–8.5]	6.5 [5.0–8.0]	7.5 [6.0–9.0]	<0.001
Histologic type				0.146
Well/moderately differentiated	258 (86.9)	153 (86.0)	105 (88.2)	
Poorly differentiated	22 (7.4)	13 (7.3)	9 (7.6)	
Mucinous	13 (4.4)	11 (6.2)	2 (1.7)	
Signet-ring cell	0 (0.0)	0 (0.0)	0 (0.0)	
Other	4 (1.3)	1 (0.6)	3 (2.5)	
Pathologic T category				<0.001
T0–2	2 (0.7)	2 (1.1)	0 (0.0)	
T3	128 (43.2)	94 (52.8)	34 (28.8)	
T4a	73 (24.7)	42 (23.6)	31 (26.3)	
T4b	93 (31.4)	40 (22.5)	53 (44.9)	
Pathologic N category				0.863
pN0	147 (49.5)	86 (48.3)	61 (51.3)	
pN1	87 (29.3)	54 (30.3)	33 (27.7)	
pN2	63 (21.2)	38 (21.3)	25 (21.0)	
Harvested lymph nodes	31 [23–39]	31 [23–41]	30 [22–39]	0.389
Lymphovascular invasion	151 (50.8)	89 (50.0)	62 (52.1)	0.723
Perineural invasion	58 (19.5)	31 (17.4)	27 (22.7)	0.261
MSI-high (of tested)[g]	12/92 (13.0)	10/63 (15.9)	2/29 (6.9)	0.327

Data are median [interquartile range] or n (%). Percentages use the column total unless a denominator is shown or stated below. P values are from the Mann–Whitney U test for continuous variables and the chi-square or Fisher exact test for categorical variables. The cohort comprises all resections of clinical T4 colon cancer, elective and emergency; rectal cancers are described in Table 3. Operative approach is the initially intended approach.

[a] Obstruction at presentation and its preoperative management; "resection without decompression" denotes obstructed patients resected without prior stent or stoma, including emergency resections.

[b] Patients with obstruction or perforation at presentation, or who underwent emergency surgery.

[c] Right-sided: cecum to mid-transverse colon; left-sided: distal transverse colon to rectosigmoid. Not classifiable in 8 patients.

[d] Patients may have had more than one organ resected; organ subcategories are not tested.

[e] 30-day complication managed by reoperation or radiologic/endoscopic intervention. The registry does not record a formal Clavien–Dindo grade, so this is a proxy for grade ≥ III.

[f] Adjuvant chemotherapy status unrecorded in 0 patient.

[g] Mismatch-repair/MSI testing was performed in 92 patients.

Missing data: initial CEA 7, estimated blood loss 89, pathologic T stage 1.

ASA, American Society of Anesthesiologists; CEA, carcinoembryonic antigen; MIS, minimally invasive surgery; MSI, microsatellite instability; NOS, not otherwise specified.

Table 2. Pathologic confirmation of clinical T4 stage and preoperative predictors of pathologic T4 disease

	n	pT4a	pT4b	pT3	pT2[a]	pT4 confirmed, n (%)
A. Pathologic T category by preoperative characteristics						
All patients	304	75	94	132	3	169 (55.6)
Tumor site (P = 0.491)						
Colon	293	73	91	127	2	164 (56.0)
Rectum	11	2	3	5	1	5 (45.5)
Clinical T category (P = 0.091)						
cT4a	171	46	40	84	1	86 (50.3)
cT4b	41	7	19	14	1	26 (63.4)
cT4, not otherwise specified[b]	91	22	35	34	0	57 (62.6)
Initial CEA (P <0.001)						
≥5 ng/mL	145	42	55	47	1	97 (66.9)
<5 ng/mL	152	32	38	80	2	70 (46.1)
Clinical node status (P = 0.523)						
Positive	278	68	85	122	3	153 (55.0)
Negative	26	7	9	10	0	16 (61.5)
Presentation (P = 0.011)						
Elective, no obstruction or perforation	178	40	50	85	3	90 (50.6)
Elective, after obstruction or perforation	92	28	35	29	0	63 (68.5)
Emergency resection	34	7	9	18	0	16 (47.1)
Period of surgery (P = 0.403)						
2011–2015	90	22	33	35	0	55 (61.1)
2016–2020	170	43	49	75	3	92 (54.1)
2021–2022	44	10	12	22	0	22 (50.0)
Operative approach[c] (P <0.001)						
MIS	185	43	42	97	3	85 (45.9)
Open	119	32	52	35	0	84 (70.6)

	Univariable OR (95% CI)	P	Multivariable OR (95% CI)	P
B. Logistic regression for pathologic T4 confirmation, colon cancer (n = 293; pT4, n = 164)				
Age (per 10 years)	1.16 (0.98–1.37)	0.094	1.13 (0.94–1.36)	0.201
Male sex	0.95 (0.60–1.50)	0.814	0.90 (0.54–1.49)	0.685
Clinical T4b (vs T4a)	1.60 (0.79–3.28)	0.194	1.87 (0.87–4.02)	0.111
Clinical T4 NOS (vs T4a)	1.47 (0.88–2.45)	0.141	1.60 (0.91–2.80)	0.100
Initial CEA ≥5 ng/mL	2.64 (1.64–4.25)	<0.001	2.29 (1.38–3.79)	0.001
Clinical node positive	0.69 (0.30–1.63)	0.400	0.78 (0.31–1.96)	0.598
Right-sided tumor	0.89 (0.56–1.42)	0.636	1.00 (0.60–1.68)	0.994
Emergency resection	0.67 (0.33–1.37)	0.268	0.79 (0.36–1.71)	0.544
Obstruction, elective resection	1.87 (1.10–3.17)	0.020	1.41 (0.77–2.58)	0.268
Perforation, elective resection	3.26 (0.68–15.61)	0.140	3.07 (0.60–15.81)	0.180

Patients who did not receive neoadjuvant therapy and had a recorded pathologic T category (n = 304); pathologic T stage is not altered by treatment in this group. P values in panel A are from chi-square or Fisher's exact tests for pT4 confirmation across categories.

Initial CEA was missing in 7 patients; they are omitted from the CEA rows of panel A and classified as <5 ng/mL in panel B.

[a] No tumor in this cohort was pT0, pTis, or pT1; all three were pT2.

[b] Before 2016, clinical T4 was recorded without subclassification; period of surgery was therefore not entered in the multivariable model, because it was collinear with this category.

[c] Operative approach was selected by the surgeon partly on the basis of suspected invasion and is shown for description only; it was not entered in the model.

Multivariable model: all listed variables entered simultaneously; apparent area under the receiver operating characteristic curve, 0.68. Obstruction and perforation managed electively are compared with elective resection without either.

CEA, carcinoembryonic antigen; CI, confidence interval; MIS, minimally invasive surgery; OR, odds ratio.

Table 3. Characteristics and outcomes of clinical T4 colon and rectal cancer by tumor location and approach

Variable	Colon (n = 297)			Rectum (n = 86)		P, colon vs rectum[b]
	MIS (n = 178)	Open (n = 119)	P[a]	MIS (n = 78)	Open (n = 8)	
Presentation						
Age, years	66.0 [58.2–76.0]	70.0 [60.0–80.0]	0.143	58.5 [54.0–70.8]	64.5 [56.2–68.0]	<0.001
ASA class III–IV	12 (6.7)	16 (13.4)	0.053	3 (3.8)	1 (12.5)	0.159
Obstruction	55 (30.9)	49 (41.2)	0.069	11 (14.1)	4 (50.0)	0.002
Decompressed before resection (stent or diverting stoma)[c]	21 (11.8)	13 (10.9)	0.817	8 (10.3)	2 (25.0)	0.963
Perforation	4 (2.2)	20 (16.8)	<0.001	4 (5.1)	2 (25.0)	0.737
Emergency surgery	0 (0.0)	34 (28.6)	<0.001	0 (0.0)	0 (0.0)	0.001
Preoperative staging						
Local staging modality	CT	CT	—	MRI	MRI	—
Clinical T category			0.010			<0.001
cT4a	112 (62.9)	56 (47.1)		27 (34.6)	4 (50.0)	
cT4b	17 (9.6)	23 (19.3)		24 (30.8)	2 (25.0)	
cT4 NOS	48 (27.0)	40 (33.6)		27 (34.6)	2 (25.0)	
Clinical node positive	164 (92.1)	108 (90.8)	0.675	73 (93.6)	7 (87.5)	0.666
Tumor distance from anal verge, cm	—	—	—	6.0 [2.5–8.0]	10.0 [7.8–11.5]	—
Neoadjuvant therapy						
Neoadjuvant treatment			0.345			<0.001
None	177 (99.4)	117 (98.3)		8 (10.3)	3 (37.5)	
Long-course chemoradiotherapy	0 (0.0)	0 (0.0)		58 (74.4)	5 (62.5)	
Short-course radiotherapy	0 (0.0)	0 (0.0)		11 (14.1)	0 (0.0)	
Chemotherapy alone	1 (0.6)	2 (1.7)		1 (1.3)	0 (0.0)	
Operative						
Robotic approach (of MIS)	0/178 (0.0)	—	—	4/78 (5.1)	—	0.008
Conversion to open (of MIS)	9/178 (5.1)	—	—	5/78 (6.4)	—	0.766
Combined organ resection	27 (15.2)	46 (38.7)	<0.001	30 (38.5)	5 (62.5)	0.003
30-day complication	36 (20.2)	46 (38.7)	<0.001	32 (41.0)	7 (87.5)	0.002
Clavien–Dindo ≥ III (reoperation or intervention)[d]	8 (4.5)	9 (7.6)	0.265	3 (3.8)	5 (62.5)	0.237
Pathology						
Pathologic T category, untreated patients[c]			<0.001			0.095
T0–2	2 (1.1)	0 (0.0)		1 (12.5)	0 (0.0)	
T3	93 (52.5)	34 (29.1)		4 (50.0)	1 (33.3)	
T4a	42 (23.7)	31 (26.5)		1 (12.5)	1 (33.3)	
T4b	40 (22.6)	51 (43.6)		2 (25.0)	1 (33.3)	
ypT category, after neoadjuvant therapy			0.083			0.714
T0–2	0 (0.0)	0 (0.0)		12 (17.1)	0 (0.0)	

Variable	Colon (n = 297)			Rectum (n = 86)		P, colon vs rectum[b]
	MIS (n = 178)	Open (n = 119)	P[a]	MIS (n = 78)	Open (n = 8)	
T3	1 (100.0)	0 (0.0)		36 (51.4)	0 (0.0)	
T4a	0 (0.0)	0 (0.0)		4 (5.7)	0 (0.0)	
T4b	0 (0.0)	2 (100.0)		17 (24.3)	5 (100.0)	
R0 resection	171 (96.1)	115 (96.6)	1.000	73 (93.6)	6 (75.0)	0.142
Radial (circumferential) margin involved[f]	8/163 (4.9)	14/106 (13.2)	0.015	15/78 (19.2)	2/8 (25.0)	0.003
Oncologic outcomes						
Any recurrence	28 (15.7)	33 (27.7)	0.012	33 (42.3)	5 (62.5)	<0.001
Locoregional recurrence (alone or with distant)	4 (2.2)	4 (3.4)	0.718	5 (6.4)	1 (12.5)	0.095
Peritoneal metastasis	9 (5.1)	3 (2.5)	0.373	4 (5.1)	0 (0.0)	0.764
5-year overall survival, % (95% CI)[g]	79.7 (72.0–85.5)	63.5 (53.1–72.1)	0.002	60.7 (47.9–71.3)	45.0 (10.8–75.1)	0.044
5-year recurrence-free survival, % (95% CI)[g]	74.7 (66.9–80.9)	50.8 (40.8–60.0)	<0.001	51.6 (39.7–62.2)	37.5 (8.7–67.4)	0.013

Data are n (%) or median [interquartile range]. Percentages use the column total as denominator unless a denominator is shown.

[a] MIS versus open within colon cancer: chi-square or Fisher exact test (categorical), Mann–Whitney U test (continuous), log-rank test (survival). MIS and open are not compared statistically within rectal cancer because only 8 rectal resections were open; rectal data are descriptive.

[b] All colon versus all rectal cancers, irrespective of approach.

[c] Obstructed patients decompressed by self-expanding metallic stent or diverting stoma before definitive resection; shown as a proportion of all patients in the column.

[d] Defined as a 30-day complication managed by reoperation or radiologic/endoscopic intervention. The registry does not record a formal Clavien–Dindo grade, so this is a proxy for grade ≥ III; grade IV–V events managed without intervention are not captured.

[e] Excludes the 78 patients who received neoadjuvant therapy (colon 3, rectum 75), whose ypT stage is shown separately. Pathologic T stage was missing for 1 untreated open colon resection.

[f] Among patients with recorded radial margin status (not described in 28 colon resections).

[g] Kaplan–Meier estimates with log–log 95% confidence intervals, restricted to the 383 patients with complete operation and last-contact dates (colon MIS 178, colon open 119, rectum MIS 78, rectum open 8); P values are log-rank tests over the entire follow-up. Recurrence-free survival counts recurrence or death from any cause as an event. Estimates are crude and include emergency resections.

Clinical T stage was assigned with contrast-enhanced CT for colon cancer and pelvic MRI for rectal cancer. Tumor distance from the anal verge is reported for rectal cancer only.

ASA, American Society of Anesthesiologists; CI, confidence interval; CT, computed tomography; MIS, minimally invasive surgery (laparoscopic or robotic, analyzed by initial approach); MRI, magnetic resonance imaging; NOS, not otherwise specified.

Table 4. Characteristics of patients undergoing elective resection for clinical T4 colon cancer, by surgical approach

Variable	Overall (n = 263)	MIS (n = 178)	Open (n = 85)	P
Demographics				
Age, years	67 [59–78]	66 [58–76]	68 [59–80]	0.478
Male sex	143 (54.4)	98 (55.1)	45 (52.9)	0.747
Body mass index, kg/m²	23.1 [20.9–25.4]	23.5 [21.2–25.6]	22.5 [20.3–24.5]	0.014
ASA class				0.648
I	84 (31.9)	60 (33.7)	24 (28.2)	
II	160 (60.8)	106 (59.6)	54 (63.5)	
III	19 (7.2)	12 (6.7)	7 (8.2)	
Current or former smoker	36 (13.7)	23 (12.9)	13 (15.3)	0.601
Diabetes mellitus	62 (23.6)	43 (24.2)	19 (22.4)	0.747
Period of surgery				0.204
2011–2015	80 (30.4)	48 (27.0)	32 (37.6)	
2016–2020	139 (52.9)	98 (55.1)	41 (48.2)	
2021–2022	44 (16.7)	32 (18.0)	12 (14.1)	
Presentation and preoperative staging				
Initial CEA, ng/mL	4.9 [2.5–12.0]	4.1 [2.3–9.4]	7.8 [3.1–15.8]	0.001
Obstruction and its management[a]				0.331
No obstruction	178 (67.7)	123 (69.1)	55 (64.7)	
Stent	29 (11.0)	21 (11.8)	8 (9.4)	
Diverting stoma	1 (0.4)	0 (0.0)	1 (1.2)	
Resection without decompression	55 (20.9)	34 (19.1)	21 (24.7)	
Perforation	10 (3.8)	4 (2.2)	6 (7.1)	0.081
Tumor sidedness[b]				0.494
Right	115 (43.7)	75 (42.1)	40 (47.1)	
Left	143 (54.4)	99 (55.6)	44 (51.8)	
Clinical T category				0.002
cT4a	147 (55.9)	112 (62.9)	35 (41.2)	
cT4b	35 (13.3)	17 (9.6)	18 (21.2)	
cT4 NOS	80 (30.4)	48 (27.0)	32 (37.6)	
Clinical node positive	244 (92.8)	164 (92.1)	80 (94.1)	0.561
Clinical TNM stage				0.561
II	19 (7.2)	14 (7.9)	5 (5.9)	
III	244 (92.8)	164 (92.1)	80 (94.1)	
Neoadjuvant chemotherapy	3 (1.1)	1 (0.6)	2 (2.4)	0.245
Operative characteristics				
Laparoscopic	178/178 (100.0)	178/178 (100.0)	—	
Robotic	0/178 (0.0)	0/178 (0.0)	—	
Conversion to open	9/178 (5.1)	9/178 (5.1)	—	
Operation time, min	200 [174–234]	205 [175–240]	199 [164–219]	0.054
Estimated blood loss, mL	100 [50–150]	80 [50–100]	100 [80–200]	<0.001
Intraoperative transfusion	16 (6.1)	4 (2.2)	12 (14.1)	<0.001
Diverting ostomy	15 (5.7)	9 (5.1)	6 (7.1)	0.573
Combined organ resection[c]	67 (25.5)	27 (15.2)	40 (47.1)	<0.001
Urinary tract (bladder, ureter, kidney)	27 (10.3)	14 (7.9)	13 (15.3)	
Small bowel	12 (4.6)	1 (0.6)	11 (12.9)	
Peritoneum, omentum, or abdominal wall	16 (6.1)	7 (3.9)	9 (10.6)	
Uterus or adnexa	10 (3.8)	3 (1.7)	7 (8.2)	
Stomach or duodenum	4 (1.5)	1 (0.6)	3 (3.5)	
Liver or gallbladder	4 (1.5)	1 (0.6)	3 (3.5)	
Other (para-aortic nodes, vas deferens, etc.)	8 (3.0)	4 (2.2)	4 (4.7)	
R0 resection	252 (95.8)	171 (96.1)	81 (95.3)	0.751

Variable	Overall (n = 263)	MIS (n = 178)	Open (n = 85)	P
Postoperative course				
30-day complication	66 (25.1)	36 (20.2)	30 (35.3)	0.008
Clavien–Dindo grade ≥ III[d]	13 (4.9)	8 (4.5)	5 (5.9)	0.762
Anastomotic leakage	1 (0.4)	1 (0.6)	0 (0.0)	1.000
Reoperation	4 (1.5)	2 (1.1)	2 (2.4)	0.597
Adjuvant chemotherapy[e]	140 (53.2)	94 (52.8)	46 (54.1)	0.842
Pathology				
Tumor size, cm	7.0 [5.0–8.5]	6.5 [5.0–8.0]	8.0 [6.0–9.0]	<0.001
Histologic type				0.168
Well/moderately differentiated	227 (86.3)	153 (86.0)	74 (87.1)	
Poorly differentiated	19 (7.2)	13 (7.3)	6 (7.1)	
Mucinous	13 (4.9)	11 (6.2)	2 (2.4)	
Signet-ring cell	0 (0.0)	0 (0.0)	0 (0.0)	
Other	4 (1.5)	1 (0.6)	3 (3.5)	
Pathologic T category				<0.001
T0–2	2 (0.8)	2 (1.1)	0 (0.0)	
T3	110 (42.0)	94 (52.8)	16 (19.0)	
T4a	66 (25.2)	42 (23.6)	24 (28.6)	
T4b	84 (32.1)	40 (22.5)	44 (52.4)	
Pathologic N category				0.756
pN0	130 (49.4)	86 (48.3)	44 (51.8)	
pN1	76 (28.9)	54 (30.3)	22 (25.9)	
pN2	57 (21.7)	38 (21.3)	19 (22.4)	
Harvested lymph nodes	31 [23–40]	31 [23–41]	30 [21–39]	0.470
Lymphovascular invasion	132 (50.2)	89 (50.0)	43 (50.6)	0.929
Perineural invasion	48 (18.3)	31 (17.4)	17 (20.0)	0.612
MSI-high (of tested)[f]	12/85 (14.1)	10/63 (15.9)	2/22 (9.1)	0.723

Data are median [interquartile range] or n (%). Percentages use the column total unless a denominator is shown or stated below. P values are from the Mann–Whitney U test for continuous variables and the chi-square or Fisher exact test for categorical variables. The cohort comprises elective resections of clinical T4 colon cancer and excludes the 34 emergency resections shown in Table 1; this is the population in which both approaches were realistic options. Operative approach is the initially intended approach.

[a] Obstruction at presentation and its preoperative management; "resection without decompression" denotes obstructed patients resected without prior stent or stoma.

[b] Right-sided: cecum to mid-transverse colon; left-sided: distal transverse colon to rectosigmoid. Not classifiable in 5 patients.

[c] Patients may have had more than one organ resected; organ subcategories are not tested.

[d] 30-day complication managed by reoperation or radiologic/endoscopic intervention. The registry does not record a formal Clavien–Dindo grade, so this is a proxy for grade ≥ III.

[e] Adjuvant chemotherapy status unrecorded in 0 patient.

[f] Mismatch-repair/MSI testing was performed in 85 patients.

Missing data: initial CEA 1, estimated blood loss 82, pathologic T stage 1.

ASA, American Society of Anesthesiologists; CEA, carcinoembryonic antigen; MIS, minimally invasive surgery; MSI, microsatellite instability; NOS, not otherwise specified.

Table 5. Oncologic and surgical outcomes of elective MIS versus open resection for clinical T4 colon cancer

Outcome	MIS (n = 178)	Open (n = 85)	Crude effect (95% CI)	MIS	Open	Difference (95% CI)[b]	Hazard ratio (95% CI)
Primary outcome: recurrence-free survival							
Events, n	46	39					
3-year, %	79.8 (72.9–85.2)	60.6 (49.1–70.3)					
5-year, % (difference, percentage points)[b]	74.7 (66.9–80.9)	55.3 (43.4–65.8)		73.5 (66.1–80.3)	60.0 (48.8–71.5)	+13.5 (+0.4 to +26.9)	
Restricted mean survival time to 5 years, months				48.3	42.8	+5.5 (-0.6 to +11.7)	
Hazard ratio, MIS vs open			0.54 (0.35–0.83); P = 0.005				0.66 (0.42–1.04); P = 0.076
Secondary outcomes							
Overall survival							
Deaths, n	37	30					
3-year, %	85.7 (79.2–90.3)	78.8 (68.1–86.3)					
5-year, % (difference, percentage points)[b]	79.7 (72.0–85.5)	70.1 (57.9–79.4)		79.7 (72.5–85.9)	73.4 (62.3–82.8)	+6.3 (-6.1 to +19.3)	
Restricted mean survival time to 5 years, months				53.2	51.0	+2.2 (-2.2 to +7.2)	
Hazard ratio, MIS vs open			0.60 (0.37–0.98); P = 0.041				0.69 (0.41–1.15); P = 0.151
Peritoneal metastasis[c]							
Events, n	9	3					
3-year cumulative incidence, %	4.7	3.7		4.6	4.0	+0.6 (-6.4 to +5.8)	
5-year cumulative incidence, %	5.5	3.7		5.5	4.0	+1.4 (-5.7 to +6.7)	
Subdistribution hazard ratio, MIS vs open			1.48 (0.40–5.48); P = 0.554				1.35 (0.38–4.84); P = 0.647
Surgical outcomes							
R0 resection, %	171/178 (96.1)	81/85 (95.3)		96.0	96.7	-0.8 (-5.2 to +4.1)	
30-day complication, %	36/178 (20.2)	30/85 (35.3)		20.1	37.5	-17.4 (-29.5 to -3.4)	
Clavien–Dindo grade ≥ III, %[d]	8/178 (4.5)	5/85 (5.9)		4.2	6.6	-2.4 (-9.6 to +4.2)	

Columns 2–4 are unadjusted; columns 5–8 are weighted by stabilized inverse probability of treatment weights (IPTW). Survival and peritoneal metastasis analyses include the 263 patients with complete operation and follow-up dates (MIS 178, open 85); surgical outcomes include all 263 patients. Median follow-up (reverse Kaplan–Meier) was 61.8 months. Recurrence-free survival counts recurrence or death from any cause as an event. Operative approach was analyzed by intention to treat (9 conversions remained in the MIS group).

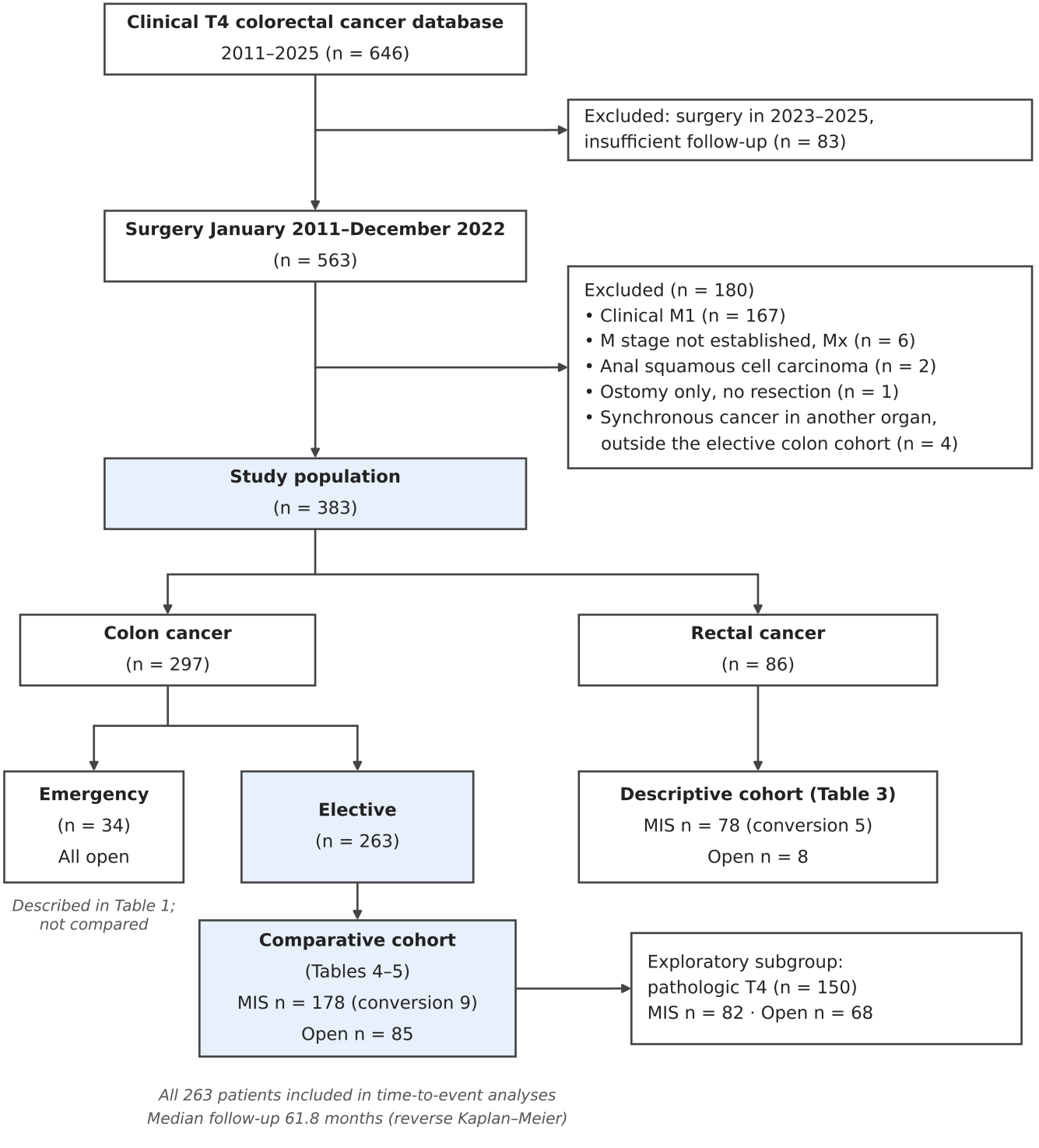
[a] Unadjusted survival estimates are Kaplan–Meier with 95% CI; crude hazard ratios are from unweighted Cox models.

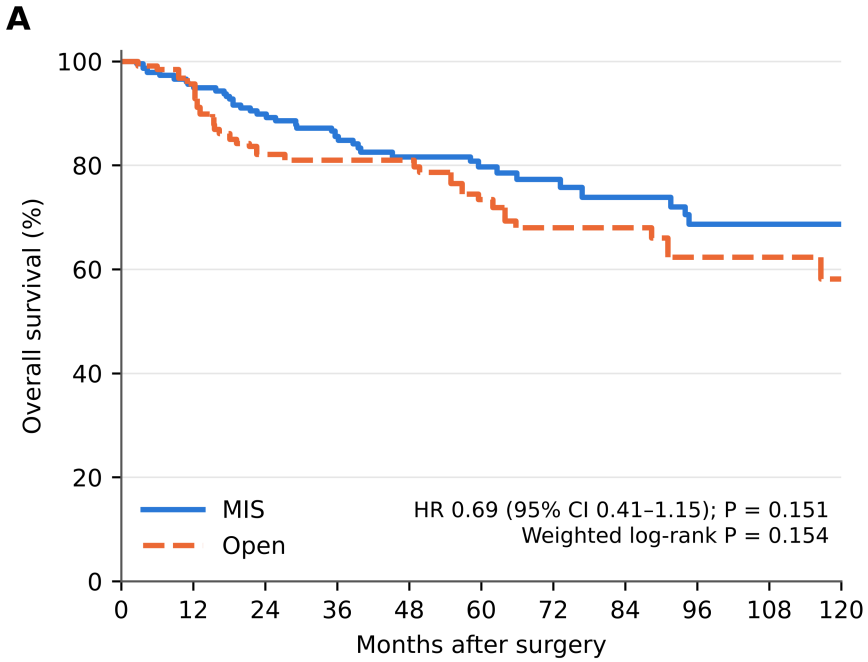
[b] MIS minus open. Confidence intervals for weighted estimates and differences are bootstrap percentile intervals (2000 resamples, with the propensity model re-fitted in each resample). Hazard ratios after weighting are from IPTW-weighted Cox models; their confidence intervals and P values are also from the bootstrap, because robust (sandwich) intervals do not account for estimation of the propensity score.

[c] Death without peritoneal metastasis treated as a competing event (Aalen–Johansen estimator); subdistribution hazard ratio from a Fine–Gray model. With 12 events, these estimates are imprecise.

[d] 30-day complication managed by reoperation or radiologic/endoscopic intervention (proxy for Clavien–Dindo grade ≥ III).

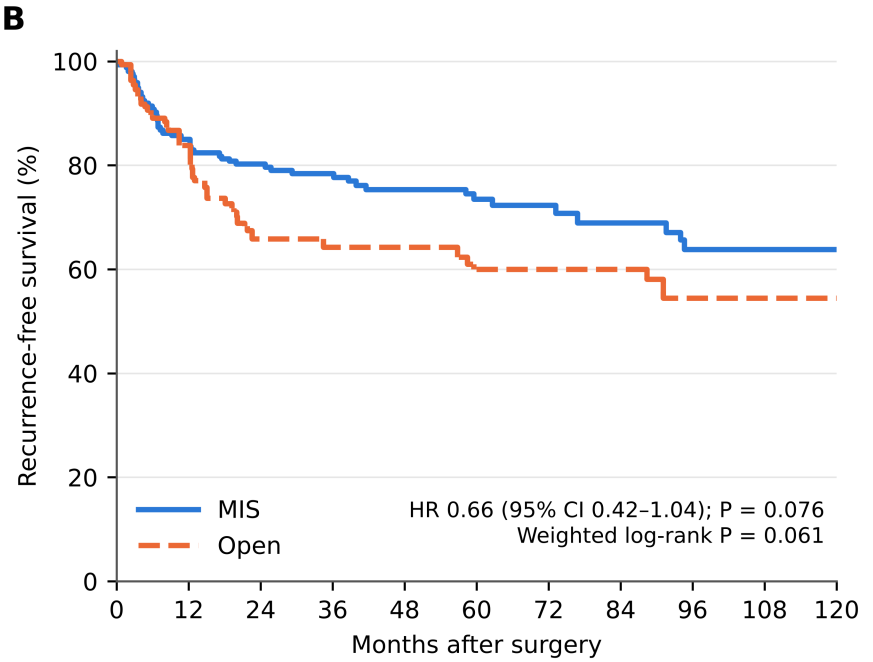
CI, confidence interval; MIS, minimally invasive surgery.


Clinical T4 colorectal cancer database
2011–2025 (n = 646)
Excluded: surgery in 2023–2025, insufficient follow-up (n = 83)
Surgery January 2011–December 2022
(n = 563)
Excluded (n = 180)
• Clinical M1 (n = 167)
• M stage not established, Mx (n = 6)
• Anal squamous cell carcinoma (n = 2)
• Ostomy only, no resection (n = 1)
• Synchronous cancer in another organ, outside the elective colon cohort (n = 4)
Study population
(n = 383)
Colon cancer
(n = 297)
Rectal cancer
(n = 86)
Emergency
(n = 34)
All open
Elective
(n = 263)
Descriptive cohort (Table 3)
MIS n = 78 (conversion 5)
Open n = 8
Described in Table 1; not compared
Comparative cohort
(Tables 4–5)
MIS n = 178 (conversion 9)
Open n = 85
Exploratory subgroup:
pathologic T4 (n = 150)
MIS n = 82 · Open n = 68
All 263 patients included in time-to-event analyses
Median follow-up 61.8 months (reverse Kaplan–Meier)



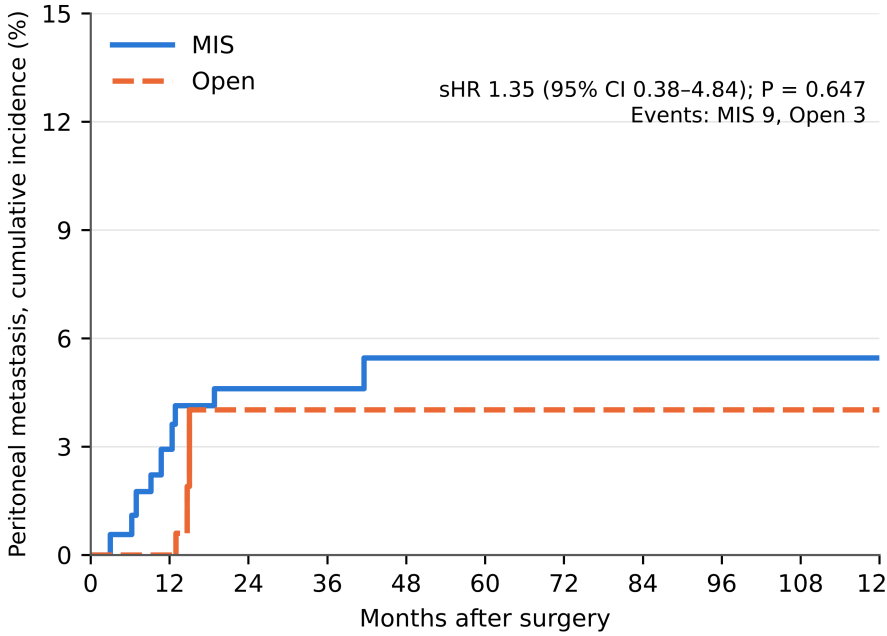
No. at risk

MIS	178	163	137	118	96	68	51	40	32	28	20
Open	85	77	59	54	49	38	28	24	20	17	10



No. at risk

MIS	178	146	123	109	92	64	49	38	30	26	18
Open	85	66	46	42	39	31	24	21	17	14	8



No. at risk

MIS	178	159	132	115	94	66	50	39	31	27	19
Open	85	77	56	52	48	37	27	23	19	16	9

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile12.docx