Surgery 176 (2024) 1598–1609

Contents lists available at ScienceDirect

Surgery

journal homepage: www.elsevier.com/locate/surg

Bowel preparation before elective right colectomy: Multitreatment machine-learning analysis on 2,617 patients

Marco Catarci, MD[a], Stefano Guadagni, MD[b,*], Francesco Masedu, PhD[c], Giacomo Ruffo, MD[d], Massimo Giuseppe Viola, MD[e], Marco Scatizzi, MD[f], the Italian ColoRectal Anastomotic Leakage (iCral) study group

[a] General Surgery Unit, Sandro Pertini Hospital, Roma, Italy
[b] General Surgery Unit, Università degli Studi dell'Aquila, L'Aquila, Italy
[c] Department of Biotechnological and Applied Clinical Sciences, Università degli Studi dell'Aquila, L'Aquila, Italy
[d] General Surgery Unit, IRCCS Sacro Cuore Don Calabria Hospital, Negrar di Valpolicella, Province of Verona, Italy
[e] General Surgery Unit, Cardinale G. Panico Hospital, Tricase, LE, Italy
[f] General Surgery Unit, Santa Maria Annunziata & Serristori Hospital, Florence, Italy

ARTICLE INFO

Article history:
Accepted 29 August 2024
Available online 25 September 2024

ABSTRACT

Background: In the worldwide, real-life setting, some candidates for right colectomy still receive no bowel preparation, some receive oral antibiotics alone, some receive mechanical bowel preparation alone, and some receive mechanical bowel preparation with oral antibiotics, with varying degrees of compliance to preoperative intravenous antibiotic prophylaxis. Previous studies mainly focused on left-sided colorectal anastomoses while less attention has been devoted to right-sided ileocolic anastomoses. When high-level evidence from randomized clinical trials is lacking, multiple-treatment propensity score weighting analysis of prospective data on the basis of generalized boosted model is superior to a simple propensity score-matching analysis and to an inverse probability weighting in terms of external validity and bias reduction.

Methods: This is an analysis on the basis of machine-learning procedures of 2,617 patients who underwent elective right colectomies.

Results: The risk of surgical-site infections (5.0% after no bowel preparation) was significantly lower after mechanical bowel preparation with oral antibiotics (4.0%, $P = .017$), significantly greater after mechanical bowel preparation alone (8.6%, $P = .019$), and comparable after oral antibiotics alone (3.9%). The risk of anastomotic leakage (3.2% after no bowel preparation) was significantly greater after oral antibiotics alone (4.8%, $P = .013$). Concerning secondary outcomes, no significant differences were recorded for the risk of overall morbidity and reoperation. The risk of readmission (3.0% after no bowel preparation) was significantly reduced after mechanical bowel preparation with oral antibiotics (1.5%, $P = .046$), and the risk of major morbidity (5.1% after no bowel preparation) was significantly greater after oral antibiotics alone (6.7%, $P = .007$).

Conclusion: This multitreatment machine-learning analysis, despite some limitations, showed that mechanical bowel preparation with oral antibiotics is associated with a decrease in surgical-site infections after elective right colectomy compared with no bowel preparation.

© 2024 Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Introduction

Surgical-site infections (SSIs) and anastomotic leakage (AL) remain major concerns of colorectal surgery, both of which are influenced significantly by preoperative bowel preparation.[1] Although the first randomized clinical trial (RCT) on this topic was published more than half a century ago,[2] followed by several RCTs and meta-analyses, the causal inference of bowel preparation

Marco Catarci is the iCral study group coordinator.

Marco Catarci (iCral study group coordinator) and Stefano Guadagni (corresponding author) share the first authorship of this paper.

The collaborators of the "iCral study group" are listed in the Acknowledgments.

* Corresponding author: Stefano Guadagni, MD, Dipartimento di Scienze Cliniche Applicate e Biotecnologiche, Università degli Studi dell'Aquila, L'Aquila, Italy, Via Vetoio, snc; 67100 L'Aquila, Italy.

E-mail address: stefano.guadagni@univaq.it (S. Guadagni).

https://doi.org/10.1016/j.surg.2024.08.039
0039-6060/© 2024 Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

remains controversial because of the lack of apodictic data.[1] Several previous studies mainly focused on high-risk left-sided colorectal anastomoses, whereas less attention has been devoted to right-sided ileocolic anastomoses. A large retrospective observational study reported that mechanical bowel preparation with oral antibiotics (MoABP) was significantly associated with reduced rates of SSI after right colectomy compared with no bowel preparation (NBP),[3] whereas a subgroup analysis[4] of a multicenter RCT,[5] a retrospective propensity score-matching analysis,[6] and an RCT[7] failed to find any difference. A recent prospective multicenter observational study, in which all enrolled patients were treated with Enhanced Recovery After Surgery (ERAS) criteria, reported that oral antibiotics alone (oA) or MoABP had no impact on postoperative complications whereas mechanical bowel preparation alone (MBP) was associated with a significantly lower rate of any complication.[8] Finally, an interesting 4-arm RCT comparing NBP with oA, MBP, and MoABP for colon resections[9] was recently closed before completion because of poor accrual.

Considering a worldwide, real-life setting, some patients still receive NBP, some oA, some MBP, and some MoABP, with varying degree of compliance to preoperative intravenous antibiotic prophylaxis (PIVAP).[10] The Italian ColoRectal Anastomotic Leakage (iCral) study group completed 2 prospective observational studies to evaluate the adherence to the ERAS colorectal pathway.[11,12] In a reappraisal of these studies,[13] the adherence rate to the NBP item was 64.1% (35.9% of cases received either MBP, oA, or MoABP), whereas PIVAP was administered in 94.1% of enrolled cases.

The low-to-moderate grade of evidence on which most scientific societies recommendations are currently based depends on multiple factors, including a great heterogeneity of type and schedule of oral antibiotics, of intravenous antibiotics and of products used for MBP as well as a small number of events per endpoint registered in the RCTs, compared with relatively small sample sizes.[1] Consequently, several scientific societies currently support MoABP for elective colorectal resections,[14–17] whereas others still recommend NBP.[18,19]

When conclusive evidence from RCTs is lacking or when researchers need to assess treatment effects on the basis of real-life data, collected through the observation of systems as they operate in normal practice without any intervention implemented by randomized assignment rules, multiple-treatment propensity score-weighting analysis on the basis of machine-learning methods performed on data from prospective observational studies offers an alternative approach for estimating treatment effects. Consequently, the iCral study group decided to evaluate whether it would be better to stay with NBP[18,19] or go toward MoABP[14–17] by estimating the effects of NBP in patients treated with PIVAP before right colectomy (treatment variable/true population of interest/ATT) in comparison with 3 other treatments (PIVAP plus oAB, PIVAP plus MBP, PIVAP plus MoABP) in a large dataset derived from 2 prospective multicenter open-label observational studies,[11,12] via a multitreatment analysis on the basis of machine-learning procedures. The multitreatment machine-learning analysis is not equivalent to propensity score matching analysis (PSMA) and does not simply provide an alternative perspective, representing a tangible improvement in terms of bias reduction and mean-squared error.[20] Compared with conventional PSMA, the machine-learning multitreatment analysis, performed through a generalized boosted model (GBM), reduces bias and improves external validity by preserving the entire sample analyzed regarding the ATT and the other treatments.[21] Finally, it enhances bias reduction compared with inverse probability weighting.[21]

Methods

Study design, participants, and setting

This is a secondary unplanned ad hoc machine-learning multitreatment analysis of patients submitted for ileocolic anastomosis selected from 2 prospective cohorts evaluated in 2 previous studies on the adherence to ERAS items.[11,12] In the 2 parent studies, a total of 8,359 patients were consecutively enrolled on the basis of explicit inclusion/exclusion criteria in 78 Italian centers, after approval of the ethics committee. Details of inclusion/exclusion criteria, modalities of data acquisition and control, ethics, trial registration numbers, and guidelines for reporting data are described in the Supplementary Materials. Particularly, exclusion criteria included incomplete data, and for this reason no missing data record was included in the 8,359-patient dataset. Moreover, during the 32-month enrolment period, no other patients who underwent colorectal surgery were excluded for reasons other than the exclusion criteria.

The present analysis focused on elective right hemicolectomies. To control imbalance derived from several treatment confounders, it included 2,617 patients (31.3%) of 8,359 available in the parent studies, enrolled in 74 centers determined by the explicit exclusion criteria reported in Figure 1. In particular, records with missing information regarding preoperative bowel preparation, or with MBP performed using anything different from polyethylene glycol were excluded, as well as patients treated without PIVAP. Any case treated in delayed urgency because of signs of obstruction and/or bleeding at admission, any anastomosis protected by a proximal stoma, patients treated with neoadjuvant therapy, perioperative steroids, dialysis, or for chronic liver diseases were excluded because these treatments were only impacting subgroups of subjects.

Four different treatment groups were considered: (1) no mechanical bowel preparation and no oral antibiotics (NBP; $n = 1,850$; 70.6%); (2) oA ($n = 208$; 8%); (3) MBP ($n = 360$; 13.8%); and (4) MoABP ($n = 199$; 7.6%). The true population of interest/ATT was the treatment variable NBP. The descriptive variables considered for the 2,617 patients are shown in Table I.[22] To optimize the effectiveness of the analysis, continuous variables were categorized according to their median values. The overall adherence percentage to the ERAS recommendations was calculated using 19 items common to both parent studies. All 2,617 patients were treated with PIVAP; however, details of intravenous antibiotic schedules were not available. All patients in the MBP and MoABP groups received products containing polyethylene glycol on the day before surgery. Patients in the oAB and MoABP groups received several different oral antibiotics schedules (Table II) all of which providing both aerobic and anaerobic coverage, not containing metronidazole in 78 patients (19%), and comparable between the 2 groups in 218 patients (53.6%).

In relation to the significant sample size differences between the 4 treatment groups, as well as for several descriptive variables, and in relation to a supposed heterogeneity in PIVAP schedules and to an undeniable heterogeneity in oral antibiotic schedules, the machine-learning multitreatment reanalysis required a specific model (GBM) to compensate for unbalancing.[21]

Adverse events

The 2,617 patients were followed up for at least 8 weeks after surgery, recording and grading any adverse events according to Clavien-Dindo[23] and the Japanese Clinical Oncology Group-

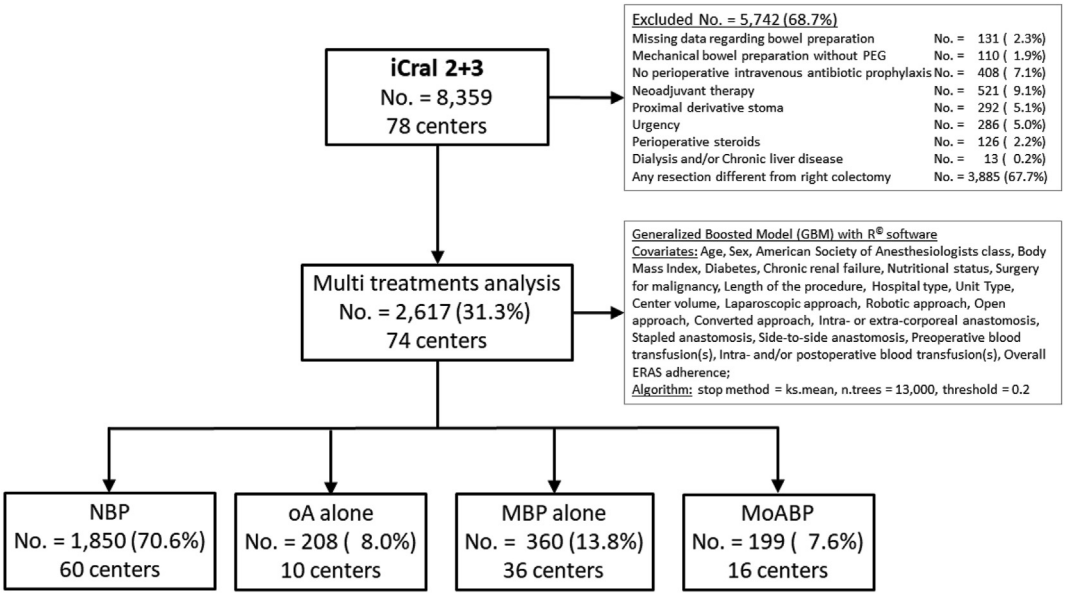

Figure 1. Study flowchart. *MBP*, mechanical bowel preparation alone; *MNA-SF*[22], Mini Nutritional Assessment–Short Form; *MoABP*, mechanical bowel preparation and oral antibiotics; *NBP*, no bowel preparation; *oA*, oral antibiotics alone; *PEG*, polyethylene glycol.

extended criteria,[24] as well as any reoperation, readmission, or death.

Outcomes

All the outcomes were calculated at 60 days after surgery. For the multitreatment analysis, the primary outcomes were SSI, according to the criteria of the Centers for Disease Control and Prevention/National Healthcare Safety Network,[25] and AL, according to the international consensus criteria.[26] Definitions of SSI are reported in the Supplementary Materials. The secondary outcomes were overall morbidity (any adverse event), major morbidity (any adverse event grade >II); reoperation (any unplanned operation); and readmission (any unplanned admission after primary discharge). Mortality (any death) and subtypes of SSI were not included in the secondary outcomes of this analysis because the absence of events in some treatment groups affects model convergence not allowing reliable estimations.

Statistical analysis

The GBM model[21] was used to estimate the propensity score weights for the binary comparisons between NBP and the other treatment arms; details are reported in the Supplementary Materials.[11,12,20,21,27,28] The analysis was performed using the "twang library" (Toolkit for Weighting and Analysis of Nonequivalent Groups,) of the software "R" (Version 4.2.2, The R Foundation for Statistical Computing, Vienna, Austria, 2022). Twenty-two covariates potentially affecting the 4 treatments variable assignments[28] were included in the model (Figure 1). For the outcome analysis, weighted logistic regression models for both primary and secondary endpoints defined as dichotomous variables, according to the baseline treatment (NBP) and the other 3 treatment arms (oA, MBP, and MoABP), were estimated using the "svyglm library" (Survey General Linear Models) of the software "R" (Version 4.2.2, The R Foundation for Statistical Computing).

Results

The population of 2,617 patients included data derived from 74 (94.9%) of the original 78 centers. The NBP group included data derived from 60 (81.0%), oA from 10 (13.5%), MBP from 36 (48.6%), and MoABP from 16 (21.6%) of the 74 centers.

In the present 2,617 right colectomy cohort, the SSI rate was 5.3%, the AL rate was 3.4%, the overall morbidity rate was 28.2%, and the mortality rate was 1.1%. Concerning AL, details about the diagnosis day, the grade, and the type of diagnosis (instrumental or clinical) are reported in Figure 2. The median time to diagnosis was 5.5 (interquartile range, 2.5, 12.5) days, the most frequent grade was IIIb, and the majority of diagnoses was instrumental (57.3%). AL diagnoses were all postoperative, and the instrumental ones were determined on the basis of intravenous-contrast computed tomography scan in 82.3% of cases, water-soluble intraluminal contrast computed tomography scan in 15.7% of cases, and water-soluble intraluminal contrast enema in 2% of cases. At univariate analysis, SSI rates were significantly different ($P = .021$) among the treatment groups; the difference was significant ($P = .042$) also regarding superficial and/or deep incisional SSI rates (Supplementary Table S1).

The types and grades of the adverse events contributing to overall morbidity and major morbidity are reported in Table III. After using the GBM, all the 22 covariates included in the model showed an optimal balance among treatment groups (Figure 3). The multitreatment-weighted logistic regression analysis for primary outcomes (Table IV) showed the risk of SSIs (5.0% after NBP) to be significantly lower after MoABP (4.0%; odds ratio [OR], 0.32; 95% confidence interval [CI], 0.13–0.82; $P = .017$), significantly greater after MBP (8.6%; OR, 2.05; 95% CI, 1.13–3.71; $P = .019$) and comparable after oA (3.9%). The AL risk (3.2% after NBP) resulted significantly greater after oA (4.8%; OR, 2.43; 95% CI, 1.21–4.89; $P = .013$).

Concerning secondary outcomes (Table IV), no significant differences were recorded for the risk of overall morbidity and reoperation. The risk of readmission (3.0% after NBP) was significantly reduced after MoABP (1.5%; OR, 0.23; 95% CI, 0.05–0.97; $P = .046$),

Table I
Descriptive analysis of the variables considered in the 2,617 patients before matching

Pattern	NBP		oA		MBP		MoABP		*P**
	n = 1,850		*n* = 208		*n* = 360		*n* = 199		
	n	%	*n*	%	*n*	%	*n*	%	
Age, yr									
≤74	992	53.6	112	53.8	186	51.7	107	53.8	.919
>74	858	46.4	96	46.2	174	48.3	92	46.2	
Sex									
Male	920	49.7	105	50.5	180	50.0	95	47.7	.946
Female	930	50.3	103	49.5	180	50.0	104	52.3	
ASA class									
I-II	1,073	58.0	118	56.7	213	59.2	114	57.3	.944
III	777	42.0	90	43.3	147	40.8	85	42.7	
Body mass index, kg/m^2									
≤25.25	908	49.1	122	58.7	179	49.7	106	53.3	.054
>25.25	942	50.1	86	41.3	181	50.3	93	46.7	
Diabetes									
Yes	329	17.8	30	14.4	66	18.3	31	15.6	.543
No	1,521	82.2	178	85.6	294	81.7	168	84.4	
Chronic renal failure									
Yes	89	4.8	8	3.8	18	5.0	12	6.0	.782
No	1761	95.2	200	96.2	342	95.0	187	4.09	
MNA-SF									
≤12	1,054	57.0	94	45.2	245	68.1	115	57.8	.000
>12	796	43.0	114	54.8	115	31.9	84	42.2	
Surgery for malignancy									
Yes	1,583	85.6	186	89.4	322	89.4	181	90.9	.031
No	267	14.4	22	10.6	38	10.6	18	9.1	
Diverticular disease	8	3.0	2	9.2	1	2.6	1	5.6	
Endometriosis	0	0	0	0	4	10.5	0	0	
Polyps	149	55.8	12	54.5	19	50.0	4	22.2	
IBD	79	29.6	3	13.6	6	15.8	3	16.7	
Other	31	11.6	5	22.7	8	21.1	10	55.5	
Laparoscopic approach									
Yes	1,332	72.0	143	68.7	220	61.1	163	81.9	.000
No	518	28.0	65	31.3	140	38.9	36	18.1	
Robotic approach									
Yes	193	10.4	14	6.7	31	8.6	4	2.0	.001
No	1,657	89.6	194	93.3	329	91.4	195	98.0	
Converted approach									
Yes	74	4.0	14	6.7	16	4.4	8	4.0	.326
No	1,776	96.0	194	93.3	344	95.6	191	96.0	
Open approach									
Yes	251	13.6	37	17.8	93	25.8	24	12.1	.000
No	1,599	86.4	171	82.2	267	74.2	175	87.9	
Anastomosis 1									
Intracorporeal	1,116	60.3	129	62.0	115	31.9	128	64.3	.000
Extracorporeal	734	39.7	79	38.0	245	68.1	71	35.7	
Anastomosis 2									
Stapled	1,616	87.3	161	77.4	252	70.0	156	78.4	.000
Handsewn	234	12.7	47	22.6	108	30.0	43	21.6	
Anastomosis 3									
Side-to-side	1,776	96.0	206	99.0	326	90.6	178	89.6	.000
Other shape	74	4.0	2	1.0	34	9.4	21	10.6	
Operation length, min									
≤155	923	49.9	110	52.9	161	44.7	118	59.3	.009
>155	927	50.1	98	47.1	199	55.3	81	40.7	
Hospital type									
Met./Ac.	1,172	63.3	129	62.0	191	53.1	181	90.9	.000
Local/regional	678	36.7	79	38.0	169	46.9	18	9.1	
Unit type									
Colorectal/oncologic	307	16.6	16	7.7	141	39.2	45	22.6	.000
General	1,543	83.4	192	92.3	219	60.8	154	77.4	
Center volume									
<4 cases/mo	441	23.8	70	33.7	167	46.4	68	34.2	.000
≥4 cases/mo	1,409	76.2	138	66.3	193	53.6	131	65.8	
Preoperative BT(s)									
Yes	182	9.8	13	6.3	38	10.6	16	8.0	.289
No	1,668	90.2	195	93.7	322	89.4	183	92.0	
Intra/postoperative BT(s)									
Yes	159	8.6	11	5.3	46	12.8	19	9.5	.017
No	1,691	91.4	197	94.7	314	87.2	180	90.5	

(*continued on next page*)

Table I (*continued*)

Pattern	NBP		oA		MBP		MoABP		*P**
	n = 1,850		*n* = 208		*n* = 360		*n* = 199		
	n	%	*n*	%	*n*	%	*n*	%	
Overall ERAS adherence (%)									
≤73.68	689	37.2	52	25.0	288	80.0	61	30.7	.000
>73.68	1,161	62.8	156	75.0	72	20.0	138	69.4	
Nutritional screening	1,354	73.2	157	75.5	216	60.0	132	66.3	
Prehabilitation	873	47.2	112	53.8	63	17.5	54	27.1	
Counseling	1,358	73.4	137	65.9	185	51.4	162	81.4	
Immune enhancing nutrition	658	35.6	106	51.0	63	17.5	36	18.1	
Antithrombotic prophylaxis	1762	95.2	200	96.2	309	85.8	182	91.5	
Preoperative carbohydrates load	1,176	63.6	122	58.7	154	42.8	110	55.3	
No preanesthesia	1,607	86.9	145	69.7	219	60.8	156	78.4	
Standard anesthesia protocol	1,562	84.4	206	99.0	275	76.4	193	97.0	
Normothermia	1,776	96.0	205	98.6	284	78.9	193	97.0	
Goal-directed fluid therapy	1,537	83.1	180	86.5	228	63.3	188	94.5	
PONV prophylaxis	1,648	89.1	203	97.6	277	76.9	184	92.5	
Multimodal analgesia	1,696	91.7	206	99.0	275	76.4	187	94.0	
No nasogastric tube	1,664	90.0	201	96.6	217	60.3	156	78.4	
Minimally invasive surgery	1,599	86.4	171	82.2	267	74.2	175	87.9	
No drains	831	44.9	131	63.0	50	13.9	77	38.7	
Urinary catheter <24–48 h	1,540	83.2	191	91.8	221	61.4	162	81.4	
Early mobilization	1,072	58.0	187	89.9	85	23.6	148	74.4	
Early oral feeding	1,027	55.5	175	84.1	57	15.8	114	57.3	
Predischarge check	1,589	85.9	168	80.8	182	50.6	176	88.4	

ASA, American Society of Anesthesiologists; *BT*, blood transfusion; *ERAS*, Enhanced Recovery After Surgery; *Extracorporeal*, anastomosis performed under direct visual control through an open access; *IBD*, inflammatory bowel disease; *Intracorporeal*, anastomosis performed under visual control through the scope; *MBP*, mechanical bowel preparation alone; *Met./Ac.*, metropolitan/academic; *MNA-SF*[22], Mini Nutritional Assessment–Short Form; *MoABP*, mechanical bowel preparation and oral antibiotics; *NBP*, no bowel preparation; *oA*, oral antibiotics alone; *PONV*, postoperative nausea/vomiting.

* *P*: χ^2 independence test with 3 degrees of freedom.

and the risk of major morbidity (5.1% after NBP) was significantly greater after oA (6.7%; OR, 2.44; 95% CI, 1.27–4.68; $P = .007$). All the details regarding the multitreatment machine-learning–adjusted comparisons are reported in Supplementary Tables S2–4.

Discussion

To the best of our knowledge, this is the first multitreatment analysis on the basis of machine-learning procedures used in a multicenter, quasi-experimental study on bowel preparation before elective right colectomy. A few studies[3–8] have focused on the impact of bowel preparation for elective right colectomy, and the present multicenter large study, regarding all patients treated with PIVAP, showed that MoABP had significantly lower rates of SSIs and readmissions compared with NBP. These findings contradict the results of an RCT on patients with colorectal cancer,[7] of a PSMA on patients with colon cancer,[6] and of 2 observational studies on patients with benign and malignant disease,[4,8] all determined on the basis of relatively small sample sizes. Our results confirm the findings of a retrospective study evaluating 45,724 patients.[3] The present multicenter study, in which the median adherence to the ERAS items was 73.68% with 2,058 patients not receiving MPB, also showed a significantly greater risk of SSI for MBP compared with NBP, contradicting the results of the Minimally-Invasive Right Colectomy Anastomosis (MIRCAST) study, in which MBP was associated with a lower incidence of any complication and in which all participating centers treated their patients using ERAS criteria, although the percentage of patients receiving MBP was 35.3%.[8] Different SSI definitions, different surveillance strategies, especially for postdischarge events, and different patient populations with different SSI risk profiles make the rates of SSI in colon surgery hardly comparable across different institutions and countries, ranging from 3.9%[29] to 26%[30] in studies published more than 10 years ago. The 5.3% SSI rate observed in this study is well within the range (4.3–13%) recorded in studies published during the last 10 years.[3,4,6–8]

Regarding the risk of AL, the present study observed that oA alone, compared with NBP, was associated with a greater risk of AL and major morbidity rates, also contradicting the findings of the MIRCAST study.[8] After the estimation of the propensity score weights, preoperative blood transfusion(s) was the only variable that, independently from oA preparation, was significantly associated with a greater risk of AL ($P = .016$), confirming the findings of previous iCral studies.[31,32] As the severity of complications, comprised into major morbidity rates, may be skewed between groups and not captured by aggregate analysis, a detailed list of adverse events is reported in Table III.

The present real-life cohort is potentially affected by 2 types of unbalancing: different treatment group sample sizes and heterogeneity among treatment groups. The first one, affecting the power of the analysis, has been addressed using a logistic survey regression model based on weights calculated by the GBM algorithm, considering that the number and the types of covariates impact on the effective sample size, that is, an estimate of the sample size required to achieve the same level of precision as would be expected to be obtained by a simple random sample. The choice of the 22 covariates in the present study was determined by both clinical considerations and the estimate of the best pairwise comparison to optimize the analysis power. Unbalancing from heterogeneity among treatment groups, affecting the analysis bias, has been addressed choosing a GBM algorithm calculating 13,000 trees in order to optimize the balancing according to the Kolmogorov-Smirnov (KS.mean) statistics, minimizing the distance of the weighted distributions of the 22 covariates (Figure 3).

Several clinical variables contribute to SSI and AL rates after right colectomy: many are patient-related risk factors (comorbidities) that affect host responsiveness, and others result from clinical interventions or behaviors during perioperative patient care.

Table II
Oral antibiotics schedules in the oA and MoABP groups

Oral antibiotic(s)	Administration schedule	oA ($n = 208$)		MoABP ($n = 199$)		*T*-test for proportions comparison
		No. of patients	% of patients	No. of patients	% of patients	*P*
Metronidazole (500 mg)	Started 2 d preoperatively, TID	57	27.0	3	1.51	.334
Paromomycin (250 mg)	Started 2 d preoperatively, BID					
Metronidazole (500 mg)	Started 1 d preoperatively, TID	30	14.4	16	8.0	.550
Cefazolin (2,000 mg)	Started 1 d preoperatively, OD					
Metronidazole (500 mg)	Started 1 d preoperatively, TID	45	21.6	8	4.0	.234
Trimethoprim (160 mg)/sulfamethoxazole (800 mg)	Started 1 d preoperatively, TID					
Metronidazole (500 mg)	Started 1 d preoperatively, TID	24	11.5	1	0.5	.724
Neomycin plus Bacitracin (300 mg)	Started 1 d preoperatively, TID					
Metronidazole (500 mg)	Started 3 d preoperatively, BID	18	8.7	1	0.5	.767
Amoxicillin (1,000 mg)	Started 3 d preoperatively, BID					
Metronidazole (250 mg)	Started 1 d preoperatively, TID	9	4.3	4	2.0	.854
Ciprofloxacin (500 mg)	Started 1 d preoperatively, BID					
Metronidazole (500 mg)	Started 7 d preoperatively, TID	1	0.5	1	0.5	1.00
Rifaximin (400 mg)	Started 7 d preoperatively, BID					
Metronidazole (250 mg)	Started 1 d preoperatively, BID	0	0	24	12.1	n.e.
Amoxicillin (1,000 mg)	Started 1 d preoperatively, BID					
Paromomycin (250 mg)	Started 4 d preoperatively, QID	22	10.6	0	0	n.e.
Paromomycin (1,000 mg)	Started 1 d preoperatively, OD	0	0	7	3.5	n.e.
Metronidazole (250 mg)	Started 1 d preoperatively, TID	2	1.0	0	0	n.e.
Rifaximin (200 mg)	Started 1 d preoperatively, BID					
Metronidazole (500 mg)	Started 1 d preoperatively, BID	0	0	28	14.1	n.e.
Rifaximin (200 mg)	Started 1 d preoperatively, BID					
Metronidazole (1,000 mg)	Started 1 d preoperatively, TID	0	0	5	2.5	n.e.
Rifaximin (400 mg)	Started 1 d preoperatively, TID					
Metronidazole (500 mg)	Started 1 d preoperatively, BID	0	0	52	26.1	n.e.
Paromomycin (500 mg)	Started 1 d preoperatively, BID					
Rifaximin (400 mg)	Started 1 d preoperatively, BID					
Rifaximin (400 mg)	Started 1 d preoperatively, TID	0	0	37	18.6	n.e.
Amoxicillin (1,000 mg)	Started 3 d preoperatively, TID	0	0	4	2.0	n.e.
Neomycin plus Bacitracin (300 mg)	Started 1 d preoperatively, TID	0	0	8	4.0	n.e.

BID, 2 times per day; *MoABP*, mechanical bowel preparation plus oral antibiotics; *n.e.*, test not executable because there were cells with insufficient values; *oA*, oral antibiotics; *OD*, once daily; *QID*, 4 times per day; *TID*, 3 times per day.

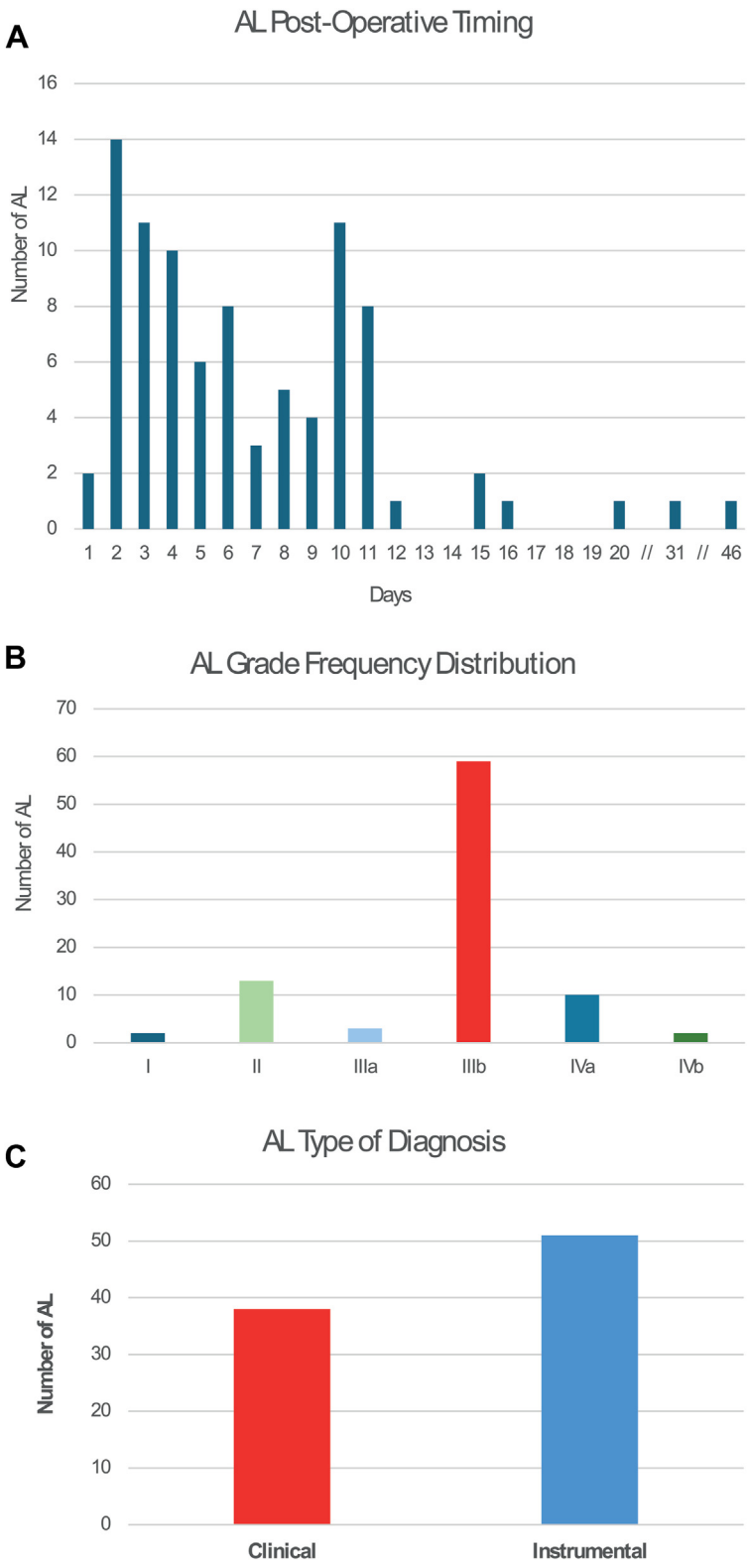

Figure 2. Details of AL, including diagnosis day (A), the grade (B), and the type of diagnosis (C). *AL*, anastomotic leakage.

Therefore, our choice of 22 covariates favored clinical considerations over statistical significance. This choice was possible thanks to the large sample size (2,617 patients) whereas a previous PSMA,[6] with a smaller sample size (238 patients enrolled in 10 years), used only 5 covariates (age, sex, American Society of Anesthesiologists class, diabetes, intermittent hemodialysis) and a caliper of 0.2, which is not sufficient to minimize the differences between groups. In particular, hospital type, surgical unit type, and center volume were included to account for the potential imbalance of multicenter, clustered data; adherence to the ERAS pathway to account

Table III
Adverse events contributing to overall morbidity (OM, any adverse event) and major morbidity (MM, any adverse event grade >II) after elective right hemicolectomy in 2,617 patients

Adverse event	NBP (n = 1,850)		oA (n = 208)		MBP (n = 360)		MoABP (n = 199)	
	OM, %	MM, %	OM, %	MM, %	OM, %	MM, %	OM, %	MM, %
Anastomotic leakage	3.2	2.6	4.8	4.3	4.7	3.9	1.5	1.0
sdiSSIs	3.3	0.3	2.4	0.5	6.4	0.3	2.5	0.0
Deep wound dehiscence	0.3	0.2	0.5	0.0	0.0	0.0	0.0	0.0
Abdominal collection/abscess	1.6	0.8	1.0	0.5	2.8	0.8	1.5	0.0
Small bowel obstruction	1.7	1.0	1.4	0.5	2.5	1.4	3.0	2.0
Anastomotic bleeding	2.2	0.5	3.8	0.0	1.1	0.0	0.5	0.5
Abdominal bleeding	1.1	0.7	0.0	0.5	1.7	1.1	1.0	0.0
Small bowel perforation	0.3	0.3	0.0	0.0	0.0	0.0	0.0	0.0
Trocar/wound site bleeding	0.4	0.0	0.0	0.0	0.3	0.0	0.5	0.0
Anemia	5.9	0.1	3.4	0.5	6.1	0.3	6.0	0.0
Paralytic ileus	5.0	0.1	4.3	0.0	6.7	0.0	3.0	0.0
Fever	3.1	0.1	5.8	0.0	3.6	0.0	3.0	0.0
DVT/pulmonary embolism	0.4	0.2	0.0	0.0	0.3	0.0	0.0	0.0
Neurologic	0.6	0.1	0.0	0.0	0.8	0.0	0.0	0.0
Pneumonia and pulmonary failure	1.8	0.5	4.8	0.5	2.5	0.6	2.0	0.5
Urinary retention	0.7	0.0	0.0	0.0	0.8	0.0	0.0	0.0
Urinary tract infection	0.1	0.0	0.5	0.5	0.6	0.0	0.0	0.0
Acute renal failure	0.5	0.1	1.4	0.0	1.4	0.0	1.0	0.0
Acute mesenteric ischemia	0.0	0.0	0.0	0.0	0.3	0.3	0.0	0.0
Acute peptic ulcer/erosive gastritis	0.2	0.1	0.0	0.0	0.3	0.0	0.0	0.0
Cardiac dysfunction and failure	1.5	0.3	1.4	1.0	1.9	0.6	1.0	0.5
Other	5.6	1.0	4.3	0.5	4.2	0.8	6.5	0.5

DVT, deep venous thrombosis; *MBP*, mechanical bowel preparation; *MM*, major morbidity; *MoABP*, mechanical bowel preparation and oral antibiotics; *NBP*, no bowel preparation; *oA*, oral antibiotics; *OM*, overall morbidity; *sdiSSIs*, superficial and/or deep incisional surgical-site infections.

for the potential imbalance of perioperative management; and pre- and intra-postoperative blood transfusion(s) to account for transfusion-related morbidity.[32] Resections for benign and malignant diseases, 4 approach types (laparoscopic, robotic, converted, open), intracorporeal (anastomosis performed under visual control through the scope) or extracorporeal (anastomosis performed under direct visual control through an open access) anastomoses, stapled or hand-sewn anastomoses, side-to-side or different fashion anastomoses, and operation length were included on the basis of controversial findings reported in literature regarding SSI, AL, and overall morbidity.[33–39] Finally, age, sex, American Society of Anesthesiologists class, body mass index, diabetes, chronic renal failure, and nutritional status were added to account for patient's imbalance.

Concerning the schedule heterogeneity in oA and MoABP treatment groups of the present analysis, it has to be noted that this is a real-life cohort of patients treated in 74 centers adhering to ERAS recommendations that, as it is known, exclude the use of oA and MBP. In 407 patients of the present cohort, treated in different centers, speculative reasons opposed the ERAS recommendations, as in similar other studies performed in centers adhering to ERAS protocols,[7,8] specifically evaluating right colectomy. Regarding the studies with findings that contradict the present analysis, in Finland[4] and Israel[6] neomycin and metronidazole, at different dosages but in the day preceding the operation, were used, whereas in the study from China,[7] streptomycin and metronidazole were administered in the 3 days before surgery. Other studies[3,8] did not report the specific antibiotic regimen used for each patient. A recent Bayesian network meta-analysis[10] reported that neomycin and metronidazole was the most frequent regimen used in RCTs among 10 different regimens with 29 different schedules. This regimen, like the kanamycin and metronidazole regimen, was superior to other regimens in significantly reducing rates of SSIs compared with MBP alone.[10] In the present study, Italian centers used 12 different regimens with 17 different schedules but, due to the small number of SSIs and AL events in each oral antibiotic and administration schedule subgroup, it was not possible to conclude which antibiotic and administration schedule is better for preventing SSIs and AL.

An important strength of the present study is represented by the large number of prospectively enrolled patients in a well-defined time-lapse and in a large number of centers, representing a wide sample of surgical units performing right hemicolectomy in Italy. Although the multicenter nature of the data may be a definite source of clustering bias, it is undoubtedly representative of real-life clinical practice.

Study limitations

The generalizability of the findings to different clinical settings and patient populations is limited by the impact on study outcomes of potential residual, known or unknown, unmeasured confounding factors, some of which affect both internal and external validity of the present analysis. Concerning the internal validity of the study, limitations include a relevant heterogeneity of oral antibiotic schedules, a supposed heterogeneity of PIVAP schedules, no information regarding patient tolerance and completion of MBP, heterogeneity of health-acquired infections preventive bundle (preoperative whole-body bathing, hair removal, and skin decontamination), no information of performing surgeon experience, and the specific Italian health care context that entrusts patients with intestinal preparation. Concerning the external validity of the study, limitations include majority of the items considered in the exclusion criteria reported in Figure 1 (except missing data regarding bowel preparation). In conclusion, this multitreatment machine-learning analysis, despite the limitations mentioned,

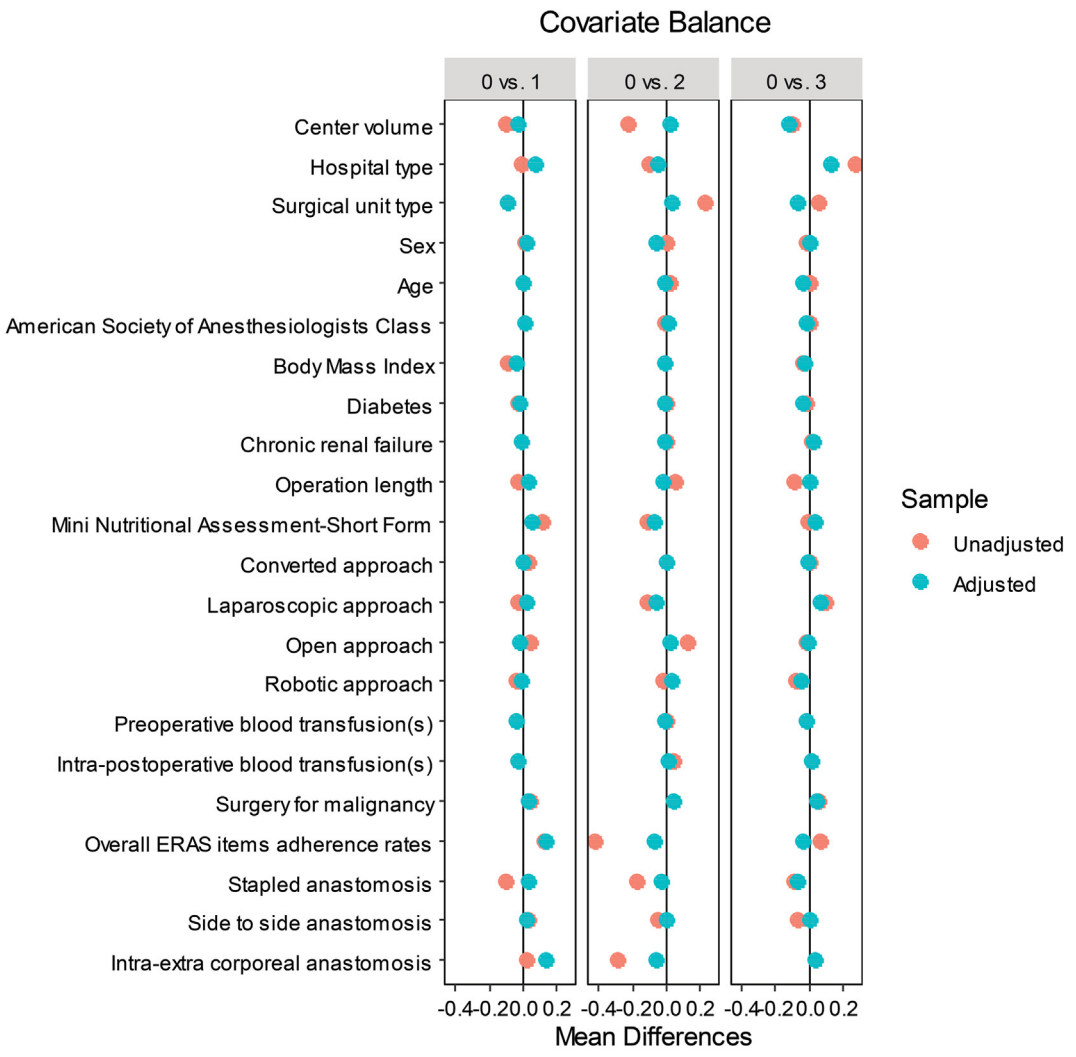

Figure 3. Love plot Kolmogorov-Smirnov mean differences of covariates before and after adjustment using a machine-learning technique, comparing the reference treatment (no bowel preparation, named "0" in the figure) with the other 3 treatments (oral antibiotics alone, named "1"; mechanical bowel preparation alone, named "2"; mechanical bowel preparation and oral antibiotics, named "3"); *ERAS*, Enhanced Recovery After Surgery.

Table IV
Multitreatment-weighted logistic regression analysis for outcomes

Outcome/treatment	NBP (n = 1,850) OR (95% CI); P	oA (n = 208) OR (95% CI); P	MBP (n = 360) OR (95% CI); P	MoABP (n = 199) OR (95% CI); P
Primary outcomes				
SSIs	5.0%	3.9%	8.6%	4.0%
	Reference	0.54 (0.22–1.37); P = .196	2.05 (1.13–3.71); P = .019	0.32 (0.13–0.82); P = .017
AL	3.2%	4.8%	4.7%	1.5%
	Reference	2.43 (1.21–4.89); P = .013	0.66 (0.32–1.38); P = .268	0.39 (0.11–1.43); P = .154
Secondary outcomes				
Overall morbidity	27.9%	29.3%	31.9%	22.6%
	Reference	1.14 (0.79–1.65); P = .480	1.39 (0.92–2.09); P = .120	0.78 (0.48–1.28); P = .324
Major morbidity	5.1%	6.7%	6.1%	3.0%
	Reference	2.44 (1.27–4.68); P = .007	0.81 (0.39–1.67); P = .567	0.73 (0.25–2.16); P = .572
Reoperation	4.4%	5.3%	6.1%	2.0%
	Reference	1.78 (0.89–3.57); P = .105	0.80 (0.38–1.70); P = .561	0.62 (0.19–2.03); P = .432
Readmission	3.0%	1.4%	1.9%	1.5%
	Reference	0.36 (0.10–1.32); P = .123	0.60 (0.22–1.62); P = .312	0.23 (0.05–0.97); P = .046

AL, anastomotic leakage; *DVT*, deep venous thrombosis; *MBP*, mechanical bowel preparation; *MM*, major morbidity; *MoABP*, mechanical bowel preparation and oral antibiotics; *NBP*, no bowel preparation; *oA*, oral antibiotics; *OM*, overall morbidity; *SSI*, surgical-site infection.

showed that MoABP is associated with a decrease in SSIs after elective right colectomy compared with NBP.

Funding/Support

The authors declare no funding or support.

Conflicts of Interest/Disclosure

The authors declare no competing interests.

Acknowledgments

Collaborators (clinical investigators) of the iCral study group are: Paolo Ciano, MD (General Surgery Unit, Sandro Pertini Hospital, Roma, Italy), Michele Benedetti, MD (General Surgery Unit, Sandro Pertini Hospital, Roma, Italy), Leonardo Antonio Montemurro, MD (General Surgery Unit, Sandro Pertini Hospital, Roma, Italy), Marco Clementi, MD (General Surgery Unit, University of L'Aquila, L'Aquila, Italy; Department of Applied Clinical Sciences and Biotechnology, University of L'Aquila, L'Aquila, Italy), Elisa Bertocchi, MD (General Surgery Unit, IRCCS Sacro Cuore Don Calabria Hospital, Negrar di Valpolicella (VR), Italy), Gaia Masini, MD (General Surgery Unit, IRCCS Sacro Cuore Don Calabria Hospital, Negrar di Valpolicella (VR), Italy), Amedeo Altamura, MD (General Surgery Unit, Cardinale G. Panico Hospital, Tricase (LE), Italy), Francesco Rubichi, MD (General Surgery Unit, Cardinale G. Panico Hospital, Tricase (LE), Italy), Marco Migliore, MD (Oncologic Surgery Unit, Candiolo Cancer Institute, FPO-IRCCS, Candiolo (TO), Italy), Daniele Parlanti, MD (General Surgery Unit, Infermi Hospital, Rimini, Italy), Gabriele Vago, MD (General Surgery Unit, Infermi Hospital, Rimini, Italy), Antonio Sciuto, MD (General Surgery Unit, ASL Napoli 2 Nord, Pozzuoli (NA), Italy), Ugo Pace, MD (Colorectal Surgical Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori, "Fondazione Giovanni Pascale IRCCS-Italia", Naples, Italy), Andrea Fares Bucci, MD (Colorectal Surgical Oncology, Istituto Nazionale per lo Studio e la Cura dei Tumori, "Fondazione Giovanni Pascale IRCCS-Italia", Naples, Italy), Michele Simone, MD (Department of Surgical Oncology, IRCCS Istituto Tumori "Giovanni Paolo II", Bari, Italy), Diletta Cassini, MD (General Surgery Unit, ASST Ovest Milanese, Legnano (MI), Italy), Lorenzo Pandolfini, MD (General Surgery Unit, Santa Maria Annunziata & Serristori Hospital, Florence, Italy), Alessandro Falsetto, MD, Ferdinando Ficari, MD (General Surgery and IBD Unit, Careggi University Hospital, Firenze, Italy), Francesco Giudici, MD (General Surgery and IBD Unit, Careggi University Hospital, Firenze, Italy), Fabio Cianchi, MD (General Surgery and IBD Unit, Careggi University Hospital, Firenze, Italy), Alberto Patriti, MD (Department of Surgery, Marche Nord Hospital, Pesaro e Fano (PU), Italy), Marcella Lodovica Ricci, MD (Department of Surgery, Marche Nord Hospital, Pesaro e Fano (PU), Italy), Walter Siquini, MD (General Surgery Unit, S. Lucia Hospital, Macerata, Italy), Alessandro Cardinali, MD (General Surgery Unit, S. Lucia Hospital, Macerata, Italy), Stefano D'Ugo, MD, PhD, FEBS, FACS (General Surgery Unit, "V. Fazzi" Hospital, Lecce, Italy), Marcello Spampinato, MD, PhD, FEBS (HPB) (General Surgery Unit, "V. Fazzi" Hospital, Lecce, Italy), Stefano Scabini, MD (General & Oncologic Surgery Unit, IRCCS "San Martino" National Cancer Center, Genova, Italy), Alessandra Aprile, MD (General & Oncologic Surgery Unit, IRCCS "San Martino" National Cancer Center, Genova, Italy), Domenico Soriero, MD (General & Oncologic Surgery Unit, IRCCS "San Martino" National Cancer Center, Genova, Italy), Marco Caricato, MD, FACS (Colorectal Surgery Unit, Policlinico Campus BioMedico, Roma, Italy), Gabriella Teresa Capolupo, MD, FACS (Colorectal Surgery Unit, Policlinico Campus BioMedico, Roma, Italy), Giusto Pignata, MD (2nd General Surgery Unit 2, Spedali Civili di Brescia, Brescia, Italy), Jacopo Andreuccetti, MD (2nd General Surgery Unit 2, Spedali Civili di Brescia, Brescia, Italy), Ilaria Canfora, MD (2nd General Surgery Unit 2, Spedali Civili di Brescia, Brescia, Italy), Andrea Liverani, MD (General Surgery Unit, Regina Apostolorum Hospital, Albano Laziale (RM), Italy), Giuseppe Lamacchia, MD (General Surgery Unit, Regina Apostolorum Hospital, Albano Laziale (RM), Italy), Claudia Franceschilli, MD (General Surgery Unit, Regina Apostolorum Hospital, Albano Laziale (RM), Italy), Roberto Campagnacci, MD (General Surgery Unit, "C. Urbani" Hospital, Jesi (AN), Italy), Angela Maurizi, MD (General Surgery Unit, "C. Urbani" Hospital, Jesi (AN), Italy), Pierluigi Marini, MD (General & Emergency Surgery Unit, San Camillo-Forlanini Hospital, Roma, Italy), Grazia Maria Attinà, MD (General & Emergency Surgery Unit, San Camillo-Forlanini Hospital, Roma, Italy), Ugo Elmore, MD (Gastrointestinal Surgery Unit, IRCCS San Raffaele Scientific Institute Università Vita-Salute San Raffaele, Milano, Italy), Francesco Puccetti, MD (Gastrointestinal Surgery Unit, IRCCS San Raffaele Scientific Institute Università Vita-Salute San Raffaele, Milano, Italy), Francesco Corcione, MD (Minimally Invasive General and Oncologic and Surgery Unit, "Federico II" University, Napoli, Italy), Umberto Bracale, MD (Minimally Invasive General and Oncologic and Surgery Unit, "Federico II" University, Napoli, Italy), Roberto Peltrini, MD (Minimally Invasive General and Oncologic and Surgery Unit, "Federico II" University, Napoli, Italy), Roberto Santoro, MD (General Oncologic Surgery Unit, Belcolle Hospital, Viterbo, Italy), Pietro Amodio, MD (General Oncologic Surgery Unit, Belcolle Hospital, Viterbo, Italy), Massimo Carlini, MD, FACS (General Surgery Unit, S. Eugenio Hospital, Roma, Italy), Domenico Spoletini, MD, PhD, FACS (General Surgery Unit, S. Eugenio Hospital, Roma, Italy), Rosa Marcellinaro, MD (General Surgery Unit, S. Eugenio Hospital, Roma, Italy), Antonio Giuliani, MD (General Surgery Unit, S. Carlo Hospital, Potenza, Italy), Giovanni Del Vecchio, MD (General Surgery Unit, S. Carlo Hospital, Potenza, Italy), Mario Sorrentino, MD (General Surgery Unit, Latisana-Palmanova Hospital, Friuli Centrale University, Udine, Italy), Massimo Stefanoni, MD (General Surgery Unit, Latisana-Palmanova Hospital, Friuli Centrale University, Udine, Italy), Giovanni Ferrari, MD (General Oncologic and Mininvasive Surgery Unit, Great Metropolitan Niguarda Hospital, Milano, Italy), Pietro Maria Lombardi, MD (General Oncologic and Mininvasive Surgery Unit, Great Metropolitan Niguarda Hospital, Milano, Italy), Alberto Di Leo, MD (General Oncologic and Mininvasive Surgery Unit, Great Metropolitan Niguarda Hospital, Milano, Italy), Lorenzo Crepaz, MD (General and Minimally Invasive Surgery Unit, San Camillo Hospital, Trento, Italy), Augusto Verzelli, MD (General Surgery Unit, Profili Hospital, Fabriano (AN), Italy), Andrea Budassi, MD (General Surgery Unit, Profili Hospital, Fabriano (AN), Italy), Giuseppe Sica, MD (Minimally Invasive Surgery Unit, Policlinico Tor Vergata University Hospital, Roma, Italy), Giulia Bagaglini, MD (Minimally Invasive Surgery Unit, Policlinico Tor Vergata University Hospital, Roma, Italy), Stefano Rausei, MD (General Surgery Unit, Gallarate Hospital (VA), Gallarate, Italy), Silvia Tenconi, MD (General Surgery Unit, Gallarate Hospital (VA), Gallarate, Italy), Davide Cavaliere, MD (General & Oncologic Surgery Unit, AUSL Romagna, Forlì (FC), Italy), Leonardo Solaini, MD (General & Oncologic Surgery Unit, AUSL Romagna, Forlì (FC), Italy), Giorgio Ercolani, MD (General & Oncologic Surgery Unit, AUSL Romagna, Forlì (FC), Italy), Gian Luca Baiocchi, MD, FACS (General Surgery Unit 3, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy), Sarah Molfino, MD (General Surgery Unit 3, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy), Marco Milone, MD (General & Endoscopic Surgery Unit, "Federico II" University, Napoli, Italy), Giovanni Domenico De Palma, MD (General & Endoscopic Surgery Unit, "Federico II" University, Napoli, Italy), Giovanni Ciaccio, MD (General Surgery Unit, S. Elia Hospital, Caltanissetta, Italy), Paolo Locurto, MD (General

Surgery Unit, S. Elia Hospital, Caltanissetta, Italy), Giovanni Domenico Tebala, MD (General Surgery Unit, S. Maria Hospital, Terni, Italy), Antonio Di Cintio, MD (General Surgery Unit, S. Maria Hospital, Terni, Italy), Luigi Boni, MD, FACS (General Surgery Unit, Fondazione IRCCS Ca' Granda, Policlinico Maggiore Hospital, Milano, Italy), Elisa Cassinott, MD (General Surgery Unit, Fondazione IRCCS Ca' Granda, Policlinico Maggiore Hospital, Milano, Italy), Stefano Mancini, MD (General & Oncologic Surgery Unit, San Filippo Neri Hospital, Roma, Italy), Andrea Sagnotta, MD, PhD (General & Oncologic Surgery Unit, San Filippo Neri Hospital, Roma, Italy), Mario Guerrieri, MD (Surgical Clinic, Torrette Hospital, University of Ancona, Ancona, Italy), Monica Ortenzi, MD (Surgical Clinic, Torrette Hospital, University of Ancona, Ancona, Italy), Roberto Persiani, MD (General Surgery Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy), Alberto Biondi, MD (General Surgery Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Roma, Italy), Andrea Lucchi, MD, FACS (General Surgery Unit, "Ceccarini" Hospital, Riccione (RN), Italy), Giulia Vitali, MD (General Surgery Unit, "Ceccarini" Hospital, Riccione (RN), Italy), Dario Parini, MD (General Surgery Unit, S. Maria della Misericordia Hospital, Rovigo, Italy), Maurizio De Luca, MD (General Surgery Unit, S. Maria della Misericordia Hospital, Rovigo, Italy), Antonino Spinelli, MD (Department of Biomedical Sciences, Humanitas University, Pieve Emanuele (MI) and IRCCS Humanitas Research Hospital, Rozzano (MI), Italy), Francesco Carrano, MD (Department of Biomedical Sciences, Humanitas University, Pieve Emanuele (MI) and IRCCS Humanitas Research Hospital, Rozzano (MI), Italy), Michele Genna, MD (General Surgery Unit, University Hospital, Verona, Italy), Francesca Fior, MD (General Surgery Unit, University Hospital, Verona, Italy), Vincenzo Bottino, MD (General & Oncologic Surgery Unit, Evangelico Betania Hospital, Napoli, Italy), Antonio Ferronetti, MD (General & Oncologic Surgery Unit, Evangelico Betania Hospital, Napoli, Italy), Andrea Coratti, MD (General and Emergency Surgery Unit, Misericordia Hospital, Grosseto, Italy), Giuseppe Giuliani, MD (General and Emergency Surgery Unit, Misericordia Hospital, Grosseto, Italy), Roberto Benigni, MD (General and Emergency Surgery Unit, Misericordia Hospital, Grosseto, Italy), Dario Scala, MD (Abdominal Oncologic Surgery Unit, IRCCS CROB Basilicata Referral Cancer Center, Rionero in Vulture, (PZ), Italy), Battistino Puppio, MD (Abdominal Oncologic Surgery Unit, IRCCS CROB Basilicata Referral Cancer Center, Rionero in Vulture, (PZ), Italy), Alessio Vagliasindi, MD (Abdominal Oncologic Surgery Unit, IRCCS CROB Basilicata Referral Cancer Center, Rionero in Vulture, (PZ), Italy), Andrea Muratore, MD (General Surgery Unit, "E. Agnelli" Hospital, Pinerolo (TO), Italy), Patrizia Marsanic, MD (General Surgery Unit, "E. Agnelli" Hospital, Pinerolo (TO), Italy), Nicoletta Sveva Pipitone Federico, MD (General Surgery Unit, "E. Agnelli" Hospital, Pinerolo (TO), Italy), Maurizio Pavanello, MD (General Surgery Unit, AULSS2 Marca Trevigiana, Conegliano Veneto (TV), Italy), Carlo Di Marco, MD (General Surgery Unit, AULSS2 Marca Trevigiana, Conegliano Veneto (TV), Italy), Umberto Rivolta, MD (General Surgery Unit, Fornaroli Hospital, ASST Ovest Milanese, Magenta (MI), Italy), Camillo Leonardo Bertoglio, MD, PhD (General Surgery Unit, Fornaroli Hospital, ASST Ovest Milanese, Magenta (MI), Italy), Micaela Piccoli, MD, FACS (General Surgery Unit, Civil Hospital, Baggiovara (MO), Italy), Francesca Pecchini, MD (General Surgery Unit, Civil Hospital, Baggiovara (MO), Italy), Carlo Talarico, MD (General Surgery Unit, Villa dei Gerani Hospital, Vibo Valentia (VV), Italy), Vincenzo Greco, MD (General Surgery Unit, Villa dei Gerani Hospital, Vibo Valentia (VV), Italy), Alessandro Carrara, MD (1st General Surgery Unit, S. Chiara Hospital, Trento, Italy), Michele Motter, MD (1st General Surgery Unit, S. Chiara Hospital, Trento, Italy), Giuseppe Tirone, MD (1st General Surgery Unit, S. Chiara Hospital, Trento, Italy), Mauro Totis, MD (Colorectal Surgery Unit, San Gerardo Hospital, ASST Monza, Monza, Italy), Nicolò Tamini, MD (Colorectal Surgery Unit, San Gerardo Hospital, ASST Monza, Monza, Italy), Franco Roviello, MD (General & Oncologic Surgery Unit, AOU Senese, Siena, Italy), Riccardo Piagnerelli, MD (General & Oncologic Surgery Unit, AOU Senese, Siena, Italy), Alessandro Anastasi, MD (General Surgery Unit, San Giovanni di Dio Hospital, Firenze, Italy), Giuseppe Canonico, MD (General Surgery Unit, San Giovanni di Dio Hospital, Firenze, Italy), Gianluca Guercioni, MD (General Surgery Unit, "C. e G. Mazzoni" Hospital, Ascoli Piceno, Italy), Simone Cicconi, MD (General Surgery Unit, "C. e G. Mazzoni" Hospital, Ascoli Piceno, Italy), Giuseppe Maria Ettorre, MD (General & Transplant Surgery Unit, San Camillo-Forlanini Hospital, Roma, Italy), Marco Colasanti, MD (General & Transplant Surgery Unit, San Camillo-Forlanini Hospital, Roma, Italy), Mauro Montuori, MD (General & Mininvasive Surgery Unit, S. Pietro Hospital, Ponte San Pietro (BG), Italy), Enrico Pinotti, MD (General & Mininvasive Surgery Unit, S. Pietro Hospital, Ponte San Pietro (BG), Italy), Pierpaolo Mariani, MD (General Surgery Unit, Pesenti Fenaroli Hospital, Alzano Lombardo (BG), Italy), Roberta Carminati, MD (General Surgery Unit, Pesenti Fenaroli Hospital, Alzano Lombardo (BG), Italy), Nicolò de Manzini, MD (Surgical Clinic, University of Trieste, Trieste, Italy), Edoardo Osenda, MD (Surgical Clinic, University of Trieste, Trieste, Italy), Annibale Donini, MD (General & Emergency Surgery Unit, University of Perugia, Perugia, Italy), Luigina Graziosi, MD (General & Emergency Surgery Unit, University of Perugia, Perugia, Italy), Mariano Fortunato Armellino, MD (General & Emergency Surgery Unit, S. Giovanni di Dio e Ruggi d'Aragona Hospital, Salerno, Italy), Ciro De Martino, MD (General & Emergency Surgery Unit, S. Giovanni di Dio e Ruggi d'Aragona Hospital, Salerno, Italy), Lucio Taglietti, MD (General Surgery Unit, ASST Valcamonica, Esine (BS), Italy), Arianna Birindelli, MD (General Surgery Unit, ASST Valcamonica, Esine (BS), Italy), Gabriele Anania, MD (General & Laparoscopic Surgery Unit, University Hospital, Ferrara, Italy), Matteo Chiozza, MD (General & Laparoscopic Surgery Unit, University Hospital, Ferrara, Italy), Mariantonietta Di Cosmo, MD (General & Upper GI Surgery Unit, University Hospital, Verona, Italy), Daniele Zigiotto, MD (General & Upper GI Surgery Unit, University Hospital, Verona, Italy), Carlo Vittorio Feo, MD (General Surgery Unit, Delta Hospital, University of Ferrara, Lagosanto (FE), Italy), Fioralba Pindozzi, MD (General Surgery Unit, Delta Hospital, University of Ferrara, Lagosanto (FE), Italy), Paolo Millo, MD (General Surgery Unit, "U. Parini" Regional Hospital, Aosta, Italy), Manuela Grivon, MD (General Surgery Unit, "U. Parini" Regional Hospital, Aosta, Italy), Corrado Pedrazzani, MD (General & HPB Surgery Unit, University Hospital, Verona, Italy), Cristian Conti, MD (General & HPB Surgery Unit, University Hospital, Verona, Italy), Silvio Guerriero, MD (General Surgery Unit, "A. Murri" Hospital, Fermo, Italy), Lorenzo Organetti, MD (General Surgery Unit, "A. Murri" Hospital, Fermo, Italy), Andrea Costanzi, MD (General Surgery Unit, S. Leopoldo Hospital, Merate (LC), Italy), Michela Monteleone, MD (General Surgery Unit, S. Leopoldo Hospital, Merate (LC), Italy), Nereo Vettoretto, MD (General Surgery Unit, Spedali Civili of Brescia, Montichiari (BS), Italy), Emanuele Botteri, MD (General Surgery Unit, Spedali Civili of Brescia, Montichiari (BS), Italy), Federico Marchesi, MD (Surgical Clinic, University of Parma, Parma, Italy), Giorgio Dalmonte, MD (Surgical Clinic, University of Parma, Parma, Italy), Massimo Basti, MD (General Surgery Unit, Spirito Santo Hospital, Pescara, Italy), Diletta Frazzini, MD, Graziano Longo, MD (General Surgery Unit, Policlinico Casilino, Roma, Italy), Simone Santoni, MD (General Surgery Unit, Policlinico Casilino, Roma, Italy), Moreno Cicetti, MD (General Surgery Unit, S. Maria della Misericordia Hospital, Urbino (PU), Italy), Gabriele La Gioia, MD (General Surgery Unit, S. Maria della Misericordia Hospital, Urbino (PU), Italy),

Giuseppe Brisinda, MD (General Surgery Unit, San Giovanni di Dio Hospital, Crotone, Italy), Stefano Berti, MD (General Surgery Unit, ASL 5 Liguria POLL, La Spezia, Italy).

Data availability

All the datasets and all the instructions used with the software "R" are available upon reasonable request to the corresponding author.

CRediT authorship contribution statement

Marco Catarci: Methodology, Investigation, Data curation, Conceptualization. **Stefano Guadagni:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Francesco Masedu:** Methodology, Formal analysis, Data curation. **Giacomo Ruffo:** Investigation, Conceptualization. **Massimo Giuseppe Viola:** Investigation, Conceptualization. **Marco Scatizzi:** Investigation, Conceptualization.

Supplementary data

Supplementary material associated with this article can be found, in the online version, at [https://doi.org/10.1016/j.surg.2024.08.039].

References

1. Willis MA, Toews I, Soltau SLV, et al. Preoperative combined mechanical and oral antibiotic bowel preparation for preventing complications in elective colorectal surgery. *Cochrane Database Syst Rev*. 2023;2:CD014909.
2. Rosenberg IL, Graham NG, De Dombal FT, et al. Preparation of the intestine in patients undergoing major large-bowel surgery, mainly for neoplasms of the colon and rectum. *Br J Surg*. 1971;58:266–269.
3. Midura EF, Jung AD, Hanseman DJ, et al. Combination oral and mechanical bowel preparations decreases complications in both right and left colectomy. *Surgery*. 2018;163:528–534.
4. Koskenvuo L, Lehtonen T, Koskensalo S, et al. Mechanical and oral antibiotic bowel preparation versus no bowel preparation in right and left colectomy: subgroup analysis of MOBILE trial. *BJS Open*. 2021;5:zrab011. https://doi.org/10.1093/bjsopen/zrab011.
5. Koskenvuo L, Lehtonen T, Koskensalo S, et al. Mechanical and oral antibiotic bowel preparation versus no bowel preparation for elective colectomy (MOBILE): a multicentre, randomised, parallel, single-blinded trial. *Lancet*. 2019;394:840–848.
6. Perets M, Yellinek S, Carmel O, et al. The effect of mechanical bowel preparation on postoperative complications in laparoscopic right colectomy: a retrospective propensity score matching analysis. *Int J Colorectal Dis*. 2023;38:133. https://doi.org/10.1007/s00384-023-04409-6.
7. Lei P, Jia G, Yang X, et al. Region-specific protection effect of preoperative oral antibiotics combined with mechanical bowel preparation before laparoscopic colorectal resection: a prospective randomized controlled trial. *Int J Surg*. 2023;109:3042–3051.
8. Gómez Ruiz M, Espin-Basany E, Spinelli A, et al, on behalf of MIRCAST STUDY GROUP. Early outcomes from the minimally invasive right colectomy anastomosis study (MIRCAST). *BJS*. 2023;110:1153–1160.
9. Assistance Publique - Hôpitaux de Paris. Mechanical bowel preparation and oral antibiotics before colon cancer surgery (COLONPREP). NCT03475680. ClinicalTrials.gov – NIH – US National Library of Medicine. Available from: https://clinicaltrials.gov/ct2/show/NCT03475680. Accessed January 11, 2024.
10. Koo CH, Chok AY, Wee IJY, et al. Effect of preoperative oral antibiotics and mechanical bowel preparation on the prevention of surgical site infection in elective colorectal surgery, and does oral antibiotic regime matter? a Bayesian network meta-analysis. *Int J Colorectal Dis*. 2023;38:151.
11. Catarci M, Ruffo G, Viola MG, et al. ERAS program adherence-institutionalization, major morbidity and anastomotic leakage after elective colorectal surgery: the iCral2 multicenter prospective study. *Surg Endosc*. 2022;36:3965–3984.
12. Italian ColoRectal Anastomotic Leakage (iCral) study group. Patient-reported outcomes, return to intended oncological therapy and enhanced recovery pathways after colorectal surgery: a prospective multicenter observational investigation by the Italian ColoRectal Anastomotic Leakage (iCral 3) study group. *Ann Surg Open*. 2023;4:e267.
13. Catarci M, Ruffo G, Viola MG, et al. High adherence to enhanced recovery pathway independently reduces major morbidity and mortality rates after colorectal surgery: a reappraisal of the iCral2 and iCral3 multicenter prospective studies – Erratum. *G Chir*. 2024;44:e44. https://doi.org/10.1097/IA9.0000000000000044.
14. Holubar SD, Hedrick T, Gupta R, et al. American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) joint consensus statement on prevention of postoperative infection within an enhanced recovery pathway for elective colorectal surgery. *Perioper Med*. 2017;6:4.
15. Carmichael JC, Keller DS, Baldini G, et al. Clinical practice guidelines for enhanced recovery after colon and rectal surgery from the American Society of Colon and Rectal Surgeons and Society of American Gastrointestinal and Endoscopic Surgeons. *Dis Colon Rectum*. 2017;60:761–784.
16. Migaly J, Bafford AC, Francone TD, et al. The American Society of Colon and Rectal Surgeons clinical practice guidelines for the use of bowel preparation in elective colon and rectal surgery. *Dis Colon Rectum*. 2019;62:3–8.
17. Antoniou SA, Huo B, Tzanis AA, et al. EAES, SAGES, and ESCP rapid guideline: bowel preparation for minimally invasive colorectal resection. *Surg Endosc*. 2023;37:9001–9012. https://doi.org/10.1007/s00464-023-10477-0.
18. Gustafsson UO, Scott MJ, Hubner M, et al. Guidelines for perioperative care in elective colorectal surgery: enhanced recovery after surgery (ERAS©) society recommendations: 2018. *World J Surg*. 2019;43:659–695.
19. Ficari F, Borghi F, Catarci M, et al. Enhanced recovery pathways in colorectal surgery: a consensus paper by the Associazione Chirurghi Ospedalieri Italiani (ACOI) and the PeriOperative Italian society (POIS). *G Chir*. 2019;40(4 Suppl.):1–40.
20. Lee BK, Lessler J, Stuart EA. Improving propensity score weighting using machine learning. *Stat Med*. 2010;29:337–346.
21. McCaffrey DF, Griffin BA, Almirall D, et al. A tutorial on propensity score estimation for multiple treatments using generalized boosted models. *Stat Med*. 2013;32:3388–3414.
22. Kaiser MJ, Bauer JM, Ramsch C, et al. Validation of the Mini Nutritional Assessment Short-Form (MNA-SF): a practical tool for identification of nutritional status. *J Nutr Health Aging*. 2009;13:782.
23. Dindo D, Demartines N, Clavien PA. Classification of surgical complications. A new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240:205–213.
24. Katayama H, Kurokawa Y, Nakamura K, et al. Extended Clavien-Dindo classification of surgical complications: Japan Clinical Oncology Group postoperative complications criteria. *Surg Today*. 2016;46:668–685.
25. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control*. 2008;36:309–332.
26. Rahbari NN, Weitz J, Hohenberger W, et al. Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study Group of Rectal Cancer. *Surgery*. 2010;147:339–351.
27. Peduzzi P, Concato J, Kemper E, et al. A simulation study of the number of events per variable in logistic regression analysis. *J Clin Epidemiol*. 1996;49:1373–1379.
28. Brookhart MA, Schneeweiss S, Rothman KJ, et al. Variable selection for propensity score models. *Am J Epidemiol*. 2006;163:1149–1156.
29. Fry DE, Pine M, Jones BL, et al. Control charts to identify adverse outcomes in elective colon resection. *Am J Surg*. 2012;203:392–396.
30. Bennett-Guerrero E, Pappas TN, Koltun WA, et al. Gentamicin–collagen sponge for infection prophylaxis in colorectal surgery. *N Engl J Med*. 2010;363:1038–1049.
31. Italian ColoRectal Anastomotic Leakage (iCral) study group. Risk factors for adverse events after elective colorectal surgery: beware of blood transfusions. *Updates Surg*. 2020;72:811–819.
32. Catarci M, Guadagni S, Masedu F, et al, Italian ColoRectal anastomotic leakage (iCral) study group. Blood transfusions and adverse events after colorectal surgery: a propensity-score-matched analysis of a hen-egg issue. *Diagnostics*. 2023;13:952.
33. Zheng J, Zhao S, Chen W, et al. Comparison of robotic right colectomy and laparoscopic right colectomy: a systematic review and meta-analysis. *Tech Coloproctol*. 2023;27:521–535.
34. Martinek L, You K, Giuratrabocchetta S, et al. Does laparoscopic intracorporeal ileocolic anastomosis decreases surgical site infection rate? A propensity score-matched cohort study. *Int J Colorectal Dis*. 2018;33:291–298.
35. Kerber KM, Hetjens S, Reißfelder C, et al. Oncological right hemicolectomy in a trimodal comparison: open surgery versus laparoscopic procedures with extra- and intracorporeal anastomosis technique. *Int J Colorectal Dis*. 2024;39:14. https://doi.org/10.1007/s00384-023-04587-3.
36. Cheong C, Kim NW, Lee HS, et al. Intracorporeal versus extracorporeal anastomosis in minimally invasive right hemicolectomy: systematic review and meta-analysis of randomized controlled trials. *Ann Surg Treat Res*. 2024;106:1–10. https://doi.org/10.4174/astr.2024.106.1.1.
37. Gao J, Gu X, Pang M, et al. Risk factors for anastomotic leak and postoperative morbidity after right hemicolectomy for colon cancer: results from a prospective, multi-centre, snapshot study in China. *BJS*. 2024;111:znad316. https://doi.org/10.1093/bjs/znad316.
38. Jessen M, Nerstrøm M, Wilbek TE, et al. Risk factors for clinical anastomotic leakage after right hemicolectomy. *Int J Colorectal Dis*. 2016;31:1619–1624.
39. Espin E, Vallribera F, Kreisler E, et al. Clinical impact of leakage in patients with handsewn vs stapled anastomosis after right hemicolectomy: a retrospective study. *Colorectal Dis*. 2020;22:1286–1292. https://doi.org/10.1111/codi.15098.