

Regimen-Specific Bowel Preparation and Early Postoperative C-Reactive Protein Elevation After Laparoscopic Hysterectomy: A Propensity Score-Matched Cohort Study

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Research Article

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Abstract

Background: Studies of bowel preparation in gynecologic surgery have mainly focused on whether preparation is used and on postoperative complications. Less is known about whether different preparation regimens carry different perioperative inflammatory signals. We evaluated whether lactulose enema was associated with postoperative C-reactive protein (CRP) elevation compared with mechanical enema after laparoscopic hysterectomy.

Methods: This single-center retrospective cohort study analyzed 1,238 patients who underwent laparoscopic total hysterectomy at Fujian Maternity and Child Health Hospital between January 2018 and December 2022. The primary exposure was bowel preparation type. The primary outcome was postoperative CRP elevation, defined from institutional records as CRP >10 mg/L within 24-48 hours after surgery. Propensity-score matching, weighted analysis, multivariable logistic regression, subgroup analysis, restricted cubic splines, and E-value analysis were used to assess robustness.

Results: Postoperative CRP elevation occurred in 276 patients (22.3%). Before matching, CRP elevation was more frequent after lactulose enema than after mechanical enema (183/712 [25.7%] vs 93/526 [17.7%]; odds ratio [OR], 1.61; 95% confidence interval [CI], 1.22-2.13). Matching retained 501 pairs and improved the maximum absolute standardized mean difference from 0.309 to 0.094. In the matched cohort, lactulose enema remained associated with CRP elevation (123/501 [24.6%] vs 89/501 [17.8%]; paired OR, 1.47; 95% CI, 1.09-1.97). Weighted, adjusted, subgroup, spline, and E-value analyses supported a directionally consistent association.

Conclusions: Lactulose enema was associated with a higher likelihood of postoperative CRP elevation than mechanical enema in this retrospective laparoscopic hysterectomy cohort. The findings are hypothesis-generating and suggest that future perioperative studies should record bowel preparation as a regimen-specific exposure rather than as a binary variable.

Trial registration: Not applicable.

Background

Bowel preparation remains one of the more variable elements of perioperative care in gynecologic surgery. Enhanced recovery after surgery (ERAS) pathways in gynecologic oncology and broader perioperative medicine emphasize selective interventions, protocol quality, shortened hospitalization, and recovery-centered care [1–6]. Within this framework, bowel preparation is not a neutral background step. It may affect hydration, bowel distension, discomfort, sleep, anxiety, anesthetic readiness, and postoperative recovery, all of which are relevant to anesthesiology.

Most gynecologic discussions of bowel preparation have asked whether mechanical bowel preparation is necessary. AAGL guidance prioritizes selective, recovery-oriented perioperative steps rather than routine interventions that add patient burden [7]. A systematic review of gynecologic surgery found limited evidence that routine mechanical bowel preparation improves clinically meaningful perioperative outcomes [8]. These data are important, but they leave a practical question unresolved: when some form of bowel preparation is still used in local pathways, should different regimens be treated as equivalent exposures?

Recent gynecologic literature has moved toward regimen- and setting-specific outcomes, including surgical-site infection, discontinuation of mechanical bowel preparation in ERAS initiatives, robot-assisted laparoscopy, oral-antibiotic preparation, and prehabilitation [9–13]. However, early postoperative inflammatory response has received less attention as a perioperative endpoint. CRP is not specific for infection, but it is widely used as a pragmatic

marker of postoperative inflammatory burden and surgical stress [14, 15]. Hysterectomy-specific data and inflammation-modifying anesthesia studies further support the relevance of inflammatory markers in minimally invasive gynecologic surgery [16, 17].

The present study was designed to address a narrower gap than the broader question of bowel preparation in hysterectomy. We examined whether two commonly used enema-based regimens, lactulose enema and mechanical enema, were associated with different early postoperative CRP-elevation profiles. This distinction matters because many datasets record bowel preparation as present or absent, which can obscure regimen-level differences and limit perioperative inference.

Because bowel preparation strategy is selected nonrandomly in routine care, observational comparisons require explicit causal assumptions and transparent propensity-score reporting [18–20]. We therefore framed this analysis as a regimen-comparison and documentation study rather than as a definitive practice-changing trial. The objective was to compare lactulose enema with mechanical enema in relation to postoperative CRP elevation after laparoscopic hysterectomy using propensity-score matching and multiple sensitivity analyses.

Methods

Study design and setting

We performed a single-center retrospective cohort study using perioperative records from Fujian Maternity and Child Health Hospital, Fuzhou, China. The source cohort included patients who underwent laparoscopic total hysterectomy between January 2018 and December 2022. Ethics approval and consent status are specified in the Declarations section.

Participants

The analytic dataset included 1,238 patients with available bowel preparation type and postoperative CRP-elevation status. Patients were classified according to bowel preparation type: lactulose enema or mechanical enema. The analytic export did not retain diagnosis, indication for hysterectomy, surgeon-level practice patterns, antibiotic exposure, ERAS adherence, or detailed surgical-complexity variables. These limitations were considered explicitly in interpretation.

Exposure, outcome, and covariates

The primary exposure was bowel preparation type, with mechanical enema treated as the reference regimen. The primary outcome was postoperative CRP elevation, recorded as a binary variable. According to the institutional source definition, postoperative CRP elevation was defined as a CRP concentration > 10 mg/L, typically measured within 24–48 hours after surgery. The analytic dataset contained the binary CRP-elevation indicator rather than serial absolute CRP values.

The primary propensity-score model included preoperative variables plausibly associated with both preparation selection and postoperative inflammatory response: age, body mass index, temperature, heart rate, respiratory rate, diastolic blood pressure, systolic blood pressure, hemoglobin, white blood cell count, platelet count, and neutrophil-to-lymphocyte ratio. Intraoperative variables including surgical duration, vasoactive drug use, infusion quantity, and

blood loss were reserved for secondary adjusted models because they may lie downstream of preoperative preparation choice.

Statistical analysis

Propensity scores for receipt of lactulose enema were estimated using logistic regression. One-to-one nearest-neighbor matching without replacement was performed using a caliper of 0.08 standard deviations of the logit of the propensity score. Covariate balance was assessed with standardized mean differences (SMDs), with an absolute SMD < 0.10 considered acceptable.

No a priori sample size calculation was performed because of the retrospective design; the available cohort included 276 outcome events, and model complexity was constrained accordingly.

The main analysis compared postoperative CRP elevation between bowel preparation groups before and after matching. Weighted and multivariable logistic regression models were used as sensitivity analyses. Prespecified subgroup analyses examined age, body mass index, hemoglobin, neutrophil-to-lymphocyte ratio, surgical duration, and vasoactive drug use. Residual confounding was explored with E-value analysis based on the adjusted risk ratio from g-computation [21]. Restricted cubic spline analyses were used to assess nonlinearity for body mass index, surgical duration, and infusion quantity [22]. An exploratory parsimonious perioperative prediction model was retained as a supplementary analysis rather than the central manuscript focus, with calibration interpreted according to contemporary prediction-model guidance [23].

Use of AI-assisted tools

During preparation of the submission package, an AI language model was used for language editing, formatting support, and journal-specific checklist organization. The authors reviewed and approved all manuscript content, verified the reported data and citations, and remain fully responsible for the work.

Results

Cohort characteristics

Among 1,238 patients, 712 (57.5%) received lactulose enema and 526 (42.5%) received mechanical enema. Postoperative CRP elevation occurred in 276 patients (22.3%). The overall study flow is summarized in Fig. 1.

Before matching, baseline differences were most apparent for age, heart rate, and hemoglobin. After matching, 501 pairs were retained, corresponding to 70.4% of the lactulose group and 95.2% of the mechanical-enema group. The maximum absolute SMD improved from 0.309 before matching to 0.094 after matching. Covariate balance is illustrated in Fig. 2 and summarized in Table 1.

Table 1
Baseline covariate balance before and after propensity-score matching

Covariate	Lactulose before	Mechanical before	SMD before	Lactulose after PSM	Mechanical after PSM	SMD after
Age, years	40.68 (11.22)	43.77 (8.63)	-0.309	43.99 (9.06)	43.35 (8.42)	0.073
Body mass index, kg/m ²	22.71 (3.47)	22.71 (2.83)	-0.001	22.68 (3.16)	22.75 (2.82)	-0.024
Body temperature, deg C	36.32 (2.25)	36.50 (0.28)	-0.113	36.49 (0.28)	36.50 (0.27)	-0.026
Heart rate, beats/min	81.36 (15.08)	78.43 (11.96)	0.216	79.74 (14.23)	79.40 (10.16)	0.028
Respiratory rate, breaths/min	18.92 (6.01)	18.25 (1.74)	0.152	18.20 (2.56)	18.38 (1.07)	-0.094
Diastolic blood pressure, mmHg	75.09 (13.50)	74.49 (10.31)	0.050	75.15 (15.06)	75.10 (8.70)	0.004
Systolic blood pressure, mmHg	114.49 (20.60)	115.42 (15.73)	-0.051	115.20 (22.67)	115.86 (12.68)	-0.036
Hemoglobin, g/L	120.03 (16.66)	116.83 (17.92)	0.184	118.88 (17.02)	117.37 (17.94)	0.087
White blood cell count, 10 ⁹ /L	5.81 (1.72)	5.73 (1.55)	0.049	5.78 (1.86)	5.73 (1.53)	0.029
Platelet count, 10 ⁹ /L	267.19 (61.21)	266.48 (69.57)	0.011	263.42 (59.52)	267.13 (70.53)	-0.057
Neutrophil-to-lymphocyte ratio	1.88 (0.98)	1.96 (0.99)	-0.082	1.98 (1.09)	1.96 (1.00)	0.018

Main outcome

In the unmatched cohort, CRP elevation occurred more often after lactulose enema than after mechanical enema (183/712 [25.7%] vs 93/526 [17.7%]; OR, 1.61; 95% CI, 1.22–2.13; P = 0.0006).

The association persisted after matching. In the matched cohort, CRP elevation occurred in 123/501 (24.6%) and 89/501 (17.8%), respectively, with a paired OR of 1.47 (95% CI, 1.09–1.97; P = 0.0113). Effect estimates across the main and sensitivity analyses are summarized in Table 2, with the corresponding visual summary provided as Supplementary Fig. 3.

Table 2
Association between bowel preparation type and postoperative CRP elevation

Analysis	Lactulose events/n	Mechanical events/n	Lactulose risk (%)	Mechanical risk (%)	Effect	Estimate	95% CI	P value
Unmatched crude comparison	183/712	93/526	25.7	17.7	Odds ratio	1.61	1.22–2.13	0.0006
Propensity-score matched comparison	123/501	89/501	24.6	17.8	Paired odds ratio	1.47	1.09–1.97	0.0113
Stabilized IPTW	weighted	weighted	26.6	17.1	Weighted odds ratio	1.76	1.33–2.34	< 0.0001
Adjusted logistic regression	276/1238 total outcomes	reference			Adjusted odds ratio	1.77	1.32–2.38	0.0001
Extended adjusted model	276/1238 total outcomes	reference			Adjusted odds ratio	1.89	1.39–2.56	< 0.0001

Secondary and exploratory analyses

The direction of effect was consistent across prespecified strata (Supplementary Fig. 4), although no multiplicative interaction reached conventional significance. The most pronounced association was seen among operations lasting < 2 hours (OR, 4.70; 95% CI, 2.51–8.79), whereas the estimate was attenuated among patients with hemoglobin < 110 g/L (OR, 0.94; 95% CI, 0.49–1.82). The smallest interaction P value was observed for hemoglobin (P = 0.0832), supporting heterogeneity as a descriptive finding rather than evidence of statistically significant effect modification.

The three-dimensional adjusted risk surface illustrated how postoperative CRP-elevation risk varied jointly across surgical duration and infusion quantity (Fig. 3). Restricted cubic spline line profiles suggested largely monotonic risk relationships for body mass index and surgical duration, whereas infusion quantity showed borderline evidence of nonlinearity (P for nonlinearity = 0.0614) with steeper model-based risk increases at higher volumes (Fig. 4). Representative adjusted risks for infusion quantity were 1,000 mL: 18.1%; 1,500 mL: 21.6%; 2,000 mL: 31.8%; 2,500 mL: 45.2%. These patterns were consistent with a perioperative interpretation in which bowel preparation type operates alongside patient and intraoperative stressors.

The g-computation-adjusted risk ratio comparing lactulose enema with mechanical enema was 1.57 (95% CI, 1.28–1.92), corresponding to an E-value of 2.52 for the point estimate and 1.88 for the lower confidence limit. As a supplementary exploratory analysis, the parsimonious perioperative prediction model achieved modest discrimination (apparent area under the receiver operating characteristic curve, 0.708; bootstrap-corrected area under the curve, 0.696), indicating that bowel preparation type remained informative within a broader perioperative risk framework. The predicted-probability density plot showed a right-shifted distribution after lactulose enema compared with mechanical enema (median predicted risk, 23.1% vs 14.9%; Fig. 5).

Discussion

This study found that lactulose enema was associated with a higher likelihood of postoperative CRP elevation than mechanical enema after laparoscopic hysterectomy. The association was directionally stable after propensity-score matching, inverse-probability weighting, conventional adjustment, extended adjustment, subgroup assessment, and E-value analysis. The study does not establish causality and should not be used alone to change practice. Its main contribution is more specific: it shows that bowel preparation should be analyzed and documented as a regimen-specific perioperative exposure rather than treated as a simple yes-or-no variable.

This distinction is important because previous work has already challenged routine bowel preparation in gynecologic surgery. An analysis that only repeats the general message that bowel preparation may not improve hysterectomy outcomes has limited added value. The present analysis asks a different question. In hospitals where bowel preparation remains embedded in perioperative pathways, different regimens may create different physiologic and patient-experience profiles. Regimen-level variation is therefore relevant to anesthesiology, ERAS implementation, and postoperative inflammatory monitoring even when the surgical procedure itself is common.

The single-institution design is both a limitation and a useful context. Local perioperative pathways often contain embedded habits that are not visible in multicenter administrative datasets. A single hospital cohort can detect such practice-level signals with more consistent laboratory timing, surgical environment, and data definitions. At the same time, these strengths do not solve generalizability. The results should be viewed as a signal that supports prospective multicenter measurement, not as proof that one enema strategy is superior across institutions.

Several explanations remain plausible. Clinicians may have selected lactulose for patients or cases that already carried higher inflammatory risk. Regimen-related bowel distension, osmotic fluid shifts, discomfort, sleep disruption, or perioperative anxiety may also have contributed indirectly. A third possibility is that preparation type marked unmeasured local practice patterns, including antibiotic decisions, case complexity, surgeon preference, or postoperative monitoring thresholds. These explanations cannot be separated in this dataset, but each points to the same methodological issue: future perioperative datasets should capture the exact preparation regimen, timing, indication, and co-interventions.

The secondary analyses add context but should not be overinterpreted. The stronger estimate in shorter operations may mean that a preoperative exposure is more visible when operative trauma is less dominant. The attenuated estimate among patients with lower hemoglobin may reflect competing sources of perioperative vulnerability. Interaction tests were not significant, so these are signals for future stratification rather than subgroup-specific recommendations. Likewise, the spline analyses suggest that bowel preparation type was embedded in a broader stress environment. Infusion quantity showed the clearest suggestion of nonlinear risk acceleration, while body mass index and surgical duration were more gradual.

The E-value analysis helps frame, but not eliminate, residual confounding. An unmeasured confounder associated with both exposure selection and CRP elevation by risk ratios of approximately 2.52-fold each would be required to fully explain away the adjusted association. The unresolved question is whether missing variables such as surgical diagnosis, bowel involvement, antibiotic regimen, ERAS adherence, surgeon preference, or postoperative monitoring thresholds could be strong enough and imbalanced enough to account for the signal.

The regimen-specific interpretation is consistent with evidence from other surgical fields showing that bowel preparation effects depend on the details of the regimen rather than the broad label of preparation [24, 25]. Gynecologic implementation literature also supports a cautious, context-aware interpretation. Sustained ERAS experience after minimally invasive gynecologic oncology surgery and implementation reports in general gynecologic practice show that pathway adoption remains uneven in real-world settings [26, 27]. Surveys from gynecologic

oncology and deep endometriosis practice show similar variation in perioperative management, including preparation and nutrition-related decisions [28, 29].

The biomarker endpoint requires restraint. CRP is not a complication diagnosis, and a binary CRP-elevation variable is blunt. Still, inflammatory indices are increasingly used to summarize postoperative risk in gynecologic cohorts, including laparoscopic hysterectomy populations [30]. The value of the current endpoint is not that it identifies infection or readmission; it captures early postoperative inflammatory burden when more granular recovery outcomes were unavailable. For the same reason, the exploratory prediction model should not be used clinically. It showed that bowel preparation type retained information beside other perioperative variables, but external validation, serial CRP measurement, procedure-level predictors, and patient-centered outcomes would be required before any prediction-oriented use.

Several limitations are central to interpretation. The analytic dataset did not include diagnosis, indication for hysterectomy, bowel involvement, antibiotic exposure, ERAS adherence, surgeon-level practice patterns, or detailed surgical-complexity measures. The outcome was based on a binary CRP threshold and did not retain serial absolute CRP values, fever, culture results, imaging, complications, length of stay, pain, nausea, bowel function, readmission, or reoperation. Matching, weighting, E-values, and consistency checks improve transparency, but they do not convert an observational comparison into a randomized trial.

The next study should be deliberately narrower and more clinically textured. A prospective minimally invasive gynecologic cohort should record indication for bowel preparation, exact regimen, timing, antibiotic co-interventions, diagnosis, procedure, bowel involvement, route of surgery, surgeon preference, and ERAS adherence. Serial CRP should be paired with nausea, bloating, pain, bowel recovery, diet tolerance, length of stay, infection, readmission, and satisfaction. That design would address the more important question raised here: not simply whether bowel preparation is used, but which preparation strategy, for which patient, in which operation, and at what recovery cost.

Conclusions

In this retrospective laparoscopic hysterectomy cohort, lactulose enema was associated with a higher likelihood of postoperative CRP elevation than mechanical enema. The finding is hypothesis-generating and should not be interpreted as evidence for immediate practice change. For perioperative and anesthesiology research, the main implication is that bowel preparation strategy should be treated as a regimen-specific exposure and documented alongside other perioperative stressors in future prospective studies.

Abbreviations

CI
confidence interval
CRP
C-reactive protein
ERAS
enhanced recovery after surgery
IPTW
inverse probability of treatment weighting
OR
odds ratio

PSM
propensity-score matching
SMD
standardized mean difference.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Fujian Maternity and Child Health Hospital (approval number: 2023KY148). The requirement for written informed consent was waived by the ethics committee because the study used retrospective de-identified perioperative data and involved no additional patient contact or intervention.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analyzed during the current study are not publicly available because they contain sensitive perioperative clinical information and are subject to patient privacy and institutional restrictions. De-identified aggregate data may be available from the corresponding author on reasonable request, subject to approval by Fujian Maternity and Child Health Hospital and the relevant ethics governance process. Analysis scripts used to generate aggregate statistical outputs and figures may be available from the corresponding author on reasonable request, subject to institutional review.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

YZ contributed to conceptualization, methodology, formal analysis, visualization, and drafting of the manuscript. XW contributed to data curation, investigation, validation, and project administration. LZ contributed to conceptualization, supervision, methodology, funding acquisition, and critical revision of the manuscript. JW contributed to supervision, resources, project administration, and critical revision of the manuscript. All authors read and approved the final manuscript.

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Figures

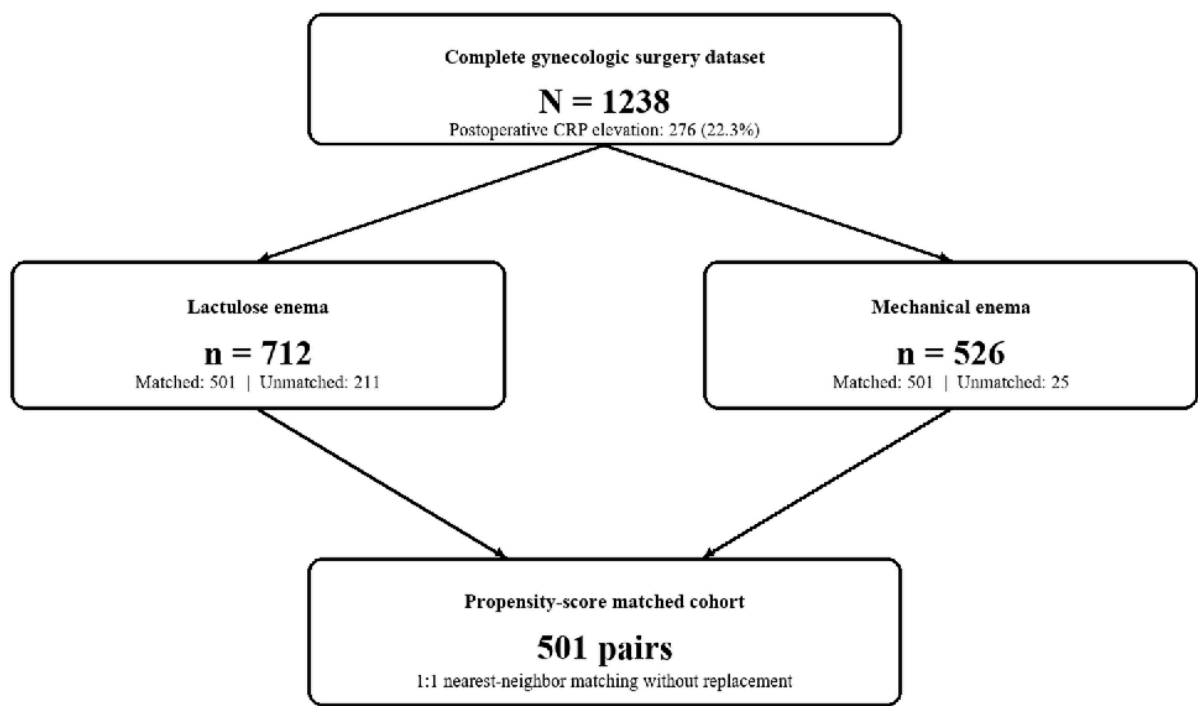


Figure 1

Study flow diagram. Flow of patients from the complete perioperative dataset into exposure groups and the propensity-score matched cohort.

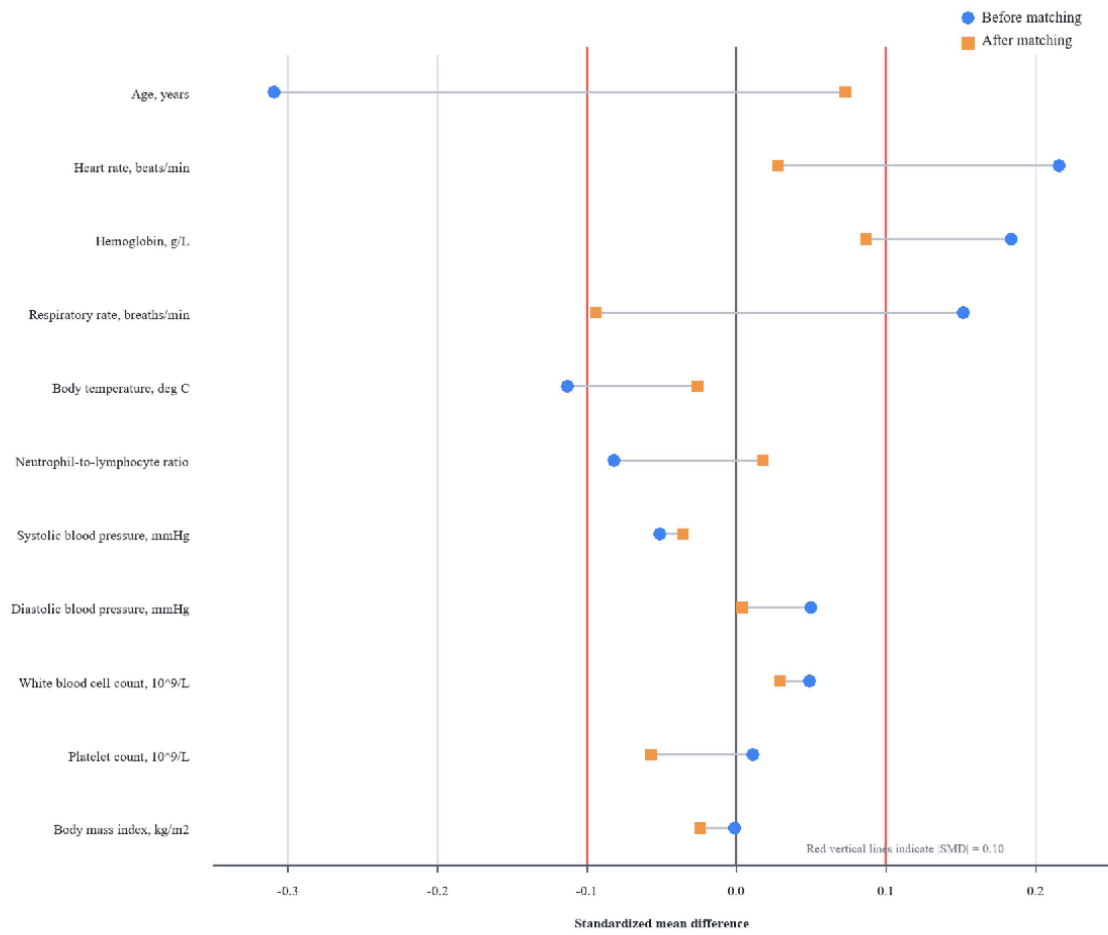


Figure 2

Covariate balance before and after matching. Love plot showing standardized mean differences for propensity-score covariates before and after matching. The dashed line indicates the conventional 0.10 threshold for acceptable balance.

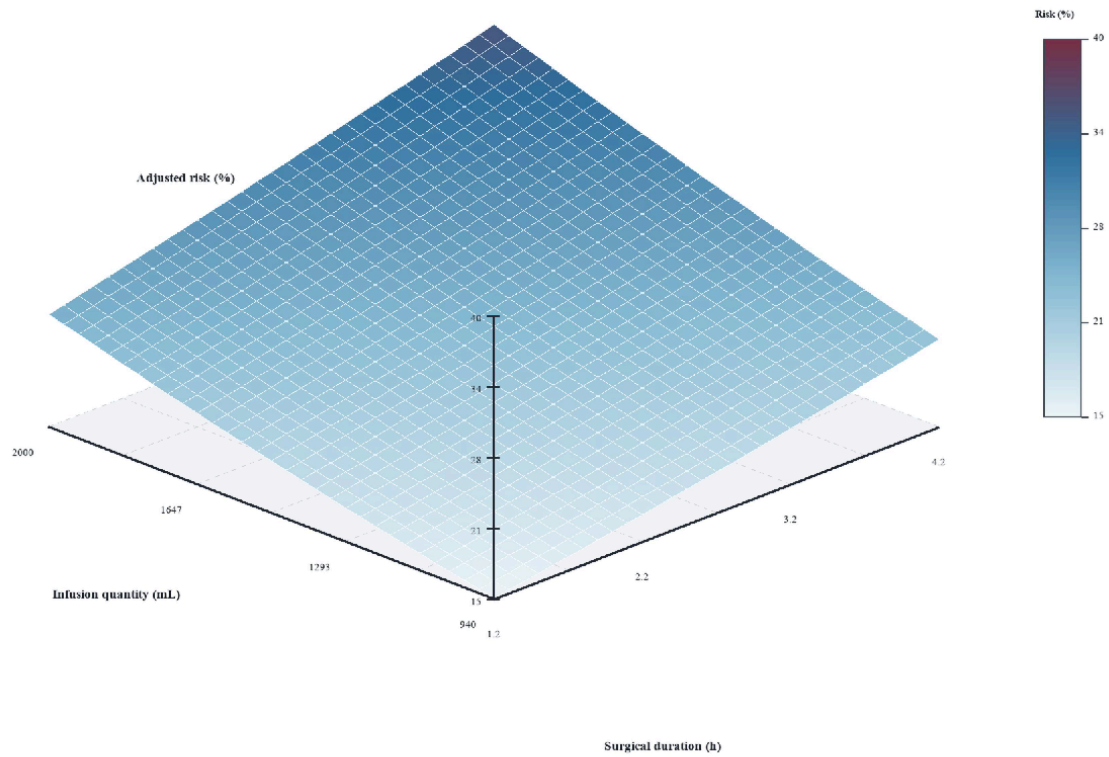


Figure 3

Three-dimensional adjusted risk surface. Model-based adjusted probability of postoperative CRP elevation across surgical duration and infusion quantity. The surface was estimated by g-computation from the extended multivariable model.

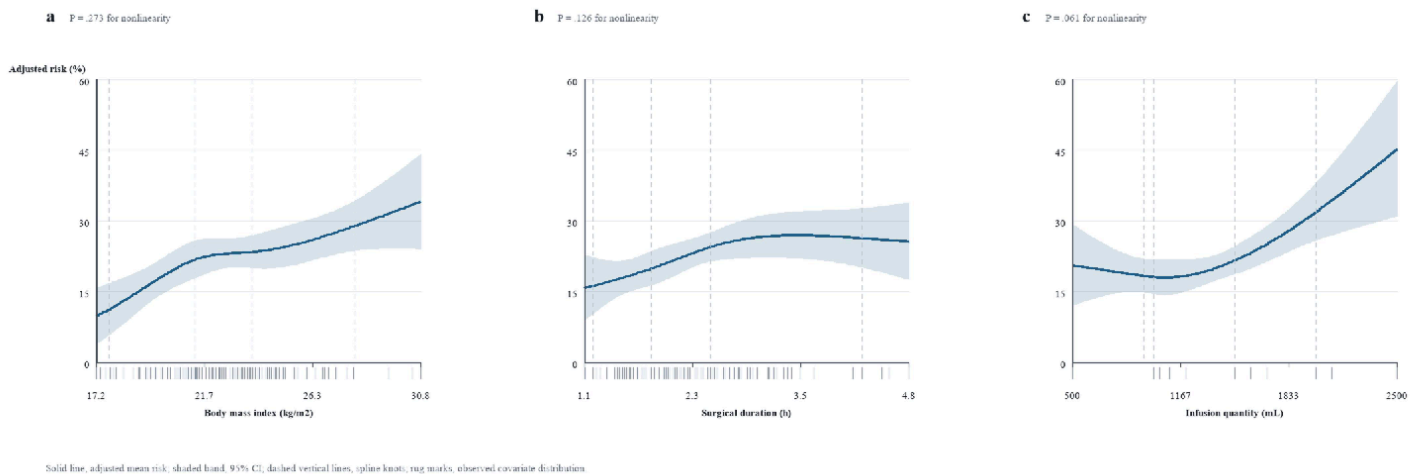


Figure 4

Adjusted risk line profiles. Restricted cubic spline line plots showing model-based adjusted risk of postoperative CRP elevation across body mass index, surgical duration, and infusion quantity. Shaded bands indicate 95% confidence intervals; dashed vertical lines indicate spline knots; rug marks indicate the observed covariate distribution.

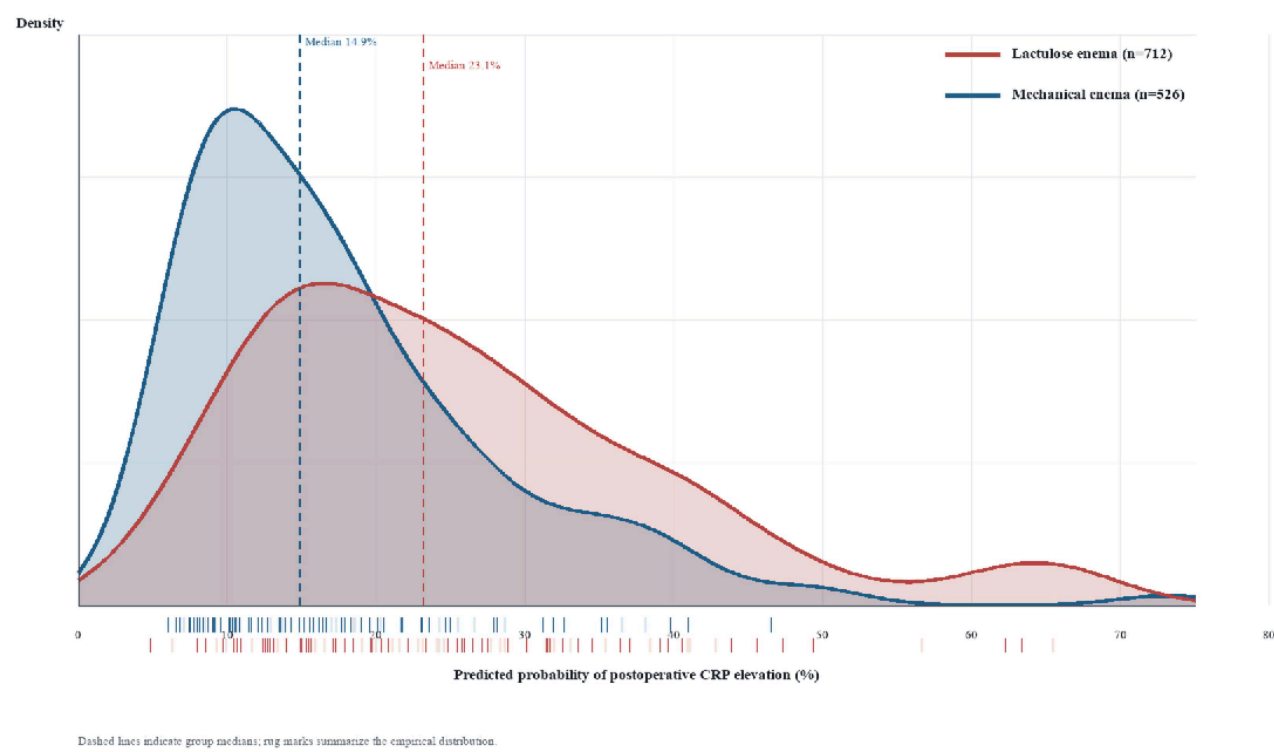


Figure 5

Predicted-probability density. Probability density plot showing the distribution of individual model-predicted probabilities of postoperative CRP elevation by bowel-preparation regimen. Dashed lines indicate group medians; rug marks indicate the empirical distribution.

Supplementary Files

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- [SupplementaryFigure1Figure6predictionperformance600dpi.pdf](#)
- [SupplementaryFigure2Figure7riskgroupbarchart600dpi.pdf](#)
- [SupplementaryFigure3SupplementaryFigure3primaryeffectconsistency600dpi.pdf](#)
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