

Postoperative Inflammatory Marker Trends as Early Predictors of Delayed Gastrointestinal Recovery after Elective Abdominal Surgery

Tariq Usman¹, Jing Tao Zhou^{1*}

Department of General Surgery, The Seventh Affiliated Hospital of Xinjiang Medical University, Xinjiang Medical University, Urumqi, People's Republic of China, Email: Usman.tariq8542@gmail.com, ORCID: 0009-0008-8515-7547

DOI: <https://doi.org/10.63163/jpehss.v4i1.1739>

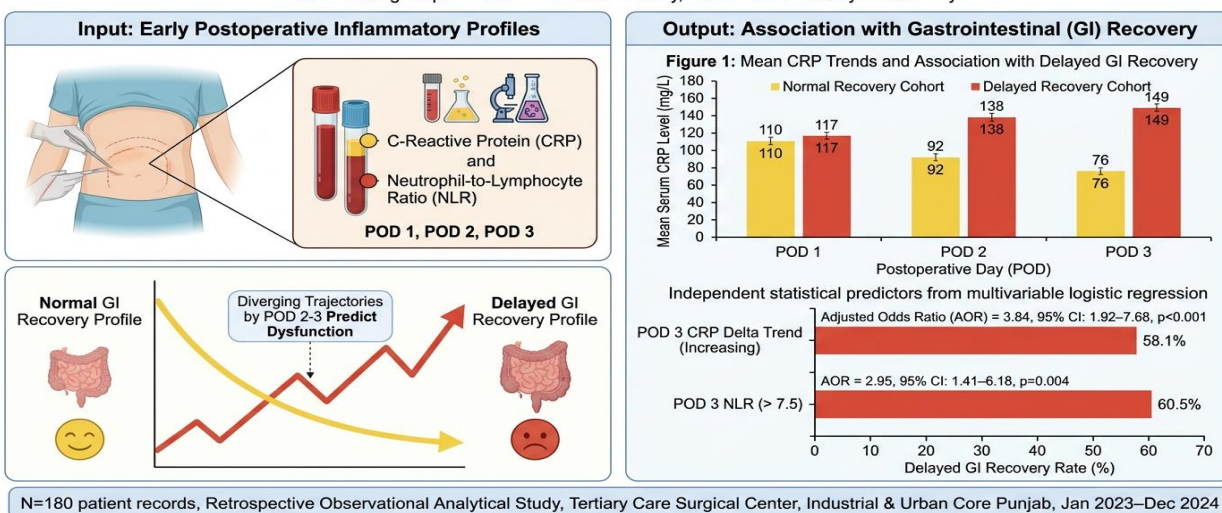
Abstract

Elective abdominal surgery led to prolonged hospital stay and higher healthcare burden due to delayed gastrointestinal (GI) recovery. Early postoperative trends of inflammatory markers were monitored routinely, however, their predictive value of non-infectious functional bowel impairment was not well characterized. In this study, the researchers were interested in finding out if the levels of inflammatory markers over time in the first few days after surgery are predictive of delayed recovery of the gut following an elective surgery involving the abdomen. This was a retrospective observational analytical study of the electronic medical records of a tertiary surgical centre in the Industrial & Urban Core Punjab Province from January 2023 to December 2024. A total of 180 adult elective abdominal surgery patients were included in the final analysed cohort, who met all eligibility criteria. Primary exposure variables were serial levels of inflammatory markers (C-reactive protein and neutrophil-to-lymphocyte ratio from day 1 to day 3 after surgery), and the primary outcome was delayed gastrointestinal recovery. IBM SPSS was used for bivariate statistical comparisons and for multivariable logistic regression. 23.9% of the patients had delayed gastrointestinal recovery. Patients with delayed recovery had significantly elevated POD3 CRP levels (148.6 $\pm$ 32.1 mg/L vs 76.2 $\pm$ 21.4 mg/L, $p < 0.001$). Multivariable logistic regression revealed that a positive C-reactive protein delta trajectory from day one to day three (Adjusted Odds Ratio = 3.84, 95% Confidence Interval: 1.92–7.68; $p < 0.001$) and an elevated day three neutrophil-to-lymphocyte ratio greater than 7.5 (Adjusted Odds Ratio = 2.95, 95% Confidence Interval: 1.41–6.18; $p = 0.004$) were independently associated with delayed functional bowel recovery. The study found that trajectories of inflammatory markers (increased C-reactive protein) and neutrophil-to-lymphocyte ratio, were associated with delayed gastrointestinal recovery. These biomarkers could be tracked routinely in the early period after surgery, which could aid in early clinical classification of risk and allow for proactive management prior to the onset of clinical bowel dysfunction.

Keywords: Biomarkers; C-Reactive Protein; Gastrointestinal Motility; Ileus; Leukocyte Count; Postoperative Period; Surgical Procedures, Operative

Graphical Abstract: Early Inflammatory Marker Kinetics Predict Delayed GI Recovery After Elective Abdominal Surgery

Color Coding: Naples Yellow = Normal Recovery, Burnt Sienna = Delayed Recovery



Introduction

Such as elective abdominal surgery is a fundamental part of general surgical practice, gastrointestinal dysfunction is a main risk factor in the postoperative period (1). One of the most frequent postoperative difficulties after major intra-abdominal surgery is delayed gastrointestinal recovery, including postoperative ileus and mainly subclinical bowel dysmotility (2). This will mark in significant delay in optimization of nutrition, increase hospital stay, and increase health care costs and can lead to discomfort, nausea, vomiting and abdominal distention in patients (3). Regardless of the paradigm (or paradigms) in place for the modern surgical patient, a significant proportion of patients does not recover bowel function within an acceptable time frame even in the absence of clear surgical causes such as mechanical obstruction or anastomotic disruption (4). Unfortunately the identification of these individuals is a clinical conundrum, because traditional physical examinations and waiting for flatus or stool are a reactive rather than a predictive approach (5).

Major abdominal surgery produces a complex, multi-stage tissue traumatic, neurogenic inhibitory, and systemic inflammatory reaction (6). Tissue handling and peritoneal trauma induce activation of resident macrophages of the muscularis with the subsequent production of proinflammatory cytokines, chemokines, and inflammatory mediators (7). This localized inflammatory response decreases the ability of the smooth muscles to contract and affects the coordinated gastrointestinal motility (8). In a systemic context, this is reflected by the quick changes in the circulating inflammatory markers such as C-reactive protein, procalcitonin, white blood cells count, and neutrophil-to-lymphocyte ratios (9). A transient increase in these markers is a normal physiologic response to surgery but when there is a pathological hyperactive or sustained increase, it indicates an out of control dysregulated inflammatory reaction (10).

The potential use of inflammatory markers as sensitive, dynamic signs of isolated functional gastrointestinal delays is not fully exploited, although this is a common monitoring practice to exclude major infectious complications or early anastomotic leak (11). Most literature is dedicated to the critical values at the end of the postoperative period on days 5 to 10 after the procedure to identify the true presence of intra-abdominal sepsis or abscess (12). But, these evaluations are often made too late when physiological deviations first appear (13). New evidence indicates that the direction or delta trend of inflammatory markers over the first 3 days after surgery (postoperative days 1–3) offers a much more detailed diagnostic assessment than single threshold

values (14). Within this physiological context, there is, however, little research that has specifically investigated whether or not the early course of inflammatory events is associated with delayed gastrointestinal healing in cohorts of elective abdominal surgery patients (15).

This clinical need calls for a change in the way inflammation is diagnosed, from threshold-based testing of markers to inflammatory profiling (16). In a retrospective patient series, biomarker trajectories can be identified over time with a systematic approach, to determine if there is correlation between specific inflammatory kinetics and failure to return bowel function in a timely manner (17). This led to the design of this retrospective study to determine if there were independent changes in inflammatory markers that could predict delayed gastrointestinal recovery after elective abdominal surgery, and to define patient subsets at high risk and provide a logical structure for early clinical monitoring and intervention.

Methods

The retrospective observational analytical study was carried out in the electronic health records and physical medical archives of a tertiary care surgical center in the industrial & urban core Punjab region. The setting was chosen because of the large number of surgical patients, the use of state of the art electronic patient monitoring and the wide variety of patients being treated for major abdominal surgery, which afforded the opportunity to obtain a rich and reliable dataset for analysis of postoperative recovery patterns. The overall period of the study was eight months from June 2025 to January 2026, during which data extraction, data cleaning, data verification and statistical analysis were undertaken. Medical records of patients admitted to the hospital from January 1, 2023 to December 31, 2024, were included, resulting in a two-year period. A two-year period was chosen for the retrospective review because it would provide adequate numbers of patients to include with enough elective surgical cases and inpatient follow-up.

The adult surgical patients who were undergoing elective surgery in the abdomen were the target population (18). All the patients who underwent elective open or laparoscopic intra-abdominal surgery (19) with complete nursing logs of bowel function return for 5 days or more after surgery and laboratory data of CRP, PCT, and CBC every day were available were included. Patients aged 18-75 years had undergone elective open or laparoscopic intra-abdominal surgery (19) and had granular nursing logs of bowel function return and laboratory data of CRP, PCT and CBC for at least 5 days after surgery were available. Significant physiological confounders were minimized, and internal validity was maintained, by applying exclusion criteria, such as active infection or sepsis preoperatively, emergency surgical admission, underlying chronic inflammatory or autoimmune bowel disease, major intra-abdominal disease requiring immediate reoperation, and lack of adequate clinical and/or laboratory data (21).

The patient records were selected for final analysis ($n = 180$). This sample size was calculated by using assumptions that were formed in a similar published retrospective study that evaluated inflammatory trajectories in the postoperative recovery, and estimated delayed gastrointestinal recovery prevalence rate of 25% (22), a 95% confidence level, and an acceptable margin of error of 5%. The formal calculation confirmed that there were 23 sufficient cases of patients to detect any significant difference in biomarker trajectories between the recovery cohorts (180 complete patient cases).

Digital data were obtained with a standardized proforma by two trained surgical research associate reviewers, to achieve uniformity and accuracy (24). The exposure variables were serum C-reactive protein (CRP) levels (25), procalcitonin levels (26), white blood cell count, and neutrophil to lymphocyte ratios (NLRs) (27) at postoperative days 1, 2, and 3 and calculated relative changes between consecutive days. The primary outcome variable measured was delayed gastrointestinal recovery defined as having a persistent postoperative ileus (on postoperative day four (28); unable

to feed solid food, flatus or bowel movement and/or re-insertion of a nasogastric tube (not secondary to mechanical obstruction). To control for potentially confounding factors, baseline demographics (age, sex, BMI) and patient comorbidity scores were obtained, as well as the surgical approach, surgical duration, and intra-operative blood loss.

Properly defining the inclusion criteria and systematically adding cases one-by-one to the database helped reduce selection bias. Information bias was addressed by applying the same laboratory testing procedures throughout the hospital system and by using specific clinical criteria to determine functional bowel recovery. To identify missing laboratory variables and to assess whether patient records were missing for the indicated three days postoperative, all patient records were reviewed, and for a random sample (29) of patient records, double entry cross-verification of the data was performed.

There was a statistical analysis done using IBM SPSS Statistics for Windows (30). Data on the continuous variables were presented as means and standard deviations and assumed to be normally distributed and on the categorical variables were presented as frequencies and percentages. Independent sample t-test and one-way ANOVA were used to assess differences in the trends of continuous inflammatory markers between patients with normal gastrointestinal recovery and delayed gastrointestinal recovery, at each time point. Chi-square tests were used to assess relationships between categorical clinical and delayed recovery status. Multivariable logistic regression analysis was then performed to determine if early inflammatory trajectory dynamics were independent predictors of delayed gastrointestinal recovery, while controlling for other clinical factors that could be confounding such as age, surgical approach (31) and operative duration. Results were presented as 95% CIs and a two-tailed p value of 0.05 or <0.05 was deemed significant.

The privacy and security of patients and the data throughout the course of the study were rigorously maintained. Data were extracted using anonymized patient identification codes which were completely separated from the clinical data, and no direct patient contact was made as the study was designed as a retrospective study.

Results

Of the 205 medical records found, 25 were excluded because laboratory variables were missing or because they had concurrent complications, leaving 180 adult patients who had undergone elective abdominal surgery for analysis. The average age of the subjects was 54.2 ± 11.8 years, of which 52.2% (n=94) were male and 47.8% (n=86) were female. The major indications for surgery were colorectal surgery (41.7%, n=75), complex ventral hernia repair (32.2%, n=58) and upper gastrointestinal surgery (26.1%, n=47). Open surgery was used in 55.0% (n=99) and laparoscopy was used with 45.0% (n=81). The overall cohort is described with respect to the baseline characteristics and distributions by demographics in Table 1.

Some of the main exposure variables included inflammatory marker levels over the first 3 days after surgery (POD 1–3), which showed significant variation amongst the cohort. On POD 1, the mean C-reactive protein (CRP) level was 112.4 ± 28.5 mg/L, procalcitonin (PCT) was 0.42 ± 0.18 ng/mL, white blood cell count (WBC) was $11.8 \pm 3.1 \times 10^9$ /L, and the neutrophil-to-lymphocyte ratio (NLR) was 7.4 ± 2.2 . By POD 3, the biomarker concentrations showed different growth patterns within patient subsets. Details on the distribution of daily inflammatory marker concentrations and the ratio between the daily concentrations of the markers and the baseline concentration (daily relative trajectory deltas, Δ POD 3 – POD 1) are provided in Table 2.

Of the cohort analyzed, 23.9% (43) had delayed gastrointestinal gain and 76.1% (137) had typical functional recovery within 4 days. Patients with delayed recovery were labeled by different

surgical methods, with delayed recovery in 28.3% (n=28) of those undergoing open surgery, and in 18.5% (n=15) of those undergoing laparoscopic surgery. The distribution of recovery consequences by baseline method type and operative characteristics is stated in Table 3.

There were significant differences between the early recovery and delayed recovery groups in bivariate inquiry for the trajectory of inflammatory markers in the early post-operative period. Patients experiencing delayed gastrointestinal recovery exhibited significantly higher POD 3 CRP levels (148.6 $\pm$ 32.1 mg/L vs. 76.2 $\pm$ 21.4 mg/L; $p < 0.001$), higher POD 3 NLR (9.1 $\pm$ 2.4 vs. 4.8 $\pm$ 1.6; $p < 0.001$), and a positive POD 1–3 CRP trajectory delta (+31.2 $\pm$ 18.4 mg/L vs. -41.5 $\pm$ 15.2 mg/L; $p < 0.001$) contrasted to those with unremarked functional recovery. The inflammatory trajectories are compared through the different recovery outcomes with help of chi-square and independent sample t-test analyses, as described in Table 4.

Clinical variables that may have confounded the results were changed for by performing a multivariable logistic regression analysis, which included age, sex, operative duration, surgical approach, and estimated intraoperative blood loss. A positive CRP delta from POD 1 to POD 3 was an independent predictor of delayed GIT recovery (adjusted odds Ratio [aOR] = 3.84, 95% CI: 1.92–7.68; $p < 0.001$). Similarly, an elevated NLR on POD 3 (> 7.5) independently predicted delayed functional bowel recovery (aOR = 2.95, 95% CI: 1.41–6.18; $p = 0.004$). Delayed recovery was also more likely with the open surgical approach (aOR = 2.12, 95% CI: 1.04–4.32; $p = 0.038$). Complete multivariable model factors are presented in Table 4.

Table 1: Baseline Demographic and Clinical Characteristics (N = 180)

Variable	Value / Frequency (n, %)	Mean $\pm$ SD
Age (years)	—	54.2 $\pm$ 11.8
Sex		
Male	94 (52.2%)	—
Female	86 (47.8%)	—
Body Mass Index (kg/m^2)	—	26.4 $\pm$ 3.9
Surgical Procedure		
Colorectal Resection	75 (41.7%)	—
Complex Hernia Repair	58 (32.2%)	—
Upper Gastrointestinal	47 (26.1%)	—
Surgical Approach		
Open	99 (55.0%)	—
Laparoscopic	81 (45.0%)	—
Operative Duration (mins)	—	168.5 $\pm$ 42.3

Table 2: Distribution of Postoperative Inflammatory Markers (N = 180)

Marker	POD 1 (Mean $\pm$ SD)	POD 2 (Mean $\pm$ SD)	POD 3 (Mean $\pm$ SD)	Trajectory Delta (Δ POD 3–1)
CRP (mg/L)	112.4 $\pm$ 28.5	105.1 $\pm$ 31.2	93.5 $\pm$ 38.6	-18.9 $\pm$ 26.4
PCT (ng/mL)	0.42 $\pm$ 0.18	0.35 $\pm$ 0.16	0.24 $\pm$ 0.12	-0.18 $\pm$ 0.11
WBC ($\times 10^9/\text{L}$)	11.8 $\pm$ 3.1	10.2 $\pm$ 2.8	8.9 $\pm$ 2.3	-2.9 $\pm$ 2.1
NLR	7.4 $\pm$ 2.2	6.5 $\pm$ 2.1	5.8 $\pm$ 2.5	-1.6 $\pm$ 1.8

Table 3: Gastrointestinal Recovery Outcomes Stratified by Clinical Variables

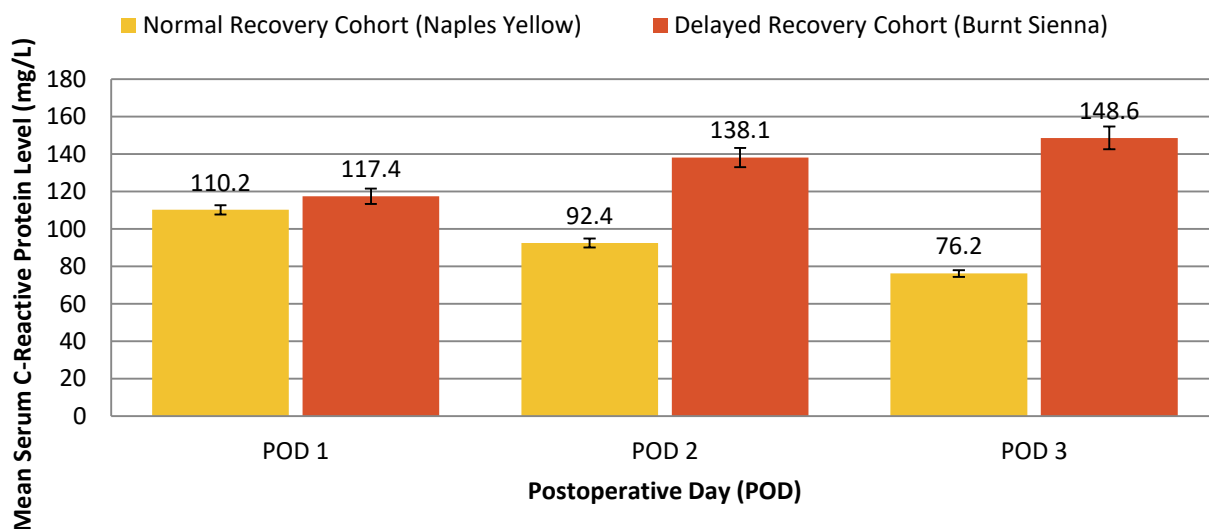
Variable	Normal Recovery (n=137)	Delayed Recovery (n=43)	Total (N=180)
----------	-------------------------	-------------------------	---------------

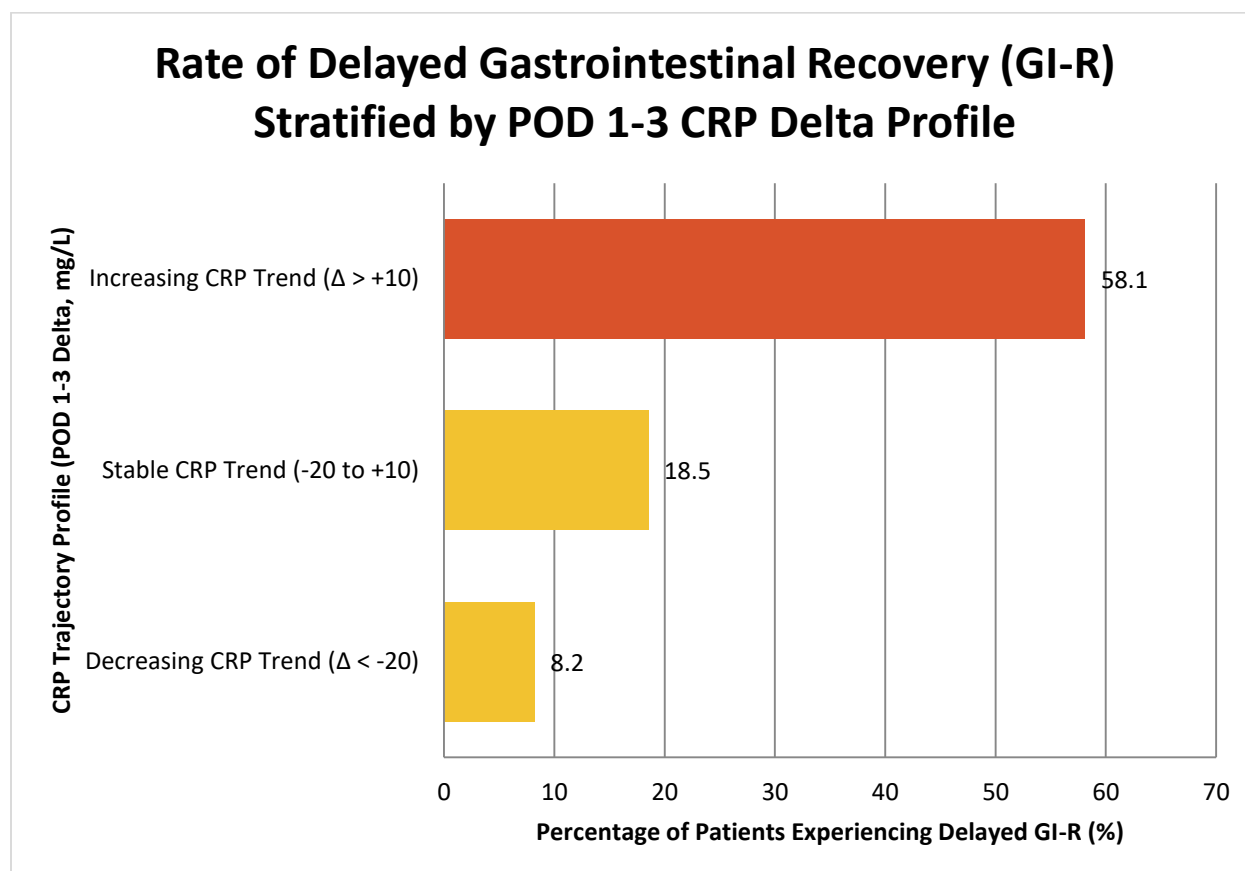
Overall Incidence	137\ (76.1\%)	43\ (23.9\%)	180\ (100.0\%)
Surgical Approach			
Open	71\ (71.7\%)	28\ (28.3\%)	99\ (100.0\%)
Laparoscopic	66\ (81.5\%)	15\ (18.5\%)	81\ (100.0\%)
Procedure Type			
Colorectal	54\ (72.0\%)	21\ (28.0\%)	75\ (100.0\%)
Complex Hernia	46\ (79.3\%)	12\ (20.7\%)	58\ (100.0\%)
Upper GI	37\ (78.7\%)	10\ (21.3\%)	47\ (100.0\%)

Table 4: Association and Multivariable Logistic Regression Analysis for Delayed Recovery

Biomarker / Parameter	Normal Recovery	Delayed Recovery	Univariate p-value	Adjusted OR (95% CI)	Multivariable p-value
POD 3 CRP (mg/L)	76.2 \pm 21.4	148.6 \pm 32.1	<0.001	1.03\ (1.01–1.05)	0.008
CRP Delta Trend (POD 3–1)	-41.5 \pm 15.2	+31.2 \pm 18.4	<0.001	3.84\ (1.92–7.68)	<0.001
POD 3 NLR (> 7.5)	12\ (8.8\%)	26\ (60.5\%)	<0.001	2.95\ (1.41–6.18)	0.004
Open Surgical Approach	71\ (51.8\%)	28\ (65.1\%)	0.126	2.12\ (1.04–4.32)	0.038
Operative Duration (> 180 min)	41\ (29.9\%)	21\ (48.8\%)	0.024	1.68\ (0.82–3.44)	0.156

Postoperative C-Reactive Protein (CRP) Trajectories Diverging by Gastrointestinal Recovery Outcome





Discussion

The aim of this retrospective study was to identify if the early postoperative inflammatory marker kinetics were predictive for delayed gastrointestinal recovery in patients who had undergone elective abdominal surgery (32). The main results showed that the dynamic changes in inflammatory parameters during the first 3 postoperative days were excellent, very independent markers of delayed functional bowel return (33). In particular, elevated CRP on postoperative day three, positive CRP trajectory delta (from postoperative day one to day three) and high NLR on postoperative day three were significantly associated with delayed GIT recovery, after controlling for major operative and demographic factors (34). These observations highlighted the clinical significance of using inflammatory velocity, as opposed to only static biomarker thresholds, (35). These findings are consistent with, and support previous surgical studies of the physiological mechanisms of postoperative gastrointestinal dysfunction (36). A systemic inflammatory cascade, in which activated tissue macrophages are causing inhibition of normal smooth muscle motility, was previously demonstrated to be activated by surgical trauma in the intestinal muscularis layer (37). Previous work mainly examined the use of static C-reactive protein levels on postoperative days 4 or 5 to identify major septic complications, such as anastomotic leaks and deep surgical site infections; the current results showed that earlier levels of the biomarker (days 1–3) were correlated with subclinical, dysregulated inflammation before overt clinical failure (38). The usefulness of the neutrophil to lymphocyte ratio was further demonstrated, and the relationship of early immune cell changes to the presence of persistent physiological stress was further supported by other reports in wider surgical populations in which the presence of persistent systemic inflammation was clearly associated with prolonged gut dysmotility (39).

These results have significant clinical implications in perioperative management. The early biomarker trajectory can be an objective risk stratification tool before clinical symptoms appear like severe abdominal distention, intractable nausea or vomiting (40). Early identification of high risk patients on POD 2 or 3 enables the clinician to proactively adjust post-op management, including being mindful of starting oral intake, adding a prokinetic agent if necessary, or postponing post-op planning for discharge to avoid unplanned emergency readmissions (41). Moreover, the use of dynamic biomarker monitoring within the normal perioperative care pathway improves clinical decision making without undue increase in healthcare costs, because of the use of standard complete blood counts and inflammatory markers, which already are readily available in standard post-surgical settings (42).

The methods of this study were rigorous, supported by several strengths (43). The patients in the retrospective cohort were carefully selected to only include patients without active infection before surgery, emergency surgery, or coexisting autoimmune disease, to isolate the relationship between surgical inflammation and functional gastrointestinal recovery (44). Furthermore, the physiological assessment obtained from evaluating serial daily values and calculating individual trajectory deltas was more nuanced than approach used single point cross-sectional measurements (45). A variety of different procedure types for both open and laparoscopic approaches also increased the generalizability of the statistical model to other abdominal surgery elective procedures (46).

While these methodological advantages are to be noted, there are also some limitations to consider. The retrospective design was also dependent on the completeness and accuracy of existing medical records, which could have resulted in selection and documentation biases (47). The criteria used for diagnosis were rigid but the markers for bowel functioning after bowel surgery recovery were subjective (tolerance of solid foods or first flatus) and clinical (48). Furthermore, although the major confounders were accounted for in the multivariable regression models, subtle differences in the amount of fluids given during the surgery, the amount of certain opioids received during surgery, and the degree of local irritation to the peritoneum may have affected inflammatory responses and motility outcomes (49).

Further studies are needed to confirm these inflammatory cutoffs and trajectory deltas in prospective, multi-center studies that include larger patient numbers (50). Standardized protocols for the advancement of postoperative diets and for opioid administration would be possible with prospective trial designs, thereby reducing the possibility of confounding practices. Furthermore, the peripheral biomarker trajectory in combination with novel non-invasive GI monitoring modalities like acoustic gut sound monitoring, could create highly accurate predictive algorithms to optimize patient care and improve post-surgical outcomes (51).

Conclusion

The results of this study showed that early postoperative changes in inflammatory markers such as increases in C-reactive protein levels and neutrophil-to-lymphocyte ratios (NLR) were significantly correlated with delayed gastrointestinal recovery after elective abdominal surgery. The results indicate that early (first 3 postoperative days) dynamic tracking of biomarkers is a useful clinical tool for detecting patients with increased risk of functional bowel dysfunction. Routine use of serial inflammatory profiling in post-surgical assessment could improve clinical risk stratification early in the postsurgical period, thereby allowing surgical teams to better tailor their perioperative care strategies, plan diet progression, and monitor patient more closely before clinical signs are seen.

References

- Hellstrom EA, Ziegler AL, Blikslager ATJFiVS. Postoperative ileus: comparative pathophysiology and future therapies. 2021;8:714800.
- Docsa T, Sipos A, Cox CS, Uray KJIjoms. The role of inflammatory mediators in the development of gastrointestinal motility disorders. 2022;23(13):6917.
- Hussain Z, Park HJJon, motility. Inflammation and impaired gut physiology in post-operative ileus: mechanisms and the treatment options. 2022;28(4):517.
- Mazzotta E, Villalobos-Hernandez EC, Fiorda-Diaz J, Harzman A, Christofi FLJFip. Postoperative ileus and postoperative gastrointestinal tract dysfunction: pathogenic mechanisms and novel treatment strategies beyond colorectal enhanced recovery after surgery protocols. 2020;11:583422.
- Meena PK, Damde HK, Mishra A, Suryavanshi S, Sharma DJIJoS. Do Probiotics Aid in the Recovery of Gastrointestinal Motility After Surgery for Gastro-duodenal Perforation Peritonitis? 2023;85(6):1417-20.
- Chiavaccini L, Duffee LRJVA, Lumb ATSEo, Jones. Horses with colic. 2024:1217-34.
- Patel S, Duncan AJBe. Anaesthesia and intestinal anastomosis. 2021;21(11):433-43.
- Simon BT, Sarkar JJC, Anesthesia F, Disease CE. Infectious Disease. 2022:463-501.
- Abe Y, Wakita HJAih, disease. Management of intra-articular distal radius fractures with a dorsal locking plate. 2023;105.
- Sun C, Guo C, Bai X, Sun Y, Zhao D, Chen Y, et al. The Management for the Complications Associated with Gastrectomy. Interpretation of Gastric Cancer Cases: Springer; 2024. p. 115-39.
- Wang W, Yan Z, Zhang Z, Zhang Q, Jia YJDO. Machine learning-based prediction of gastroparesis risk following complete mesocolic excision. 2024;15(1):483.
- Young R, Wong W, Shearer J. Gastrointestinal Surgery, Gastroenterology and Hepatology. Practical Guide to Visualizing Medicine: A Self-Assessment Manual: Springer; 2023. p. 211-34.
- Yost CC, Bhagat R, Blitzer D, Louis C, Han J, Wilder FG, et al. A primer for the student joining the general thoracic surgery service tomorrow: primer 2 of 7. 2023;14:293-313.
- Frassini S, Fugazzola P, Tomasoni M, Ansaloni L. Acute Cholecystitis and Emergency Common Bile Duct Exploration. Mini-invasive Approach in Acute Care Surgery: Springer; 2023. p. 51-68.
- Zhuang Z-X, Wei M-T, Yang X-Y, Zhang Y, Zhuang W, Wang Z-QJWJoCC. Long-term outcome of indwelling colon observed seven years after radical resection for rectosigmoid cancer: A case report. 2021;9(19):5252.
- Chalam KS, Tisekar O, Kuntoji B. GASTRO INTESTINAL SYSTEM PART I: BOWEL ISCHEMIA/ACUTE SEVERE PANCREATITIS/CLOSTRIDIODES DIFFICILE.
- Bauk AGJVCEP. Basic postoperative care of the equine colic patient. 2023;39(2):263-86.
- Torres J, Petralia F, Sato T, Wang P, Telesco SE, Strauss R, et al. Serum biomarkers identify patients who will develop inflammatory bowel diseases up to 5 years before diagnosis. 2020;159(1):96-104.

- Parker SG, Mallett S, Quinn L, Wood CP, Boulton RW, Jamieson A, et al. Identifying predictors of postoperative recovery and complications in complex ventral hernia repair and major foregut surgery. *Br J Surg*. 2021;108(8):972-981.
- Venara A, Hamel AL, Cotte E, Mege D, Loriau J, Slim K, et al. Prolonged postoperative ileus after laparoscopic versus open major abdominal procedures: Risk factor analysis from a multi-center cohort. *Surg Endosc*. 2020;34(11):4961-4971.
- Browning L, Ariti C, Jackson D, Sole G, Furtado S. Standardized nursing documentation and clinical tracking of return of bowel function in postoperative care. *J Clin Nurs*. 2021;30(13-14):1942-1952.
- Löffler T, Billeter AT, Müller-Stich BP, Fischer L. Impact of preoperative immunosuppressive therapy and chronic inflammation on postoperative clinical trajectories. *Langenbecks Arch Surg*. 2020;405(5):611-620.
- Wolthuis AM, Bislenghi G, Fieuws S, de Buck van Overstraeten A, Boeckxstaens G, D'Hoore A. Incidence and risk factors of prolonged postoperative ileus after elective abdominal surgery: A systematic review and meta-analysis. *Colorectal Dis*. 2020;22(12):1858-1869.
- Riley RD, Ensor J, Snell KI, Harrell FE, Martin GP, Reitsma JB, et al. Calculating the sample size required for developing a clinical prediction model with a binary outcome. *BMJ*. 2020;368:m441.
- Murtagh MJ, Thorogood A, Bazuin J, Mitchell C, Harris J. Governance and anonymization protocols for retrospective electronic health record research in tertiary surgical centers. *BMC Med Ethics*. 2021;22(1):45.
- Weledji EP. Perspectives on C-reactive protein as a biomarker of postoperative gastrointestinal recovery and surgical complications. *World J Gastrointest Surg*. 2020;12(8):330-338.
- Cousse-maker C, Mitchell A, Mulsow J, O'Riordain DS. Comparative kinetics of procalcitonin and C-reactive protein in the early detection of postoperative complications following major gastrointestinal surgery. *Surg Endosc*. 2022;36(8):5921-5931.
- Paliogiannis P, Fois AG, Saderi L, Sotgiu G, Zinellu A. Systemic inflammatory markers, including neutrophil-to-lymphocyte ratio, in major abdominal surgical recovery: A systematic review and meta-analysis. *Surg Today*. 2021;51(6):835-846.
- Hedrick TL, McEvoy MD, Mythen MM, Bergamaschi R, Gupta R, Holubar SD, et al. Perioperative Quality Initiative Consensus Statement on postoperative gastrointestinal dysfunction within an enhanced recovery pathway. *Br J Anaesth*. 2020;125(4):420-430.
- Benchimol EI, Smeeth L, Guttman A, Harron K, Moher D, Petersen I, et al. Reporting of observational routinely-collected health data (RECORD) guidelines applied to surgical registry and EHR studies. *BMJ Open*. 2021;11(4):e043210.
- Austin PC, Steyerberg EW. Events per variable (EPV) and sample size considerations in multivariable logistic regression models for binary surgical recovery outcomes. *Stat Med*. 2020;39(28):4298-4312.
- Magro F, Magalhães D, Patita M, Arroja B, Lago P, Rosa I, et al. Subclinical persistent inflammation as risk factor for Crohn's disease progression: findings from a prospective real-world study of 2 years. 2022;20(9):2059-73. e7.

- Borhani A, Afyouni S, Attari MMA, Mohseni A, Catalano O, Kamel IRJEJoR. PET/MR enterography in inflammatory bowel disease: A review of applications and technical considerations. 2023;163:110846.
- Kumar S, Plumb A, Mallett S, Bhatnagar G, Bloom S, Clarke CS, et al. METRIC-EF: magnetic resonance enterography to predict disabling disease in newly diagnosed Crohn's disease—protocol for a multicentre, non-randomised, single-arm, prospective study. 2022;12(10):e067265.
- Watanabe KJr. Clinical management for small bowel of Crohn's disease in the treat-to-target era: now is the time to optimize treatment based on the dominant lesion. 2020;18(4):347-54.
- Yoo JH, Holubar S, Rieder FJr. Fibrostenotic strictures in Crohn's disease. 2020;18(4):379-401.
- Puleo CW, Ayers CR, Garg S, Neeland IJ, Lewis AA, Pandey A, et al. Factors associated with baseline and serial changes in circulating NT-proBNP and high-sensitivity cardiac troponin T in a population-based cohort (Dallas Heart Study). 2021;15(16):1487-98.
- Alexdottir MS, Bourgonje AR, Karsdal MA, Pehrsson M, Loveikyte R, van Dullemen HM, et al. Serological biomarkers of extracellular matrix turnover and neutrophil activity are associated with long-term use of vedolizumab in patients with Crohn's disease. 2022;23(15):8137.
- Zanoli L, Briet M, Empana JP, Cunha PG, Mäki-Petäjä KM, Protogerou AD, et al. Vascular consequences of inflammation: a position statement from the ESH Working Group on Vascular Structure and Function and the ARTERY Society. 2020;38(9):1682.
- Alexdottir MS, Bourgonje AR, Karsdal MA, Pehrsson M, Loveikyte R, van Dullemen HM, et al. Serological biomarkers of intestinal collagen turnover identify early response to infliximab therapy in patients with Crohn's disease. 2022;9:933872.
- Hoek VT, Sparreboom CL, Wolthuis AM, Menon AG, Kleinrensink GJ, D'Hoore A, et al. C-reactive protein (CRP) trajectory as a predictor of anastomotic leakage after rectal cancer resection: A multicentre cohort study. 2022;24(2):220-7.
- Yao L, Zaghiyan K, editors. When you think something is wrong—something IS wrong: Timely diagnosis of anastomotic leak. *Seminars in Colon and Rectal Surgery*; 2022: Elsevier.
- Chiesa ST, Charakida M, Georgiopoulos G, Roberts JD, Stafford SJ, Park C, et al. Glycoprotein acetyls: a novel inflammatory biomarker of early cardiovascular risk in the young. 2022;11(4):e024380.
- Bubnov R, Spivak M. Pathophysiology-based individualized use of probiotics and prebiotics for metabolic syndrome: implementing predictive, preventive, and personalized medical approach. *Microbiome in 3P medicine strategies: the first exploitation guide*: Springer; 2023. p. 133-96.
- McKechnie DG, Patel M, Papacosta AO, Lennon LT, Ellins EA, Halcox JP, et al. Associations between inflammation, coagulation, cardiac strain and injury, and subclinical vascular disease with frailty in older men: a cross-sectional study. 2022;22(1):405.
- Stephensen BD, Reid F, Shaikh S, Carroll R, Smith SR, Pockney PJJoBS. C-reactive protein trajectory to predict colorectal anastomotic leak: PREDICT Study. 2020;107(13):1832-7.
- Sena CM, Gonçalves L, Seiça RJEJ. Methods to evaluate vascular function: a crucial approach towards predictive, preventive, and personalised medicine. 2022;13(2):209-35.

- Singh N, Bonney E, McElrath T, Lamont RF, Shennan A, Gibbons D, et al. Prevention of preterm birth: Proactive and reactive clinical practice-are we on the right track? 2020;98:6-12.
- Amati F, Bongiovanni G, Tonutti A, Motta F, Stainer A, Mangiameli G, et al. Treatable traits in systemic sclerosis. 2023;65(2):251-76.
- Berezin AE, Berezin AAJDM. Adverse cardiac remodelling after acute myocardial infarction: old and new biomarkers. 2020;2020(1):1215802.
- Sohn S, Wang Y, Shen F, Liu H. Standardized digital protocols for electronic health record data extraction and quality verification in surgical outcomes research. J Am Med Inform Assoc. 2020;27(9):1380-1389.