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A Pilot Exploratory Study Examining the Association Between Preoperative Circulating Cell-Free DNA Levels and Postoperative Organ Dysfunction in Acute Abdomen

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Research Article

Keywords: Sequential Organ Failure Assessment, cell-free DNA, Acute Abdomen, Sepsis, Emergency Surgery

Posted Date: November 17th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11237796/v1

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Additional Declarations: No competing interests reported.

Article type: Research article

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Abstract

Background: Circulating cell-free deoxyribonucleic acid (cfDNA) has emerged as a potential biomarker of acute cellular injury and systemic inflammation during emergency surgery for acute abdomen. In this study, we aimed to evaluate the association between preoperative circulating cfDNA levels and postoperative organ dysfunction in these patients.

Methods: Forty-six patients who underwent emergency surgery for acute abdomen between September 2019 and October 2022 were included. Preoperative plasma cfDNA levels were measured. Postoperative organ dysfunction was defined as an increase in the Sequential Organ Failure Assessment (SOFA) score of ≥ 2 on postoperative day 1 (ΔSOFA ≥ 2).

Results: Patients with ΔSOFA ≥ 2 had higher preoperative cfDNA levels than did those with ΔSOFA < 2. In an exploratory multivariable logistic regression model, both elevated preoperative SOFA scores and cfDNA levels remained significantly associated with ΔSOFA ≥ 2, although the results should be interpreted cautiously given the wide confidence intervals. The area under the receiver operating characteristic curve for cfDNA was 0.82.

Conclusions: Preoperative plasma cfDNA levels may serve as potential biomarkers associated with postoperative organ dysfunction in patients undergoing emergency surgery for acute abdomen. External validation is needed before cfDNA can be recommended for perioperative risk assessment.

Keywords: Sequential Organ Failure Assessment, cell-free DNA, Acute Abdomen, Sepsis, Emergency Surgery

Background

Inflammatory responses are triggered when the body experiences stress due to infection, surgery, or other insults that often lead to organ dysfunction [1]. Source control measures include emergency surgery for acute abdomen performed within 6 h of diagnosis, which is associated with lower mortality and shorter hospital stays than those associated with delayed intervention [2]. Accordingly, accurate preoperative risk stratification is important for guiding the allocation of critical care resources and enabling early intensive care unit (ICU)-level management of high-risk patients while avoiding unnecessary invasive interventions in lower-risk patients.

The Sequential Organ Failure Assessment (SOFA) score is a well-established and widely used tool for assessing the severity of organ dysfunction in various critical illnesses, including those arising from diverse causes of acute abdomen [3,4]. According to the Sepsis-3 definition, sepsis is characterized by infection-associated organ dysfunction, defined as an acute increase of two or more points in the SOFA score from baseline [5]. However, the SOFA score reflects the patient's condition only after the development of organ dysfunction. Thus, predicting which surgical patients with acute abdomen will develop worsening postoperative SOFA scores remains challenging.

Moreover, early identification of patients at high risk of postoperative organ dysfunction is important to enable timely intervention and improve patient outcomes.

Circulating cell-free deoxyribonucleic acid (cfDNA) has emerged as a potential biomarker for cellular and systemic inflammation [6]. cfDNA concentrations increase rapidly in response to severe infection and tissue injury, reflecting cellular damage and neutrophil extracellular trap formation; higher levels correlate with greater disease severity and poor outcomes. Martins et al. [7] were the first to report circulating cfDNA levels in the plasma of patients with sepsis, a finding that has expanded the role of cfDNA in sepsis diagnosis and prognosis [8,9]. Recent studies have reported that circulating plasma cfDNA has a sensitivity of 81% (95% confidence interval [CI], 75–86%) and a specificity of 72% (95% CI, 65–78%) for identifying sepsis in critically ill patients [10]. Moreover, metagenomic sequencing may offer an even better predictive performance, with one study reporting an area under the curve of 0.992 (95% CI, 0.969–1.000) for sepsis diagnosis [11]. We hypothesized that preoperative cfDNA levels could provide prognostic information beyond that obtained from routine clinical assessments in patients undergoing emergency surgery for acute abdomen. Therefore, this study investigated the association between preoperative circulating cfDNA levels and

postoperative organ dysfunction and explored their potential utility for perioperative risk stratification in this population.

Methods

Patient population and study design

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Research Ethics Committee of the participating hospital (19012134). Informed consent was obtained from all patients or their legal representatives. This observational study included patients who underwent emergency surgery for acute abdomen in our department. Preoperative shock was clinically defined as a persistent systolic blood pressure < 90 mmHg or mean arterial pressure < 65 mmHg despite initial fluid resuscitation or the requirement for vasopressor infusion prior to skin incision.

The SOFA score was measured preoperatively and on postoperative day 1 (POD1). Postoperative organ dysfunction was defined as an increase in the SOFA score of ≥ 2 on POD1 relative to the preoperative baseline (ΔSOFA ≥ 2). This change-based definition was chosen in accordance with the Sepsis-3 framework to specifically distinguish acute new-onset perioperative organ worsening from preexisting chronic dysfunction [5]. POD1 was selected to capture early postoperative changes in organ function.

Surgical procedures

Emergency surgical procedures were performed based on the underlying pathology and clinical condition of each patient. The procedures included colorectal resection (including Hartmann's procedure), small bowel resection, surgical relief of bowel obstruction without resection, laparoscopic omental patch repair, abdominal drainage, appendectomy, cholecystectomy, splenectomy, and hemostasis, all performed according to standard institutional protocols. The most common procedures were Hartmann's procedure (n = 9), small bowel resection including ileocecal resection (n = 9), surgical relief of bowel obstruction without resection (n = 8), laparoscopic omental patch repair (n = 3), and abdominal drainage (n = 4). Two appendectomies and two cholecystectomies were performed. Splenectomy and hemorrhage control were required in rare cases.

Measurement of plasma cfDNA

Preoperative blood sampling was performed after informed consent was obtained. Blood samples were collected in PAXGene ccfDNA tubes (Roche Diagnostics, Basel, Switzerland) and centrifuged at 1600 × *g* for 10 min at room temperature using a swing-out rotor. The supernatant was transferred to a fresh tube, and plasma aliquots were frozen at −80°C. cfDNA was extracted using the MagMAX Cell-Free DNA Isolation Kit (Thermo Fisher Scientific, Waltham, MA, USA). Plasma cfDNA concentrations were

measured using the Qubit 3.0 dsDNA High Sensitivity System (Thermo Fisher Scientific, Waltham, MA, USA).

Statistical analysis

Preoperative baseline characteristics were compared between the ΔSOFA ≥ 2 and ΔSOFA < 2 groups. The ΔSOFA ≥ 2 was chosen as a clinically meaningful indicator of organ dysfunction, consistent with its use in sepsis severity assessment [5]. Categorical variables are summarized as counts (percentages) and were compared using the chi-square test or Fisher's exact test when the expected counts were <5. Continuous variables are summarized as medians (ranges) and were compared using the Wilcoxon rank-sum test.

To evaluate the discrimination of preoperative plasma cfDNA for ΔSOFA ≥ 2, we performed receiver operating characteristic (ROC) analysis, identified the optimal cutoff from the ROC curve, and reported the area under the curve (AUC). The optimal cfDNA cut-off value was determined by maximizing the Youden index. Based on this cut-off, patients were classified into high (cfDNA-H) and low (cfDNA-L) cfDNA groups. A similar ROC curve analysis was performed for the preoperative SOFA score to identify the optimal cutoff value for discriminating between patients with and without ΔSOFA ≥ 2, and patients were categorized into SOFA-H and SOFA-L groups accordingly.

Variables showing statistically significant differences between the ΔSOFA ≥ 2 and ΔSOFA < 2 groups in the initial between-group comparisons were selected for subsequent logistic regression analyses. Univariable logistic regression analyses were performed for these selected variables, followed by an exploratory multivariable logistic regression model including the same variables. For preoperative SOFA score and cfDNA level, dichotomized variables (SOFA-H and cfDNA-H), defined using the cutoff values derived from the ROC analyses, were used in the logistic regression analyses. Thus, preoperative shock, SOFA-H, and cfDNA-H were included in the exploratory multivariable model. Odds ratios (ORs) with 95% CIs were calculated.

To assess the potential clinical utility, a decision curve analysis (DCA) was conducted for two models: (i) cfDNA-H and (ii) SOFA-H. Predicted probabilities were obtained using logistic regression analysis and net benefit was computed across threshold probabilities 0.05–0.50, as follows:

$$NB(pt) = TP/N - FP/N \times [pt/(1-pt)].$$

The treat-all and treat-none strategies were used as comparators. Decision curves were bootstrap resampling (1,000 resamples), and optimism-corrected results were reported.

The predictive performance of cfDNA-H- and SOFA-H-based risk stratifications

for ΔSOFA ≥ 2 was evaluated using multiple metrics, including sensitivity, specificity, positive predictive value, negative predictive value, accuracy, F1 score, and AUC, calculated based on the classification results at the respective cutoff values. Radar charts were constructed to visually compare the overall predictive performance of these metrics. Statistical significance was set at $P < 0.05$. Analyses were performed using JMP software for Windows (SAS Institute Inc., Cary, NC, USA).

Results

The clinical characteristics of the 46 patients are presented in **Table 1**. The median patient age was 75 years (range: 27–93 years). The study cohort comprised 27 men and 19 women. The main organs involved in surgery were the small intestine in 21 (45.7%) patients, colon in 12 (26.1%) patients, and other organs in 13 (28.3%) patients. The main causes of acute abdomen were gastrointestinal perforation (n = 18; 39.1%), bowel strangulation (n = 13; 28.3%), and other conditions (n = 15; 32.6%). Preoperative shock was observed in 15 (32.6%) patients. The median preoperative white blood cell count was 12,800/μL (range, 1,400–26,600/μL), and the median C-reactive protein level was 5.5 mg/dL (range, 0.01–40.1 mg/dL). The median preoperative SOFA score was 3

(range, 0–13), which increased to 4 (range, 0–14) on POD1. The 30-day and 90-day mortality rates were 2.2% (n = 1) and 8.7% (n = 4), respectively.

cfDNA levels and SOFA score ≥ 2 on POD 1

Preoperative cfDNA levels were higher in the ΔSOFA ≥ 2 group than in the ΔSOFA < 2 group (median, 1114 ng/mL vs. 275 ng/mL, P < 0.001) (**Fig. 1**). ROC curve analysis was performed to determine the optimal cutoff value of preoperative cfDNA levels for discriminating ΔSOFA ≥ 2 (**Fig. 2**), yielding an AUC of 0.82 and an optimal cutoff value of 746 ng/mL. Accordingly, patients were divided into cfDNA-H (> 746 ng/mL) and cfDNA-L (≤ 746 ng/mL) groups.

Preoperative risk factors associated with postoperative organ dysfunction

To understand factors influencing postoperative organ dysfunction, preoperative risk factors for ΔSOFA ≥ 2 were analyzed (**Table 2**). ROC curve analysis identified a preoperative SOFA score of ≥ 3 as the optimal cutoff for discriminating ΔSOFA ≥ 2. The AUC for preoperative SOFA score in discriminating ΔSOFA ≥ 2 was 0.74. Accordingly, patients were divided into SOFA-H (≥3) and SOFA-L (<3) groups. The rates of SOFA-H, preoperative shock, and cfDNA-H were significantly higher in the ΔSOFA ≥ 2 group than in the ΔSOFA < 2 group (SOFA-H: 15/18 [83.3%] vs. 11/28

[39.3%], P = 0.006; preoperative shock: 10/18 [55.6%] vs. 5/28 [17.9%], P = 0.011; cfDNA-H: 16/18 [88.9%] vs. 7/28 [25.0%], P < 0.001).

Preoperative factors associated with postoperative organ dysfunction

Based on the initial between-group comparisons, preoperative shock, SOFA-H, and cfDNA-H were selected for subsequent logistic regression analyses. In univariable logistic regression analyses, preoperative shock, SOFA-H, and cfDNA-H were significantly associated with ΔSOFA ≥ 2 (**Table 3**). In an exploratory multivariable logistic regression model, both SOFA-H (adjusted OR, 6.45; 95% CI, 1.09–55.21; P = 0.039) and cfDNA-H (adjusted OR, 25.91; 95% CI, 3.79–315.11; P < 0.001) remained significantly associated with ΔSOFA ≥ 2.

Subgroup analysis of risk factors for postoperative organ dysfunction stratified by gastrointestinal perforation or strangulation

In the subgroup analysis of patients with gastrointestinal perforation or strangulation, preoperative shock, SOFA-H, and cfDNA-H were significantly associated with postoperative organ dysfunction (ΔSOFA ≥ 2). In contrast, in patients without gastrointestinal perforation or strangulation, cfDNA-H remained significantly associated with ΔSOFA ≥ 2, whereas other variables were not statistically significant (**Additional file 1, Supplementary Tables 1 and 2**).

These findings suggest that the preoperative cfDNA-H classification is consistently associated with postoperative organ dysfunction across different clinical subgroups.

Potential clinical benefit of preoperative cfDNA assessed using DCA

Subgroup analysis demonstrated that cfDNA-H status was consistently associated with postoperative organ dysfunction across clinical subgroups. Based on these findings, the potential clinical utility of cfDNA-based risk stratification was evaluated using DCA. The DCA showed that risk stratification based on cfDNA-H provided a greater net clinical benefit than stratification based on SOFA-H across a wide range of threshold probabilities (**Fig. 3a**).

Overall predictive performance of cfDNA-H and SOFA-H

The radar chart analysis visually illustrated the comparative performance profiles of cfDNA-H and SOFA-H across metrics, showing higher point estimates for cfDNA-H (**Fig. 3b**).

Association between preoperative cfDNA levels and postoperative outcomes

Associations between preoperative cfDNA levels and postoperative outcomes are shown in **Table 4**. Compared with the cfDNA-L group, the cfDNA-H group showed higher use of norepinephrine (cfDNA-L vs. cfDNA-H: 13.0% vs. 78.3%, $P < 0.001$), vasopressin (4.4% vs. 52.2%, $P = 0.001$), thrombomodulin (4.4% vs. 47.8%, $P = 0.002$), and

continuous hemodiafiltration (8.7% vs. 60.9%, P < 0.001). The cfDNA-H group also had a longer duration of mechanical ventilation (median, 0 vs. 4.5 days; P < 0.001) and ICU stay (median, 0 vs. 9 days; P < 0.001). No significant differences were observed in 30-day mortality (0.0% vs. 4.4%, P = 1.000), 90-day mortality (8.7% vs. 8.7%, P = 1.000), or postoperative hospital stay (median, 14.5 days vs. 13.0 days, P = 0.669). These results indicate that elevated preoperative cfDNA levels are associated with a more severe postoperative course.

Discussion

In this exploratory pilot study, preoperative plasma cfDNA levels were identified as a potential biomarker of postoperative organ dysfunction in patients undergoing emergency surgery for acute abdomen. Elevated preoperative cfDNA levels were associated with postoperative organ dysfunction, defined as an increase in the SOFA score of ≥2 on POD1, consistent with the SOFA-based definition of organ dysfunction used in the Sepsis-3 framework. Importantly, both SOFA-H and cfDNA-H remained significantly associated with postoperative organ dysfunction in the exploratory multivariable model, whereas the association with preoperative shock was attenuated after adjustment. In addition, subgroup analysis and DCA findings support the potential role of cfDNA as an

238 exploratory biomarker for perioperative risk stratification, although these findings should
239 be interpreted cautiously given the pilot nature of the study.

240 The potential clinical utility of cfDNA observed in this pilot exploratory study
241 may be understood in light of the unique biological behavior of circulating cfDNA during
242 acute inflammatory states [6,12]. Because circulating cfDNA is rapidly cleared from the
243 bloodstream, plasma cfDNA concentration reflects ongoing cellular injury and
244 inflammatory activity at a given time point rather than accumulated pathological burden
245 [8, 13]. In patients with acute abdomen, this rapid clearance allows preoperative cfDNA
246 levels to reflect the immediate systemic impact of intra-abdominal infection, ischemia, or
247 perforation before overt postoperative organ dysfunction becomes clinically apparent.

248 From a mechanistic perspective, cfDNA released during acute abdominal
249 injury may serve as a surrogate marker of damage-associated molecular patterns
250 released during acute tissue injury and neutrophil-driven inflammatory responses
251 [14,15]. These signals can precede the measurable deterioration of organ-specific
252 parameters captured by conventional scoring systems. Accordingly, preoperative cfDNA
253 levels may reflect a transitional phase of physiological stress that bridges localized
254 abdominal disease and subsequent systemic organ dysfunction [16].

The clinical application of cfDNA in this study differs from its conventional use in oncology [9, 17]. In cancer medicine, cfDNA is mainly used to detect tumor-derived genetic alterations and monitor tumor burden or treatment response over time [18–20]. In contrast, preoperative cfDNA is not used for genomic characterization in patients undergoing emergency surgery for acute abdomen, but rather as a transient quantitative marker reflecting the severity of acute cellular injury and systemic inflammatory stress at a specific time point. This difference in clinical purpose highlights that, in this context, cfDNA should be interpreted as an indicator of physiological severity rather than as a disease-specific biomarker.

Preoperative plasma cfDNA levels may assist in perioperative risk stratification before emergency surgery for acute abdomen. Plasma cfDNA concentrations can be obtained within approximately 1.5 hours, and elevated levels may help identify patients who require close postoperative monitoring, early ICU admission, or proactive organ-supportive management. In this time-sensitive setting, cfDNA may serve as a simple adjunct to conventional clinical assessments, supporting more informed perioperative decision making without replacing established severity scores.

This study had some limitations. First, the sample size was relatively small and limited to a single center, which may restrict the generalizability of our findings; therefore,

this study should be regarded as hypothesis generating. Second, the exact number of outcome events (ΔSOFA ≥ 2) was limited to 18, resulting in a limited events-per-variable ratio that may have affected model stability in the primary analyses. To account for the modest sample size, bootstrap resampling was used for the DCA. Third, the study cohort included a heterogeneous group of surgical diagnoses with distinct pathophysiological courses. Although subgroup analyses demonstrated consistent associations, this heterogeneity may limit the direct applicability of our findings to specific disease entities, which requires confirmation in homogeneous populations. Fourth, the cfDNA levels were measured only at a single preoperative time point. Fifth, although DCA with bootstrap resampling assessed the stability of the net benefit, the model was not externally validated and requires confirmation in larger multicenter cohorts. Finally, the cutoff values were internally optimized without external validation, which carries an inherent risk of over-optimism.

Conclusions

This pilot study showed that elevated preoperative plasma cfDNA levels were associated with an increased risk of postoperative organ dysfunction in patients undergoing emergency surgery for acute abdomen. These findings suggest that

preoperative cfDNA may have potential utility for perioperative risk stratification. Although external validation is required, these findings support further investigation of cfDNA as a biomarker for perioperative risk stratification in patients with acute abdomen.

List of abbreviations

AUC: Area Under the Curve

cfDNA: Cell-Free Deoxyribonucleic Acid

cfDNA-H: High Preoperative Cell-Free DNA (> 746 ng/mL)

cfDNA-L: Low Preoperative Cell-Free DNA (≤ 746 ng/mL)

CHDF: Continuous Hemodiafiltration

CI: Confidence Interval

CRP: C-Reactive Protein

DCA: Decision Curve Analysis

ICU: Intensive Care Unit

OR: Odds Ratio

POD1: Postoperative Day 1

ROC: Receiver Operating Characteristic

SOFA: Sequential Organ Failure Assessment

SOFA-H: High Preoperative SOFA Score (≥ 3)

SOFA-L: Low Preoperative SOFA Score (< 3)

Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Nagasaki University Hospital Clinical Research Ethics Committee (Approval Number: 19012134-7). Written informed consent was obtained from all participants included in the study or their legal representatives.

Clinical trial number

Not applicable

Consent for publication

Informed consent for publication was obtained from all patients or their legal representatives.

Availability of data and materials

The datasets used and/or analyzed in the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by a JSPS Grant-in-Aid for Scientific Research C (Grant Number: 24K11935) and a Research Grant for Young Physicians in Abdominal Emergency Medicine. The funding bodies played no role in the study design, data collection, analysis, interpretation, or writing of the manuscript.

Authors' contributions

S.K. and Y.I. designed the study, analyzed the data, and wrote the initial draft of the manuscript. S.O. contributed substantially to the data interpretation. S.Y. and T.A. participated in discussions and assisted with manuscript preparation. M.H. extracted cell-free DNA under blinded conditions. S.K. measured plasma cell-free DNA concentration. K.K. supervised the study and made critical revisions. S.E. supervised patient treatment and assisted substantially with manuscript editing. All authors contributed to data collection and interpretation, critically reviewed the manuscript, and approved the final version.

Acknowledgements

The authors thank Shigeaki Ohtsuki, PhD, of the Japan Institute of Statistical Technology, for expert advice and technical support with the statistical analyses. References were identified using Open Evidence. Automated language-editing software (Paperpal) was used to improve English phrasing.

Authors' information

Not applicable.

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Figure Legends

Fig. 1 Relationship between preoperative cfDNA levels and ΔSOFA score on postoperative day 1: ΔSOFA score ≥ 2 was defined as an increase in the SOFA score of ≥ 2 points from the preoperative value to postoperative day 1.

Abbreviations: cfDNA, Cell-Free DNA; SOFA, Sequential Organ Failure Assessment.

Fig. 2 ROC curve of preoperative cfDNA levels for discriminating postoperative ΔSOFA ≥ 2: ROC curve analysis was performed to evaluate the discriminatory performance of preoperative cfDNA levels for postoperative ΔSOFA ≥ 2. The AUC was 0.82.

Abbreviations: ROC, Receiver Operating Characteristic; cfDNA, Cell-Free DNA; SOFA, Sequential Organ Failure Assessment; AUC, Area Under the Curve.

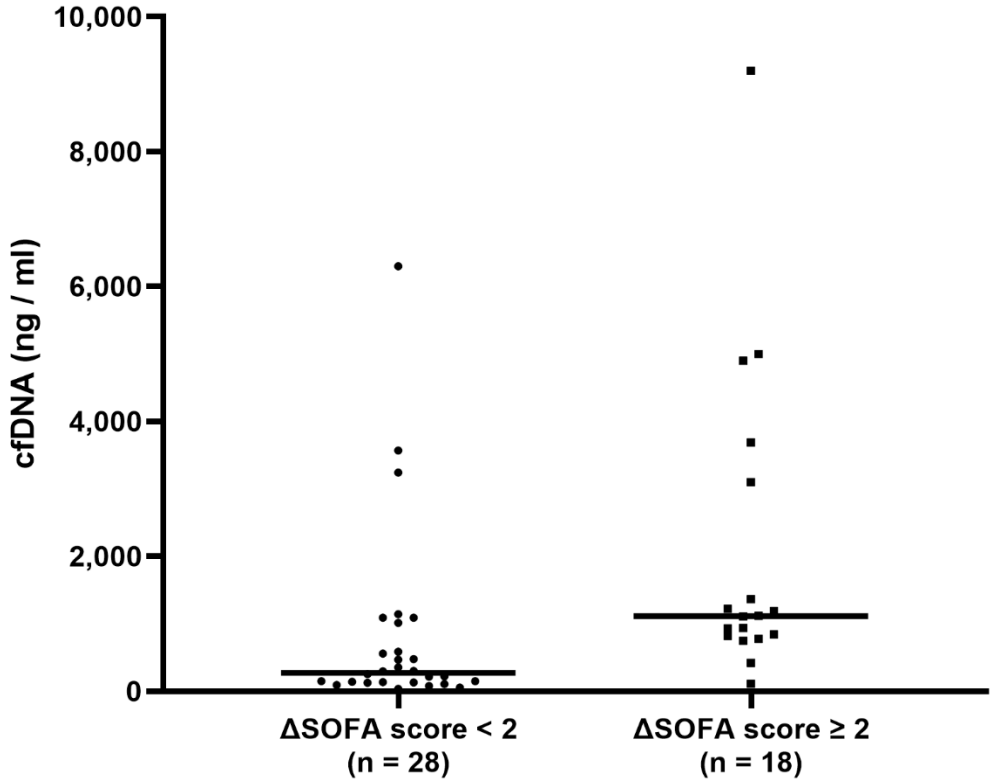
Fig. 3 Decision curve analysis and the radar charts demonstrating the comprehensive predictive performance of cfDNA-H and SOFA-H: (a) Decision curve analysis showing the net clinical benefit of the models in predicting postoperative organ dysfunction (ΔSOFA ≥ 2). The model incorporating high preoperative plasma cfDNA levels (cfDNA-H; > 746 ng/mL) provided a greater net benefit than the high preoperative SOFA score (SOFA-H; ≥ 3)-based model. The orange line shows SOFA-H with 95% CI. The blue line

437 shows cfDNA-H with 95% CI. (b) Radar charts comparing the predictive performances
438 of cfDNA-H and SOFA-H for predicting postoperative organ dysfunction (ΔSOFA ≥ 2).
439 The predictive performance was assessed using selected representative metrics, including
440 accuracy, sensitivity, specificity, PPV, NPV, F1 score, and AUC. Each axis represents a
441 performance metric, and the enclosed area reflects the overall balance of the predictive
442 performance.
443 Abbreviations: cfDNA, Cell-Free DNA; SOFA, Sequential Organ Failure Assessment; CI,
444 Confidence Interval; cfDNA-H, Preoperative Plasma Cell-Free DNA value > 746 ng/mL;
445 SOFA-H, Preoperative SOFA Score ≥ 3; AUC, Area Under the Curve; PPV, Positive
446 Predictive Value; NPV, Negative Predictive Value.
447
448
449 **Additional file 1**
450 **Supplementary table 1.** Risk factors for ΔSOFA score 2 or more in GI perforation or
451 strangulation on postoperative day 1

452 Figures

453 **Fig. 1** Relationship between preoperative cfDNA levels and ΔSOFA score on

454 postoperative day 1

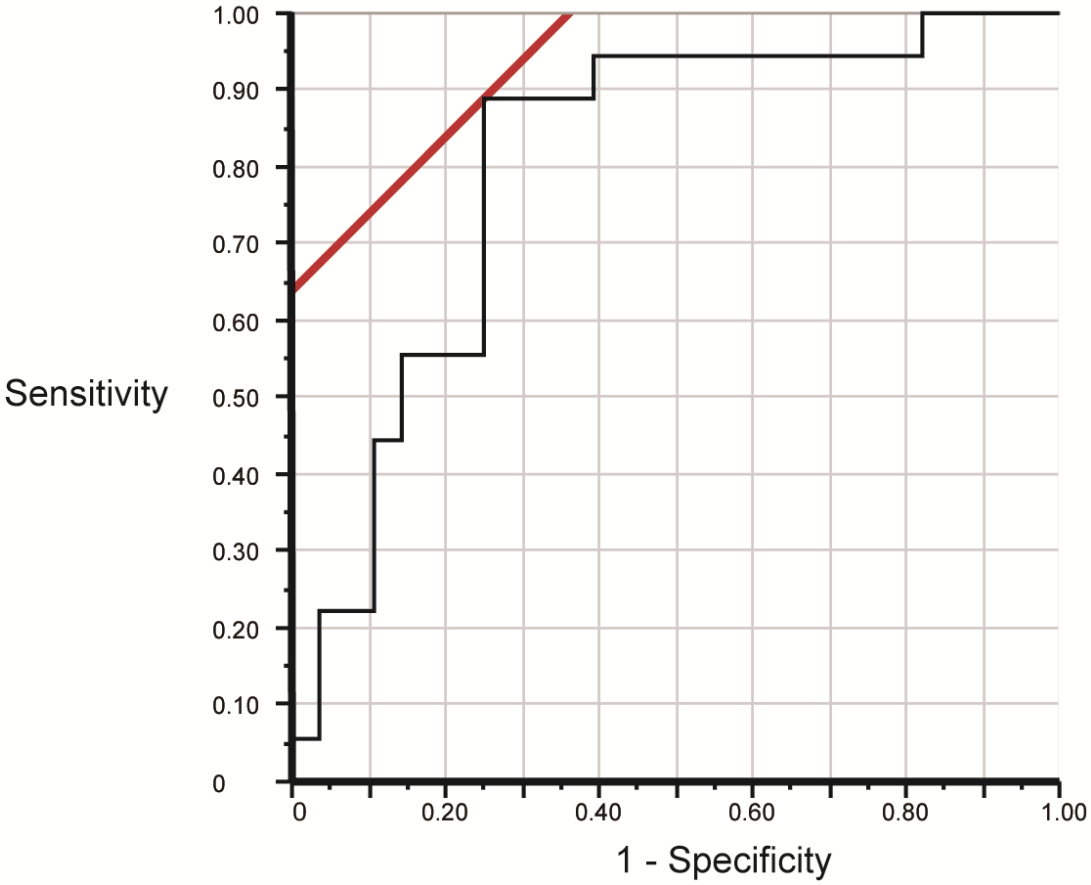


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457 **Fig. 2** ROC curve of preoperative cfDNA levels for discriminating postoperative ΔSOFA

458 ≥ 2

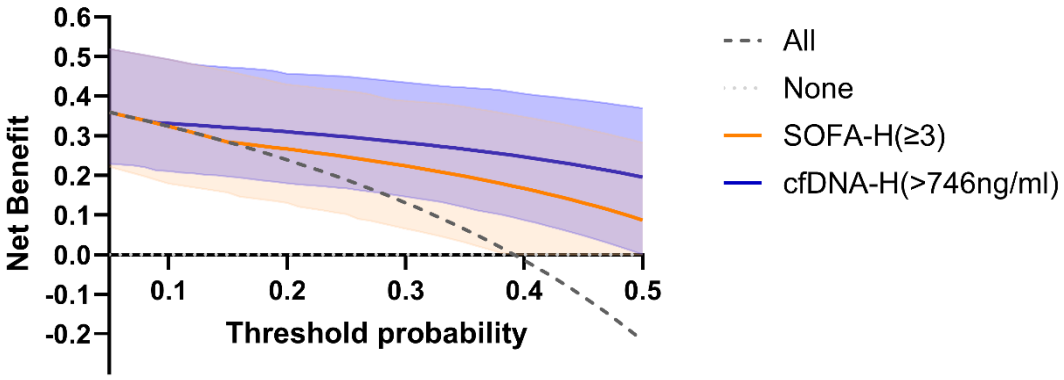


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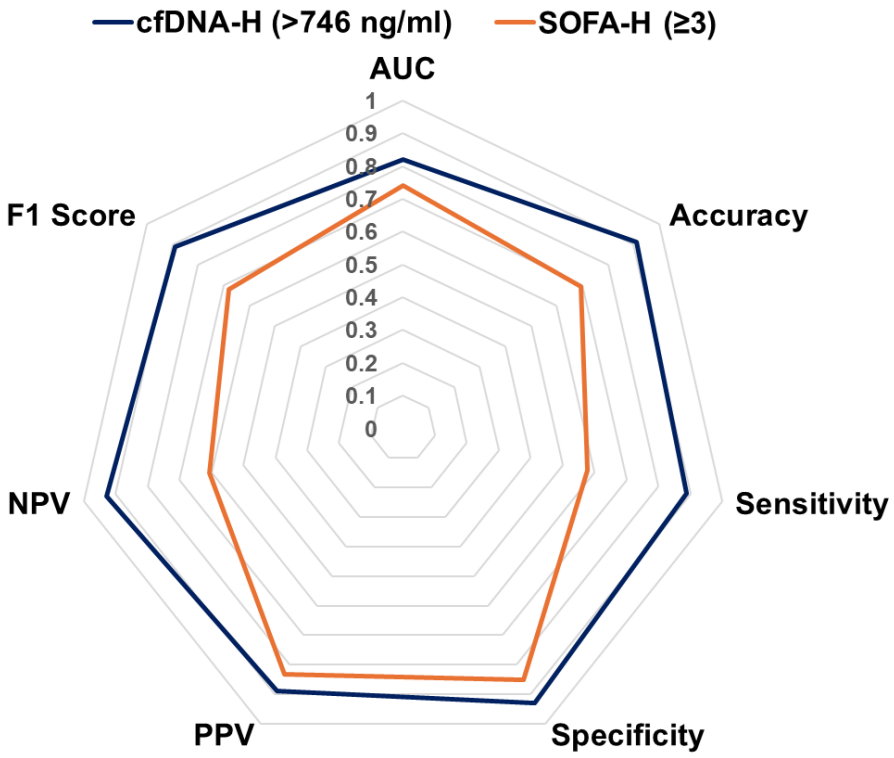
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Fig. 3 Decision curve analysis and the radar charts demonstrating the comprehensive predictive performance of cfDNA-H and SOFA-H

(a)



(b)



Tables

Table 1. Patient characteristics

Variable	Overall (n = 46)
Age (years)	75 (27–93)
Sex (male / female)	27/19
Organ - Intestine	21 (45.7%)
- Colon	12 (26.1%)
- Others	13 (28.3%)
Disease - Perforation	18 (39.1%)
- Strangulation	13 (28.3%)
- Others	15 (32.6%)
Preoperative shock	15 (32.6%)
Preoperative WBC (/μL)	12,800 (1,400–26,600)
Preoperative CRP (mg/dL)	5.50 (0.01–40.10)
Preoperative SOFA	3 (0–13)
SOFA on postoperative day 1	4 (0–14)
30-day postoperative mortality	1 (2.2%)

90-day postoperative mortality	4 (8.7%)
ICU stay (days)	3 (0–23)
Postoperative hospital stay (days)	14 (2–31)

471 Values are expressed as medians (ranges) or numbers (percentages), as appropriate.

472 SOFA, Sequential Organ Failure Assessment; ICU, Intensive Care Unit; WBC, White

473 Blood Cell; CRP, C-Reactive Protein.

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Table 2. Preoperative risk factors for ΔSOFA score of 2 or more on postoperative day 1

Risk Factor	**ΔSOFA score < 2 (n = 28)**	**ΔSOFA score ≥ 2 (n = 18)**	**P value**
Age	71 (27–90)	76 (45–93)	P = 0.241
Sex (male / female)	17 / 11	10 / 8	P = 0.767
Perforation or strangulation	19 (67.8%)	12 (66.7%)	P = 0.933
Preoperative shock	5 (17.9%)	10 (55.6%)	P = 0.011
Preoperative WBC count (/μL)	13,050 (3,200–26,600)	12,750 (1,400–22,500)	P = 0.581
Preoperative CRP (mg/dL)	3.01 (0.01–40.12)	9.03 (0.05–30.86)	P = 0.191
SOFA	2 (0–12)	5 (0–13)	P = 0.006
cfDNA (ng/mL)	275 (36.60–6300)	1,114 (114–9600)	P < 0.001
Preoperative lactate levels (mmol/L)	1.30 (0.50–7.30)	1.90 (0.60–9.50)	P = 0.262

Values are expressed as medians (ranges) or numbers (percentages), as appropriate.

WBC, White Blood Cell; CRP, C-Reactive Protein; SOFA, Sequential Organ Failure Assessment; cfDNA, Cell-Free DNA.

Table 3. Logistic regression analyses of factors associated with postoperative organ dysfunction (ΔSOFA ≥ 2)

Variable	Incidence with risk factor, n/N (%)	Incidence without risk factor, n/N (%)	Univariable			Multivariable		
			Odds ratio	95% CI	P value	Odds ratio	95% CI	P value
Preoperative shock	10/15 (66.7%)	8/31 (25.8%)	5.75	1.57–23.76	P = 0.008	1.71	0.25–16.83	P = 0.598
SOFA-H (≥3)	15/26 (57.7%)	3/20 (15.0%)	7.72	2.00–39.31	P = 0.002	6.45	1.09–55.21	P = 0.039
cfDNA-H (>746 ng/mL)	16/23 (69.6%)	2/23 (8.7%)	24.00	5.21–178.71	P < 0.001	25.91	3.79–315.11	P < 0.001

SOFA, Sequential Organ Failure Assessment; CI, Confidence Interval; cfDNA-H, Preoperative Plasma Cell-Free DNA Value > 746 ng/mL; SOFA-H, Preoperative SOFA ≥ 3

Table 4. Association between preoperative cfDNA levels and postoperative outcomes

Outcome	cfDNA-L (≤746 ng/mL) (n = 23)	cfDNA-H (>746 ng/mL) (n = 23)	P value
Norepinephrine use	3 (13.0%)	18 (78.3%)	P < 0.001
Vasopressin use	1 (4.4%)	12 (52.2%)	P = 0.001
Thrombomodulin use	1 (4.4%)	11 (47.8%)	P = 0.002
CHDF use	2 (8.7%)	14 (60.9%)	P < 0.001
30-day postoperative mortality	0 (0%)	1 (4.4%)	1.000

90-day postoperative mortality	2 (8.7%)	2 (8.7%)	1.000
Duration of mechanical ventilation (days)	0.0 (0.0–47.0)	4.5 (0.0–37.0)	P < 0.001
ICU stay (days)	0.0 (0.0–19.0)	9.0 (0.0–23.0)	P < 0.001
Postoperative hospital stay (days)	14.5 (2.0–30.0)	13.0 (2.0–31.0)	P = 0.669

2 Values are expressed as median (range) or number (percentage), as appropriate.

3 cfDNA-H; Preoperative Plasma Cell-Free DNA Value > 746 ng/mL, cfDNA-L; Preoperative Plasma Cell-Free DNA Value ≤ 746 ng/mL,

4 CHDF; Continuous Hemodiafiltration, ICU; Intensive Care Unit.

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Supplementary Files

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- Additionalfile1.docx