The Impact of Anesthesia and Surgical Intervention on Liver and Kidney Function in Patients With Gynecological Malignancies

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AIM: Gynecological malignancies are common cancers in women, with postoperative liver and kidney function impairment significantly impacting long-term prognosis. Therefore, this study aimed to evaluate the effects of anesthesia and surgical interventions on postoperative liver and kidney function in patients with gynecological malignancies and explore its association with long-term survival outcomes.
METHODS: This single-center retrospective cohort study included 153 patients who underwent surgery for ovarian cancer (50 cases), endometrial cancer (63 cases), and cervical cancer (40 cases) at Peking University International Hospital between 2018 and 2023. Demographic data, anesthesia methods (general or regional), surgical approaches (laparoscopic or open), and perioperative hepatorenal function indicators (Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Total Bilirubin (TBIL), creatinine and urea) were analyzed. Multivariate regression analysis adjusted for potential confounders, and survival models assessed long-term patient outcomes.
RESULTS: Analysis of variance (ANOVA) revealed significant differences among the three cohorts in postoperative levels of ALT ($p = 0.044$), AST ($p < 0.001$), TBIL ($p < 0.001$), creatinine ($p = 0.026$), and urea ($p < 0.001$). Within each cohort, significant postoperative elevations were observed for ALT, AST, TBIL, creatinine, and urea compared to preoperative levels (all $p < 0.05$). Intergroup comparisons revealed that cervical cancer patients exhibited the most severe biochemical disturbances (95% stage IV, $p < 0.001$), with significant postoperative decreases in red blood cell (RBC) count ($p < 0.001$), hemoglobin (Hb) levels ($p < 0.001$), and platelet count ($p = 0.003$), alongside a substantial increase in white blood cell (WBC) count ($p < 0.001$). Multivariate linear regression analysis revealed that advanced tumor stage (Stage IV vs. I) was independently associated with elevated postoperative ALT ($p = 0.001$), AST ($p < 0.001$), TBIL ($p < 0.001$), and urea ($p = 0.002$) levels; however, its association with creatinine levels did not reach statistical significance ($p > 0.05$). Further analysis demonstrated that open surgery (vs. laparoscopic) significantly predicted increased creatinine ($p = 0.002$) and urea ($p = 0.015$) levels and TBIL ($p = 0.002$), whereas no significant effects were observed on ALT or AST ($p > 0.05$). Moreover, prolonged operative time (per 10 minutes) independently contributed to elevated AST ($p = 0.015$), TBIL ($p = 0.018$), and urea levels ($p < 0.001$). Similarly, intraoperative blood loss (per 100 mL) was associated with higher AST ($p = 0.002$), TBIL ($p = 0.003$), and urea levels ($p = 0.003$), while its associations with ALT ($p = 0.083$) and creatinine ($p = 0.089$) were not significant. Notably, pathological grade (G3 vs. G1), mode of anesthesia (general vs. local anesthesia), and age were not significantly associated with these biomarkers ($p > 0.05$). Furthermore, survival analysis revealed significantly reduced 5-year survival in patients with hepatorenal dysfunction, with survival curves diverging markedly from 32 months post-surgery ($p < 0.001$).
CONCLUSIONS: Perioperative hepatorenal injury in gynecological malignancies is independently associated with tumor stage, open surgery, prolonged operative time, intraoperative blood loss, and tumor biology, and it critically impacts long-term survival. Therefore, minimally invasive techniques and optimizing perioperative management are essential to reduce organ damage and improve patient outcomes.

Keywords: gynecological malignancies; anesthesia; surgical intervention; hepatorenal function; survival analysis

Introduction

Gynecological malignancies, such as ovarian, endometrial, and cervical cancers, are the common types of cancer posing a significant threat to women's health [1]. Surgical resection is one of the primary treatment modalities for these malignancies, with both anesthesia and surgical interventions playing a crucial role in the treatment process [2,3]. However, despite their pivotal role in tumor removal and facilitating recovery, these procedures can significantly impact liver and kidney function [4]. As vital metabolic and excretory organs, the liver and kidneys are crucial for optimal postoperative recovery and favorable long-term prognosis [5,6].

In recent years, advancements in perioperative management have drawn growing attention to the impact of anesthesia and surgery on liver and kidney function. General anesthetic agents may impair liver and kidney function by inhibiting hepatic metabolic enzymes, altering renal hemodynamics, or exerting direct toxic effects [7,8]. Addition-

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ally, surgical trauma can trigger systemic inflammatory responses, ischemia-reperfusion injury, and postoperative complications (such as infections, hypotension, or drug toxicity), which can further exacerbate the burden on hepatic and renal function [9]. In patients with gynecological malignancies, these adverse events may be more pronounced due to pre-existing hepatic or renal impairment associated with the tumor or prior treatments like chemotherapy or radiotherapy [10]. However, comprehensive research and systematic analyses on perioperative liver and kidney function changes in gynecological malignancy patients remain limited.

Furthermore, the relationship between postoperative liver and kidney dysfunction and long-term patient outcomes remains inadequately elucidated. Existing evidence suggests that such dysfunction may be associated with delays in chemotherapy, dose adjustments, or even interruptions in treatment, thereby affecting the overall efficacy of tumor treatment [11,12]. However, comparative studies assessing the effects of various anesthesia methods (e.g., general anesthesia vs. regional anesthesia), surgical approaches (e.g., minimally invasive surgery vs. open surgery), and perioperative management strategies on liver and kidney function remain insufficient. More importantly, whether postoperative liver and kidney dysfunction independently affect the long-term survival of gynecological malignancy patients remains crucial that requires further exploration.

Based on the above background, this study aims to systematically evaluate the impact of anesthesia and surgical interventions on liver and kidney function in patients with gynecological malignancies, and to explore the relationship between postoperative hepatic and renal dysfunction and long-term patient outcomes. By retrospectively analyzing clinical data from patients diagnosed with ovarian, endometrial, and cervical cancers treated at Peking University International Hospital, we seek to reveal the associations between anesthesia methods, surgical approaches, and postoperative changes in liver and kidney function. Furthermore, this study intends to elucidate whether these dysfunctions impact patient survival rates. The findings will not only contribute to optimizing perioperative management strategies to reduce postoperative liver and kidney injury but also provide valuable theoretical evidence for improving the long-term prognosis of patients with gynecological malignancies.

Methods

Study Design and Research Participants

This is a single-center retrospective cohort study designed to systematically evaluate the impact of anesthesia and surgical interventions on liver and kidney function in patients with gynecological malignancies, and to explore the association between postoperative liver and kidney dysfunction and long-term patient outcomes. The study population consisted of female patients diagnosed with ovarian, endometrial, or cervical cancers who underwent surgical treatment at Peking University International Hospital between 1 January 2018, and 31 December 2023. All patients met the following inclusion criteria: (1) pathologically confirmed diagnosis of ovarian, endometrial, or cervical cancers; (2) complete pre- and postoperative liver and kidney function assessments, including Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Total Bilirubin (TBIL), creatinine and urea levels; (3) underwent surgical treatment, such as laparoscopic or open surgery, with general or local anesthesia; (4) no pre-existing severe liver or kidney dysfunction (e.g., cirrhosis, end-stage renal disease) or other significant comorbidities affecting hepatic and renal function. However, the exclusion criteria included: (1) patients who did not undergo surgical treatment; (2) patients with missing or incomplete postoperative follow-up data; (3) those with severe complications, such as cardiovascular disease or diabetes, that could significantly impact postoperative recovery; and (4) patients with missing or substantially abnormal clinical laboratory findings.

Data Collection

The baseline data for all participants were extracted from the electronic medical record system and postoperative follow-up database of Peking University International Hospital. The collected clinical data included: (1) patient demographics, such as age, tumor type, tumor stage, and pathological grade. Tumor staging was performed based on the 2018 criteria of the International Federation of Gynecology and Obstetrics (FIGO) [13]; and for consistency, stages were recorded as IA, IB, II, III, and IV, without subclassifications (e.g., IIIA, IIIB, IIIC); (2) perioperative data, such as anesthesia method, surgical approach, surgery duration, anesthesia time, intraoperative blood loss; (3) pre- and postoperative liver and kidney function indicators (ALT, AST, TBIL, creatinine, urea); (4) postoperative hematological parameters (red blood cell count, hemoglobin, white blood cell count, platelet count); and (5) long-term follow-up data, including overall survival (OS).

Follow-up Strategy

Overall survival (OS) was defined as the time from surgery date to death from any cause. Patients who remained alive at the end of the study period were censored at their last follow-up date. The follow-up period began on the day of surgery and ended on 31 December 2023, or the date of death, whichever occurred first. Patients were regularly followed up every 3 months during the first 2 years, every 6 months over the next 3 years, and annually thereafter. Follow-up evaluations included clinical examinations, imaging studies (such as computed tomography or magnetic resonance imaging), and laboratory tests (such as liver and kidney function tests and tumor markers). Data regarding disease recurrence, metastasis, and survival status were collected during each follow-up visit. Patients who missed scheduled follow-up appointments were contacted via telephone or their data were obtained through a review

of electronic medical records to ensure complete data collection.

Data Processing and Statistical Analysis

All data were analyzed using Statistical Product and Service Solutions software (version: 26.0, IBM Corporation, Armonk, NY, USA). Initially, continuous variables were tested for normality using the Shapiro-Wilk test, with normally distributed continuous variables presented as mean ± standard deviation. Multiple group comparisons were performed using a one-way analysis of variance (ANOVA). Paired pre- and postoperative data were compared using paired *t*-tests. Categorical variables were expressed as frequencies and percentages, with intergroup comparison conducted using chi-square tests (χ^2 tests) or Fisher's exact tests, as appropriate.

Multivariate linear regression models were applied to analyze changes in liver and kidney function indicators, including ALT, AST, TBIL, creatinine, and urea. These models were adjusted for potential confounding factors, including tumor stage, pathological grade, surgical approach (laparoscopic vs. open), anesthesia method (general vs. regional), surgery duration, intraoperative blood loss, and individual age.

For survival analysis, patients were stratified into "normal liver or kidney function" and "abnormal liver or kidney function" groups based on postoperative liver (ALT, AST) and kidney (creatinine) biomarkers. The abnormal liver function was defined as ALT >40 U/L or AST >35 U/L, and abnormal kidney function as creatinine >1.5× baseline or >1.5 mg/dL (the kidney disease: Improving Global Outcomes criteria). Both overall survival rates (calculated as the proportion of surviving patients at study termination) and time-to-event outcomes (including median survival time and cumulative survival probabilities) were analyzed. The Kaplan-Meier survival curves were generated to estimate median survival times, with between-group comparisons performed using the log-rank test. A *p*-value of <0.05 was considered statistically significant. Disease-free survival (DFS) data were incomplete due to limitations in follow-up documentation and were excluded from formal analysis.

Results

Comparison of Demographic Characteristics in Patients With Ovarian, Endometrial, and Cervical Cancers

This study included a cohort of 153 patients, comprising 50 cases of ovarian cancer (mean age 48.1 ± 8.5 years), 63 cases of endometrial cancer (mean age 49.3 ± 6.7 years), and 40 cases of cervical cancer (mean age 47.9 ± 9.3 years). The age differences among the three groups did not reach statistical significance ($p = 0.618$).

In terms of tumor staging, the majority of ovarian cancer patients presented with advanced disease, with 24 (48%) cases designated as stage IV and 16 (32%) cases as stage III, while stages I and II were less frequent. The stage distribution was relatively balanced among endometrial cancer patients, including 25 cases (39.7%) at stage I, 8 cases (12.7%) at stage II, 5 cases (7.9%) at stage III, and 25 cases (39.7%) at stage IV. In contrast, cervical cancer patients exhibited significant differences in the staging, with 38 cases (95%) identified at stage IV, no cases at stages I and III, and only 2 cases (5%) at stage II (Table 1). These results indicate a significantly higher proportion of advanced-stage (stage IV) cases among cervical cancer patients compared to other types of gynecological cancers, while ovarian cancer patients also show a predominance of advanced-stage (III–IV) cases.

Regarding pathological grading, most ovarian cancer patients were classified as G2, accounting for 27 cases (54%), while G1 and G3 were less frequent, with 12 cases (24%) and 11 cases (22%), respectively. Among endometrial cancer patients, pathological grading was relatively balanced, with 28 cases (44.4%) classified as G1 and 28 cases (44.4%) as G2, while only 7 cases (11.1%) were classified as G3. Among cervical cancer patients, G3 was the predominant grade, observed in 22 cases (55%), followed by G2 in 14 cases (35%), and G1 in only 4 cases (10%) (Table 1). These results indicate that the proportion of G2 cases was significantly higher in ovarian cancer, potentially highlighting the tumor's unique biological characteristics and progression mechanisms. In contrast, the relatively balanced pathological grading among endometrial and cervical cancers suggests greater variability in the malignancy of these tumors. Furthermore, the significant differences in pathological grading among different tumor types underscore the crucial role of pathological grading in assessing patient prognosis and formulating personalized treatment strategies.

Analysis of perioperative data revealed that cervical cancer patients experienced significantly higher intraoperative blood loss compared to those with ovarian and endometrial cancer (320 ± 95 mL vs. 250 ± 85 mL and 220 ± 70 mL, $p < 0.001$), and received open surgery more frequently (77.5% vs. 56% and 52.4%, $p = 0.031$). This discrepancy aligns with the high proportion of advanced-stage cervical cancer cases (95% stage IV), which often require extensive surgical resection. Additionally, surgery duration (162 ± 28 min) and anesthesia time (135 ± 25 min) were significantly longer in cervical cancer patients ($p < 0.05$). While no significant differences were observed in the choice of anesthesia method (general vs. regional) across the groups ($p = 0.609$), general anesthesia was most frequently used in cervical cancer cases (80%), likely highlighting the greater surgical complexity (Table 1).

Comparative Analysis of Preoperative and Postoperative Changes in Liver and Kidney Function in Patients With Ovarian, Endometrial, and Cervical Cancers

Preoperative and postoperative analysis of liver and kidney function markers using ANOVA showed significant differences in AST, TBIL, creatinine, and urea levels across the three cancer groups (Table 2). Furthermore, pair-wise

Table 1. Comparison of basic clinical features in patients with three cancer types.

Characteristics	Ovarian cancer (n = 50)	Endometrial cancer (n = 63)	Cervical cancer (n = 40)	χ^2/F-value	*p*-value
Age (mean ± SD)	48.1 ± 8.5	49.3 ± 6.7	47.9 ± 9.3	0.483	0.618
Stage				55.76	<0.001
I	7 (14%)	25 (39.7%)	0 (0%)		
II	3 (6%)	8 (12.7%)	2 (5%)		
III	16 (32%)	5 (8%)	0 (0%)		
IV	24 (48%)	25 (39.7%)	38 (95%)		
Pathological grade				30.98	<0.001
G1	12 (24%)	28 (44.4%)	4 (10%)		
G2	27 (54%)	28 (44.4%)	14 (35%)		
G3	11 (22%)	7 (11.1%)	22 (55%)		
Anesthesia method				0.99	0.609
General	38 (76%)	45 (71.4%)	32 (80%)		
Regional	12 (24%)	18 (28.6%)	8 (20%)		
Surgical approach				6.97	0.031
Laparoscopic	22 (44%)	30 (47.6%)	9 (22.5%)		
Open	28 (56%)	33 (52.4%)	31 (77.5%)		
Surgery duration (min)	145 ± 35	138 ± 42	162 ± 28	5.35	0.006
Anesthesia time (min)	120 ± 28	115 ± 30	135 ± 25	6.35	0.002
Intraoperative blood loss (mL)	250 ± 85	220 ± 70	320 ± 95	18.37	<0.001

Table 2. Comparative analysis of preoperative and postoperative changes in liver and kidney function in patients with ovarian, endometrial, and cervical cancers.

Indicator	Ovarian cancer preoperative	Ovarian cancer postoperative	Endometrial cancer preoperative	Endometrial cancer postoperative	Cervical cancer preoperative	Cervical cancer postoperative	F-value	*p*-value
ALT (U/L)	20.5 ± 10.3	25.4 ± 12.1*	25.85 ± 11.0	30.6 ± 13.4*	20.7 ± 5.8	30.6 ± 9.0***	3.18	0.044
AST (U/L)	17.3 ± 8.9	21.1 ± 9.7*	24.88 ± 9.1	29.72 ± 12.2*	19.2 ± 5.5	28.45 ± 8.5***	10.19	<0.001
TBIL (mg/dL)	0.77 ± 0.35	0.95 ± 0.40*	0.95 ± 0.31	1.25 ± 0.32***	0.85 ± 0.30	1.05 ± 0.28**	11.49	<0.001
Creatinine (μmol/L)	50.78 ± 9.22	54.84 ± 10.24*	48.96 ± 23.3	57.3 ± 22.4*	56.1 ± 18.3	64.3 ± 12.4*	3.73	0.026
Urea (mmol/L)	4.4 ± 2.1	5.3 ± 2.3*	4.5 ± 1.7	5.8 ± 3.5**	5.5 ± 2.1	8.4 ± 1.5***	16.41	<0.001

Note: ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; TBIL, Total Bilirubin. One-way analysis of variance was used for the comparison of the three groups of patients after the operation. Comparisons with preoperative levels, *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

comparisons revealed that, in ovarian cancer patients, postoperative levels of ALT ($p = 0.0316$), AST ($p = 0.0439$), TBIL ($p = 0.0185$), creatinine ($p = 0.0398$), and urea ($p = 0.0437$) were significantly elevated compared to preoperative levels. Similarly, in endometrial carcinoma, ALT ($p = 0.0316$), AST ($p = 0.0129$), TBIL ($p < 0.001$), creatinine ($p = 0.0427$), and urea ($p = 0.0091$) levels were significantly increased after surgery. In cervical cancer patients, postoperative ALT ($p < 0.001$), AST ($p < 0.001$), TBIL ($p = 0.0028$), creatinine ($p = 0.0215$), and urea ($p < 0.001$) levels were also significantly increased.

Comparative Analysis of Preoperative and Postoperative Changes in Hematological Indicators in Patients With Ovarian, Endometrial, and Cervical Cancers

Dynamic changes in hematological parameters in patients with ovarian, endometrial, and cervical cancers revealed significant intergroup differences in postoperative hematological indicators ($p < 0.05$). Within-group comparisons demonstrated that cervical cancer patients experienced significant postoperative decreases in red blood cell (RBC) ($p < 0.001$), hemoglobin (Hb) ($p < 0.001$), and platelet (PLT) ($p = 0.0479$), alongside a significant increase in white blood cell (WBC) ($p < 0.001$) count. In contrast, although postoperative levels of RBC, Hb, WBC, and PLT showed slight increases in the ovarian and endometrial cancer groups, these changes were statistically insignificant ($p > 0.05$, Table 3). These findings suggest that cervical cancer patients may be more susceptible to perioperative hematological changes, indicating a higher risk of anemia, inflammatory responses, or hemorrhagic complications compared to other cohorts.

Multivariate Linear Regression Analysis of Factors Associated With Postoperative Liver and Kidney Function

Multivariate linear regression analysis demonstrated that advanced tumor stage (Stage IV vs. I) was significantly associated with elevated postoperative ALT ($\beta = 8.21$, standard error (SE) = 2.15, $p < 0.001$), AST ($\beta = 9.85$, SE =

Table 3. Comparative analysis of preoperative and postoperative changes in hematological indicators in patients with ovarian, endometrial, and cervical cancers.

Indicator	Ovarian cancer preoperative	Ovarian cancer postoperative	Endometrial cancer preoperative	Endometrial cancer postoperative	Cervical cancer preoperative	Cervical cancer postoperative	F-value	*p*-value
RBC ($\times 10^{12}$/L)	4.58 ± 0.64	4.82 ± 0.72	4.32 ± 0.70	4.50 ± 0.60	4.32 ± 0.50	3.42 ± 0.55***	59.15	<0.001
Hb (g/dL)	12.3 ± 1.4	12.5 ± 1.3	12.1 ± 1.3	12.3 ± 1.2	10.4 ± 1.2	8.5 ± 1.1***	153.2	<0.001
WBC ($\times 10^{9}$/L)	6.3 ± 2.5	6.5 ± 2.3	6.5 ± 2.0	6.8 ± 2.3	7.9 ± 1.5	11.5 ± 1.7***	74.21	<0.001
PLT ($\times 10^{9}$/L)	230 ± 67	255 ± 72	264 ± 74	270 ± 80	250 ± 70	215 ± 85*	6.061	0.003

Note: RBC, red blood cell; Hb, hemoglobin; WBC, white blood cell; PLT, platelet. One-way analysis of variance was used for the comparison of the three groups of patients after the operation. Comparisons with preoperative levels, *$p < 0.05$, ***$p < 0.001$.

Table 4. Multivariate linear regression analysis of factors associated with postoperative liver and kidney function.

Variable	ALT (U/L) β (SE)	AST (U/L) β (SE)	TBIL (mg/dL) β (SE)	Creatinine (μmol/L) β (SE)	Urea (mmol/L) β (SE)
Tumor Stage (Ref: I)					
Stage IV vs. I	8.21 (2.15)***	9.85 (2.43)***	0.18 (0.05)***	4.12 (2.01)	1.25 (0.45)**
Surgical approach					
Open vs. Laparoscopic	2.15 (1.32)	3.02 (1.67)	0.12 (0.04)**	6.32 (1.98)**	0.78 (0.31)*
Surgery Duration (per 10 min)	0.05 (0.02)	0.07 (0.03)*	0.01 (0.003)*	0.03 (0.01)	0.12 (0.03)***
Intraoperative Blood Loss (per 100 mL)	0.04 (0.01)	0.06 (0.02)**	0.02 (0.006)**	0.02 (0.01)	0.08 (0.02)**
Pathological Grade (Ref: G1)					
G3 vs. G1	1.12 (1.45)	1.89 (1.82)	0.05 (0.02)	0.95 (1.20)	0.33 (0.28)
Anesthesia Method					
General vs. Regional	1.23 (0.98)	1.56 (1.22)	0.02 (0.01)	1.05 (0.75)	0.12 (0.09)
Age (per 1 year)	0.05 (0.03)	0.06 (0.04)	0.003 (0.002)	0.01 (0.01)	0.02 (0.01)

Notes: β, regression coefficient; SE, standard error. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

2.43, $p < 0.001$), TBIL ($\beta = 0.18$, SE = 0.05, $p < 0.001$), and urea ($\beta = 1.25$, SE = 0.45, $p = 0.002$) levels. However, it showed no significant association with creatinine ($\beta = 4.12$, SE = 2.01, $p = 0.058$) levels. Furthermore, compared to the laparoscopic approach, open surgery was significantly associated with increased creatinine ($\beta = 6.32$, SE = 1.98, $p = 0.002$), urea ($\beta = 0.78$, SE = 0.31, $p = 0.015$), and TBIL ($\beta = 0.12$, SE = 0.04, $p = 0.002$) levels. However, its associations with ALT ($\beta = 2.15$, SE = 1.32, $p = 0.104$) and AST ($\beta = 3.02$, SE = 1.67, $p = 0.071$) did not achieve statistical significance.

Prolonged operative time (per 10-minute increment) was independently associated with elevated AST ($\beta = 0.07$, SE = 0.03, $p = 0.015$), TBIL ($\beta = 0.01$, SE = 0.003, $p = 0.018$), and urea ($\beta = 0.12$, SE = 0.03, $p < 0.001$) levels, but not with ALT ($\beta = 0.05$, SE = 0.02, $p = 0.052$) or creatinine ($\beta = 0.03$, SE = 0.01, $p = 0.067$). Intraoperative blood loss (per 100 mL) was significantly correlated with higher AST ($\beta = 0.06$, SE = 0.02, $p = 0.002$), TBIL ($\beta = 0.02$, SE = 0.006, $p = 0.003$), and urea ($\beta = 0.08$, SE = 0.02, $p = 0.003$), whereas its associations with ALT ($\beta = 0.04$, SE = 0.01, $p = 0.083$) and creatinine ($\beta = 0.02$, SE = 0.01, $p = 0.089$) were not significant.

Interestingly, pathological grade (G3 vs. G1) showed no significant association with any of the hepatic or renal function biomarkers (ALT: $\beta = 1.12$, SE = 1.45, $p = 0.441$; AST: $\beta = 1.89$, SE = 1.82, $p = 0.301$; TBIL: $\beta = 0.05$, SE = 0.02, $p = 0.112$; creatinine: $\beta = 0.95$, SE = 1.20, $p = 0.432$; urea: $\beta = 0.33$, SE = 0.28, $p = 0.241$). Likewise, anesthesia method (general vs. regional) demonstrated no significant effects on postoperative hepatic or renal dysfunction (ALT: $\beta = 1.23$, SE = 0.98, $p = 0.211$; AST: $\beta = 1.56$, SE = 1.22, $p = 0.202$; TBIL: $\beta = 0.02$, SE = 0.01, $p = 0.089$; creatinine: $\beta = 1.05$, SE = 0.75, $p = 0.162$; urea: $\beta = 0.12$, SE = 0.09, $p = 0.183$). Additionally, Age (each increase of 1 year) and ALT ($\beta = 0.05$, SE = 0.03, $p = 0.102$); AST ($\beta = 0.06$, SE = 0.04, $p = 0.122$); TBIL ($\beta = 0.003$, SE = 0.002, $p = 0.061$); creatinine ($\beta = 0.01$, SE = 0.01, $p = 0.072$); urea ($\beta = 0.02$, SE = 0.01, $p = 0.089$) had no significant difference (Table 4).

Association Between Postoperative Liver/Kidney Dysfunction and Long-term Survival in Patients With Gynecological Malignancies

To evaluate the impact of postoperative liver and kidney dysfunction on overall survival (OS), patients were stratified into two groups based on postoperative biomarkers (ALT, AST, creatinine): "normal hepatorenal function group" (n = 78) and "poor hepatorenal function group" (n = 75). Over a median follow-up of 36 months (range: 6–60 months), 45 deaths were recorded, including 32 (42.7%) in the poor function group and 13 (16.7%) in the normal function group. Kaplan-Meier analysis revealed a significantly reduced cumulative survival probability in the poor

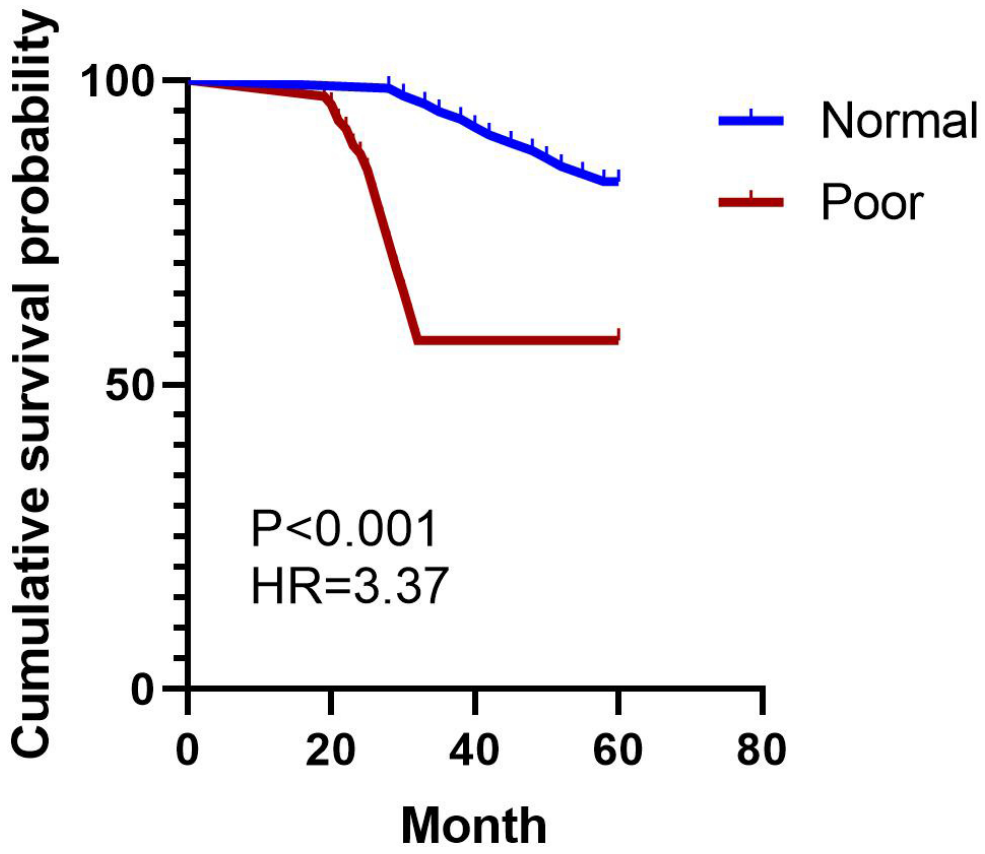

Fig. 1. Association between postoperative liver/kidney dysfunction and long-term survival in patients with gynecological malignancies. Images were created using GraphPad Prism 8 (version 8.0.2, GraphPad Software, Danaher Corporation, San Diego, CA, USA). Note: Cumulative survival probabilities and overall survival rates differ in the calculation: the former focuses on time-dependent risks, while the latter reflects endpoint event proportions. HR, hazard ratio.

function group (log-rank [Mantel-Cox] test: $\chi^2 = 15.89$, $p < 0.001$). At the end of the follow-up, the OS rates were 83.3% (65/78) in the normal function group and 57.3% (43/75) in the poor function group. The median OS was undefined in either group due to >50% of patients remaining alive at the study cutoff (censoring rates: 83.3% in the normal function group vs. 57.3% in the poor function group).

The survival curves began to diverge gradually around 24 months post-surgery, with a statistically significant increase in mortality risk in the poor function group emerging after 32 months. This separation remained sustained and clinically meaningful throughout the follow-up period (hazard ratio (HR) = 3.37, 95% confidence interval (CI): 1.85–6.12, $p < 0.001$).

These findings underscore the critical prognostic significance of the postoperative hepatorenal function in determining long-term survival outcomes among patients with gynecological malignancies. The association between postoperative liver and kidney dysfunction and long-term survival is shown in Fig. 1.

Discussion

Gynecological malignancies, including ovarian, endometrial, and cervical cancers, are among the most common cancers affecting women worldwide, with surgical resection being a primary treatment strategy [14]. However, the perioperative period poses significant risks to liver and kidney function, which are critical for postoperative recovery and long-term survival [15,16]. While the impact of anesthesia and surgical interventions on hepatorenal function has been studied in various contexts, systematic analyses focusing on gynecological cancer patients remain limited [17]. This study aimed to evaluate the effects of different anesthesia methods and surgical approaches on postoperative liver and kidney function in these patients and to explore the association between hepatorenal dysfunction and long-term survival outcomes. By addressing these gaps, our findings contribute to the growing body of evidence on perioperative organ protection and its implications for cancer survivorship.

The findings of this study demonstrated significant postoperative elevations in liver and kidney function biomarkers (ALT, AST, TBIL, creatinine, and urea) across ovarian, endometrial, and cervical cancer patients, with cervical cancer patients exhibiting the most severe biochemical disturbances. This phenomenon may be attributed to the predominance of advanced-stage cervical cancer cases (95% stage IV) and greater surgical trauma in this group, as indicated by the predominance of open surgeries (77.5%) and

higher intraoperative blood loss. Previous studies have suggested that advanced gynecological malignancies are often associated with tumor infiltration, vascular invasion, and systemic inflammation [18–20]. Consistent with our results, the available research shows that open surgery, due to extensive tissue exposure and increased inflammatory cytokine release, is more likely to elevate liver enzymes and impair renal function compared to laparoscopic approaches [21,22]. Additionally, the significant postoperative hematological alterations in cervical cancer patients, such as reduced RBC, Hb, and PLT, along with elevated WBC levels, indicate higher risks of anemia, inflammatory responses, and hemorrhagic complications, likely linked to systemic tumor burden and surgical complexity [23]. These findings underscore the need for enhanced perioperative blood management and anti-inflammatory support in advanced cervical cancer patients.

Multivariate regression revealed that open surgery (compared to laparoscopic approaches) independently predicted elevated creatinine and urea levels. Additionally, prolonged operative time (per 10 minutes) was substantially correlated with increased AST, TBIL and urea levels, while intraoperative blood loss was associated with higher AST, TBIL and urea levels. These results resonate with Shi *et al*. [24], who demonstrated that minimally invasive techniques reduce postoperative organ injury by mitigating inflammation. Prolonged operative time may contribute to tissue hypoxia and metabolic waste accumulation, whereas blood loss can directly compromise renal perfusion, exacerbating tubular damage [25,26]. These observations highlight the significance of prioritizing laparoscopic approaches, optimizing surgical efficiency, and employing goal-directed fluid management approaches to minimize blood loss and preserve hepatorenal function.

Survival analysis showed a significantly reduced 5-year survival rate in patients with postoperative hepatorenal dysfunction, consistent with findings from previous research [27–29]. Li *et al*. [29] reported that chemotherapy drugs, especially platinum-based compounds, are associated with an increased risk of acute renal insufficiency and may even aggravate or lead to renal failure in patients with gynecological tumors. Therefore, measures to prevent and treat renal dysfunction in patients with gynecological malignant tumors during chemotherapy are crucial, and the chemotherapy regimen for patients with renal dysfunction should be adjusted [29]. For example, hepatic impairment can reduce platinum drug metabolism, while renal dysfunction exacerbates nephrotoxicity, potentially creating a vicious cycle of "treatment interruption-tumor progression" [29,30]. The significantly poor survival outcomes in cervical cancer patients may stem from advanced-stage disease, postoperative complications, and reduced treatment tolerance to systemic therapies. These results emphasize that perioperative hepatorenal protection is critical for facilitating short-term recovery and enhancing long-term survival outcomes. The early detection of subclinical organ injury using advanced biomarkers, such as neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1), followed by timely clinical intervention, is strongly warranted [31,32].

Notably, this study observed no statistically significant differences in postoperative hepatic and renal function between patients who received general anesthesia and those who underwent regional anesthesia across gynecological malignancies (ovarian, endometrial, and cervical cancers). However, the higher use of general anesthesia in cervical cancer surgeries (80%) may be attributed to its ability to support systemic hemodynamic stability during more complex surgical procedures. This observation is supported by the hemodynamic mechanisms of hypervolemic anesthesia. Previous animal studies have demonstrated that hypervolemic anesthesia maintains stable mean arterial pressure while significantly increasing cardiac output and reducing total peripheral resistance, accompanied by decreased hepatic and renal vascular resistance as well as a redistribution of intrarenal blood flow toward the medulla, leading to a reduced cortical-to-medullary blood flow ratio [33,34]. These findings suggest that hypervolemic anesthesia may optimize organ function through two key pathways: (1) increased hepatic blood flow may enhance metabolic and detoxification processes, and (2) improved medullary blood flow redistribution may improve countercurrent multiplication, enhancing filtration and reabsorption efficiency. These physiological advantages offer crucial function reserves during complex surgeries.

Furthermore, previously reported neuroendocrine responses to ketamine anesthesia further support the clinical observations of this study [35]: Ketamine has been proven to stimulate the early release of atrial natriuretic peptide (significantly elevated at 10 minutes post-anesthesia), inhibit angiotensin II levels and plasma renin activity, and result in a delayed elevation in aldosterone levels (peaking at 60 minutes post-anesthesia). This dynamic response may maintain intraoperative metabolic balance through multiple mechanisms [35]: (1) atrial natriuretic peptide antagonizes the effects of angiotensin II, increasing glomerular filtration rate while inhibiting sodium reabsorption in the proximal tubule; (2) the delayed rise in aldosterone compensates for the sodium-excreting effect induced by atrial natriuretic peptide, stabilizing water-electrolyte balance through sodium conservation; and (3) ketamine may stimulate adrenocorticotropic hormone, further promoting aldosterone secretion. These mechanisms align with the findings of this study, suggesting that the neuroendocrine modulation exerted by general anesthetics such as ketamine plays a critical role in supporting physiological homeostasis during complex surgeries (e.g., radical hysterectomy for cervical cancer) by maintaining a dynamic balance within the atrial natriuretic peptide–renin-angiotensin-aldosterone system axis. This dual modulation optimizes hemodynamics (e.g., maintaining hepatic and renal perfusion) while preventing the risk of intraoperative electrolyte disturbances.

In conclusion, the advantages of general anesthesia in gynecological oncology surgeries may be primarily due to its capacity to regulate hypervolemic hemodynamics and adaptively modulate metabolic homeostasis rather than inherent differences in hepatorenal toxicity. This provides a mechanistic rationale for prioritizing general anesthesia in complex surgical interventions.

Despite its contributions, this study has several limitations that should be acknowledged.

First, the single-center study design may limit the generalizability of the findings. However, as a tertiary referral institution with standardized surgical and anesthetic protocols, our center ensures internal validity, and the results are likely applicable to similar academic medical centers. Future multicenter studies must validate these findings in diverse patient populations and healthcare settings.

Second, the retrospective design of this study resulted in an uneven distribution of tumor stages between laparoscopic and open surgery groups, with laparoscopic procedures predominantly performed in early-stage tumors and open surgeries in advanced-stage cases. This precluded a meaningful comparison between surgical approaches within the same tumor stage. Future prospective studies should stratify patients by tumor stage for a more balanced comparison and accurate assessment of laparoscopic versus open surgical outcomes.

Third, the retrospective nature of this study limited access to detailed pharmacological data, including specific anesthetic agents used (e.g., isoflurane and propofol) and their dosages. While this restricts the mechanistic understanding of anesthesia-related hepatorenal dysfunction, the study's primary aim was to evaluate the overall impact of anesthesia methods and surgical interventions. Future prospective studies should incorporate comprehensive pharmacological data to explore these mechanistic insights.

Fourth, while we adjusted for key confounders such as age and tumor stage, unmeasured variables like genetic polymorphisms in drug-metabolizing enzymes or baseline inflammatory status may have influenced patient outcomes. These factors could alter individual metabolic responses to anesthesia and surgery, affecting liver and kidney function. Future studies should consider incorporating genetic and inflammatory markers to better account for these interindividual variables. Fifth, the study's reliance on conventional biomarkers (ALT, AST, creatinine) may underestimate subclinical organ injury, as more sensitive indicators like NGAL or KIM-1 were not routinely assessed. These novel biomarkers could provide earlier and more sensitive detection of organ dysfunction, potentially leading to more prompt therapeutic interventions. Future research should integrate these advanced biomarkers to enhance the sensitivity of subclinical injury detection.

Finally, the lack of long-term and longitudinal functional assessments beyond survival outcomes limits insights into the chronic sequelae of perioperative hepatorenal injury, such as progressive fibrosis, chronic kidney disease, or the development of metabolic syndrome. Future multicenter prospective studies incorporating advanced biomarkers, imaging modalities, pharmacogenomic profiling, and extended follow-up are needed to provide a more comprehensive understanding of perioperative organ injury.

Conclusions

In conclusion, our findings highlight that (1) patients with advanced-stage gynecological malignancies are at higher risk of postoperative hepatorenal injury, necessitating personalized surgical approaches; (2) minimally invasive techniques, operative efficiency, and effective blood loss management are pivotal for preserving liver and kidney function; and (3) postoperative hepatorenal dysfunction critically impacts long-term survival, warranting the significance of integrating perioperative organ protection into comprehensive oncologic care. Future research should incorporate multi-omics technologies and novel biomarkers to optimize perioperative management and improve patient outcomes.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

JYZ and JYF contributed equally to this work and share first authorship. JYZ designed the study and collected the data. JYF performed the data analysis and wrote the manuscript. CZY contributed to the data collection and patient follow-up. ZD jointly participated in data analysis and interpretation. GYX provided technical support for the research. LY supervised the study, provided critical revisions to the manuscript, and collected data. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study strictly adheres to the ethical principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of Peking University International Hospital (2022-KY-0046). Written informed consent was obtained from all participants before data collection.

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Conflict of Interest

The authors declare no conflict of interest.

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