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Anesthesia management and outcomes of gynecologic oncology surgery

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ORIGINAL RESEARCH

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Anesthesia management and outcomes of gynecologic oncology surgery

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ABSTRACT

Objectives: This study assessed postoperative mortality, morbidity, and complications associated with anesthesia administration for gynecologic oncology abdominal surgery and investigated the risk factors for the development of these complications

Methods: We conducted a retrospective cohort study analyzing the data of patients who underwent elective gynecologic oncology surgery between 2010 and 2017. The demographic data; comorbidities; preoperative anemia; Charlson Comorbidity Index; anesthesia management; complications; preoperative, intraoperative, and postoperative periods; mortality; and morbidity were investigated. The patients were classified as surviving or deceased. Subgroup analyses of patients with endometrial, ovarian, cervical, and other cancers were performed.

Results: We analyzed 416 patients; 325 survived and 91 were deceased. The postoperative chemotherapy rates ($p < 0.001$), and postoperative blood transfusion rates ($p = 0.010$) were significantly higher in the deceased group, while the preoperative albumin levels were significantly lower in the deceased group ($p < 0.001$). Infused colloid amount was higher in the deceased group of endometrial ($p = 0.018$) and ovarian cancers ($p = 0.017$).

Conclusions: Perioperative patient management for cancer surgery requires a multidisciplinary approach led by an anesthesiologist and surgeon. Any improvement in the duration of hospital stay, morbidity, or recovery rate depends on the success of the multidisciplinary team.

PLAIN LANGUAGE SUMMARY

Cancer surgeries in the female reproductive system can sometimes cause severe complications, including death. Proper anesthesia management is crucial to reducing such negative outcomes. This study looked at patient records to understand the factors that led to bad results with anesthesia. Researchers focused on both pre-surgery preparations and post-surgery care. They found that factors like needing a blood transfusion, wound infections, getting chemotherapy after surgery, and low blood albumin levels increased the death rate. Strict monitoring of fluid balance and blood circulation during surgery improved survival chances. The work begins long before the operating theater. Anesthesiologists should carefully assess patients before surgery, and teamwork between the anesthesiologist and surgeon is vital throughout treatment. Identifying risks, taking precautions, and minimizing high-risk interventions can decrease the days passed at the hospital, improve recovery, and reduce deaths from surgery complications.

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Gynecology; oncology; anesthesia; mortality; morbidity; complication

1. Introduction

About 8.8 million people die annually from cancer worldwide. Breast, colorectal, lung, and cervical cancers are the four most common types of cancer in women. In addition to cervical cancer, other gynecological cancers, such as uterine cancers (sixth most common) and ovarian cancer (eighth most common) are also frequent [1].

According to the Turkish Cancer Statistics report, the most common cancer observed in women in 2013 was breast cancer, with an incidence rate of 45.9/100,000 individuals. Moreover, the incidence rates for gynecological cancers were 9.9/100,000 for uterine cancers (fifth most common), 7.0/100,000 for ovarian cancers (seventh most common), and 4.6/100,000 for cervical cancers (tenth most common). The same report investigated deaths linked to cancer among women in Turkey in 2009 and found that ovarian cancer was seventh accounting for 5% of deaths, uterine cancer was ninth accounting for 2.9% of deaths, and cervical cancer was tenth accounting for 2% of deaths. The latest cancer data show that gynecological cancers in Turkey are among the top ten in terms of both incidence and mortality [2].

Among those undergoing anesthesia, the proportion of patients receiving cancer treatment is increasing [3]. When patients with cancer require anesthesia, several factors must be considered, including the regional or systemic effects of anesthesia due to the comorbidities, cancer, or treatments received for cancer, as well as the direct or indirect effects of anesthesia management on cancer recurrence and metastasis. Therefore, anesthesia methods and management should be determined after careful assessment of these factors [4].

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Several substances affect patients with cancer in different ways. For instance, benzodiazepines reduce cytokine release due to their central immunomodulatory effects as well as by easing surgical stress. Additionally, midazolam can be used to treat hiccups caused by chemotherapy [3]. Propofol can inhibit tumor growth by reducing cyclooxygenase activity and stabilizing natural killer cell function. Beta receptor antagonists may decrease cancer cell metastasis by limiting their adhesion, migration, and apoptosis. However, conflicting research exists on preoperative opioid use, with some studies indicating it can either reduce or increase postoperative metastasis. Factors such as increased COX-II receptor numbers, PGE2 production, and urokinase activity in tumor cells due to opioid use might contribute to enhanced angiogenesis and metastasis. Additionally, morphine increases the urokinase activity of tumor cells, facilitating metastasis. Finally, inhalational anesthetics exert suppressive effects on the immune system and reduce NK cell function by up to 90% [3].

This study, which was completed over a period of seven years, aimed to assess postoperative mortality, morbidity, and complications associated with anesthesia administration for gynecologic oncology abdominal surgery; further, it investigated the risk factors for the development of these complications.

2. Materials and methods

This retrospective clinical study received permission from the Non-Interventional Research Ethics Committee (protocol no: 3541-GOA, decision no: 2017/21–32) and investigated the data of all patients undergoing elective gynecologic oncology abdominal surgery from August 2010 to August 2017. The study was conducted in accordance with the Declaration of Helsinki. Data were obtained from perioperative anesthesia forms in the archives and records held in clinics by gynecological clinicians and by investigating the Hospital Information Management System. The standard informed consent forms signed by the patients at admission to the hospital for their treatment, permitted the researchers to analyze retrospective data for scientific research purposes ensuring confidentiality of the personal data of the patient (any information regarding the identity of the patient); further, the researchers have obeyed the Turkish Personal Data Protection Law.

The inclusion criteria were surgical intervention for gynecological cancer and admission to the surgical ward, post-anesthesia care unit (PACU), or anesthesia intensive care unit (AICU). Patients under 18 years of age and those with missing data in their records were excluded.

2.1. Parameters assessed

2.1.1. Demographic data

Patients were classified according to their age, height, weight, American Society of Anesthesiologists (ASA) score, BMI, smoking status, alcohol use, and comorbid diseases. We also collected information on the cancer type, history of having received chemotherapy, requirement of chemotherapy for any other reason, chemotherapy agents used, and history of radiotherapy, if any.

2.1.2. Anemia

In the preoperative period, hemoglobin values of <10 g/dL and preoperative blood transfusion history were recorded.

2.1.3. Charlson comorbidity index

Comorbidity disease points were classified as 1, 2, 3, and 6.

2.1.4. Preoperative assessment

In the preoperative period, fasting duration, intestinal preparation, and venous thromboembolism were assessed. Anesthesia management data included the anesthesia method used (TIVA, regional anesthesia, opioid use, nitroprotoxide use, inhalation agent, postoperative nausea-vomiting treatment), use of nasogastric tube, hypothermia (in cases with heat probe and values recorded), lowest measurement value if hypothermia was identified, lowest measurement value if hypotension was identified, perioperative fluid treatment (blood and blood products, colloid, and crystalloid amounts), and unwanted events. The duration of anesthesia, duration of operation, and operation type (laparotomy/laparoscopic surgery) were also assessed.

2.1.5. Fluid therapy

Traditional perioperative fluid management is based on the principle of replacing fluid deficits from the preoperative period, maintenance requirements, surgical associated third space losses, and blood loss. The normal maintenance requirement has been estimated using the 4-2-1 rule (Holliday-Segar Method) protocol. Goal-directed therapy was not implemented due to the lack of necessary monitorization devices.

Fluid deficits from the preoperative period have been calculated by multiplying the hourly maintenance requirement by the duration without oral intake. Surgical-related losses are calculated as evaporation from opened spaces, redistribution to the 'third space,' and blood losses. Fifty percent of the calculated deficit amount has been administered during the first hour of the perioperative period, while the remaining fifty percent has been distributed and completed during the second and third hours of the perioperative period, along with other replacement therapies [5,6]. Colloid administration was reserved to be used for blood loss.

2.1.6. Complications

Complications included wound infections (inflammation/purulent discharge, positive swab culture), pneumonia (shading on new pulmonary radiography, purulent phlegm ± positive culture), atelectasis, pulmonary complications (other than pneumonia and atelectasis), sepsis (proven infection in addition to life-threatening organ failure, classified by an increase of two or more points in the 'Sepsis-Related Organ Failure Assessment' score), intraabdominal abscess (intraabdominal purulent collection requiring operative drainage), cardiac arrhythmia (all types of arrhythmia not present preoperatively), renal failure (urine output <0.5 ml/kg/hr), delirium (acute neuropsychiatric symptoms and findings of global disruption of brain function), and postoperative ventilation

support requirements (invasive or noninvasive ventilation). Oral intake status (date of onset, whether oral intake was tolerated or not), postoperative analgesia, and unplanned or planned PACU/AICU admission were also recorded.

2.1.7. Morbidity and mortality data

Planned PACU/AICU admission, unplanned PACU/AICU admission, duration of PACU/AICU admission, hospital admission duration, 28-day mortality, and survival rates were recorded. Postoperative 28-day mortality was considered as death related to surgical procedure; whereas 5-year survival was used for survival assessment.

2.2. Statistical analysis

Statistical analyses were performed using SPSS 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp). Frequency data were presented as numbers (n) and percentages (%). Data with continuous values are given as the mean ± standard deviation or median (minimum – maximum) considering the group numbers and statistical methods applied. Frequency data were analyzed using the chi-squared test or Fisher's exact test, according to the number of cases in each group. The distribution patterns of data with continuous variables were determined by normality tests and considering case numbers in consecutive subgroups. Data with non-normal distributions were analyzed using Kruskal – Wallis or Mann – Whitney U tests. Data with normal distributions were analyzed using the t-test or one-way analysis of variance and appropriate post hoc tests, according to the size of the subgroups. Relative risk and odds ratios were given with a 95% confidence interval after logistic regression analyes. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Patient characteristics

A total of 416 patients were assessed, the five year survival rate was 78.1% ($n = 325$) and mortality rate was 21.9% ($n = 91$). Four patients (0.96%) died within the first 28 days postoperatively, two had ovarian cancer, and the other two had endometrial cancer. Sepsis was identified as a major cause of mortality. The demographic characteristics of the patients are presented in Table 1.

Alcohol consumption and smoking were similar between the surviving and exitus patients. The difference was not statistically significant. Unfortunately, the data lacked the consumption amount of these substances in detail. Most of the patients had been classified as ASA class 2; the others (class 1 and 3) were significantly fewer. The difference between ASA scores among survivors and the exitus patients was not statistically significant.

Of the 416 patients, the most common comorbid diseases were hypertension in 182 patients (43.8%), followed by diabetes mellitus in 83 patients (20.0%), and coronary artery disease in 33 patients (7.9%). Only hypertension was associated with increased relative risk of mortality (Odds ratio for mortality (OR): 1.796, 95% confidence interval (CI): 1.077–2.994; $p = 0.025$).

For subgroup analyses, all patients were divided into three groups: those that underwent surgical intervention for endometrial cancer, ovarian cancer, and cervical cancer. For other gynecological cancers (fallopian tube, vaginal, and vulvar), subgroup analyses were not possible due to the scarcity of cases.

3.2. Outcomes of different types of gynecologic cancers

A total of 222 (53.3%) patients underwent surgery for endometrial cancer, and 181 survived, resulting in a 5-year survival rate of 81.5%. The distribution of cancer stages among patients with endometrial cancer was as follows: stage I, 64.0% ($n = 142$); stage II, 18.9% ($n = 42$); stage III, 14.4% ($n = 32$); and stage IV, 2.7% ($n = 6$). The five-year survival rates for the different stages of endometrial cancer were as follows: stage I, 95.1% ($n = 135$); stage II, 85.7% ($n = 36$); stage III, 68.8% ($n = 22$); and stage IV, 50.0% ($n = 3$). Among those that underwent surgery for endometrial cancer, the mean amount of colloid administered during the operation was 528.15 ± 328.90.16 mL. The infused colloid amount was lower among the surviving patients and the difference was statistically significant ($p = 0.018$). The difference in the rate of wound site infection was not statistically significant among patients with endometrial cancer ($p = 0.863$).

Table 1. Demographic characteristics of patients.

	Surviving patients ($n = 325$; 78.1%)	Excitus patients ($n = 91$; 29.1%)	Total	p
Age (years) (mean±SD)	55.78 ± 12.03	61.15 ± 12.40	56.95 ± 12.30	.644*
BMI (kg/m^2) (mean±SD)	3.92 ± 2.53	31.45 ± 2.68	31.00 ± 2.57	.146*
Alcohol Intake				
Present (n) (%)	16 (4.9%)	6 (6.6%)	22 (5.3%)	.529ϕ
Absent (n) (%)	309 (95.1%)	85 (93.4%)	394 (94.7%)	
Smoking				
Continues smoking (n) (%)	21 (6.5)	6 (6.6)	27 (6.5)	.802ϕ
Stopped smoking at least 4 weeks before procedure (n) (%)	112 (34.5)	28 (3.8)	140 (33.7)	
No history of smoking (n) (%)	192 (59.1)	57. (62.6)	249 (59.9)	
ASA score				
1 (n) (%)	64 (19.7)	8 (8.8)	72 (17.3)	.007**
2 (n) (%)	245 (75.4)	75 (82.4)	320 (76.9)	
3 (n) (%)	16 (4.9)	8 (8.8)	24 (5.8)	
CCI (median) (min. – max.)	2 (0–6)	2 (0–10)	2 (0–10)	.005**

Note: **Mann-Whitney U test; *t-test; ϕChi-square test BMI: body mass index; ASA: American Society of Anesthesiologists, CCI: Charlson Comorbidity Index.*

A total of 143 patients (34.3%) underwent surgery for ovarian cancer, the 5-year survival rate was 65.7%.). The distribution of cancer stages among patients with ovarian cancer was as follows: stage I, 28.0% ($n = 40$); stage II, 4.9% ($n = 7$); stage III, 51.7% ($n = 74$); and stage IV, 15.4% ($n = 22$). The five-year survival rates for the different stages of ovarian cancer were as follows: stage I, 95.0% ($n = 38$); stage II, 71.4% ($n = 5$); stage III, 55.4% ($n = 41$); and stage IV, 45.5% ($n = 10$). In this subgroup, the infused colloid amount was 6744.83 ± 431.10 mL, and a significantly higher amount was administered to the deceased group ($p = 0.017$). The overall wound site infection rate was 9.1% ($n = 13$), 5.3% among the surviving patients and 16.3% among the deceased patients; the difference was statistically significant ((OR: 3.47, 95% CI: 1.070–11.269; $p = 0.038$).

A total of 37 (8.8%) patients underwent surgery for cervical cancer, including 29 surviving and 8 deceased patients, resulting in a mortality rate of 21.60%. The distribution of cancer stages among patients with cervical cancer was as follows: stage I, 73.0% ($n = 27$); stage II, 13.5% ($n = 5$); and stage III, 13.5% ($n = 5$). The five-year survival rates for the different stages of cervical cancer were as follows: stage I, 88.9% ($n = 24$); stage II, 80.0% ($n = 4$); and stage III, 20.0% ($n = 1$). There was not any patients with stage IV cervical cancer in this cohort. The amount of colloid administration for patients with cervical cancer was 554.05 ± 349.28 mL. The difference between the administered amount to the surviving and deceased patients was not statistically significant ($p = 0.628$).

Finally, 14 (3.3%) patients underwent surgery for other gynecological cancers, including six surviving and eight deceased patients, resulting in a mortality rate of 57.1%. The incidence of peritoneal carcinomatosis was 6.4% ($n = 27$), with a mortality rate of 29.6% ($n = 8$). No significant difference was identified in the incidence rate of peritoneal carcinomatosis between the surviving and deceased patients ($p = 0.313$).

3.3. Laboratory parameters

The number of patients with preoperative anemia was 36 (8.7%), with 26 in the surviving group (8.0%) and 10 in the deceased group (11.0%) (OR: 1.540, 95% CI: 0.534–4.438; $p = 0.424$). Overall, 16 (3.8%) patients received preoperative blood transfusions. The blood transfusion rate was 3.7% among the surviving patients and 4.4% among the deceased patients (OR: 1.540, 95% CI: 0.534–4.438; $p = 0.665$) (Table 2).

The mean preoperative albumin value of the overall, surviving, and deceased groups was 3.59 ± 0.69, 3.65 ± 0.65, and 3.40 ± 0.80 g/dL, respectively. The preoperative albumin levels varied significantly between the surviving and deceased groups ($p < 0.001$). The mean preoperative total protein value of the overall, surviving, and deceased groups was 6.30 ± 1.01, 6.37 ± 0.96, and 6.07 ± 1.14 g/dL, respectively. Statistically significant differences were observed in the preoperative total protein levels between the surviving and deceased groups ($p = 0.003$).

3.4. Chemotherapy and radiotherapy

Overall, 185 (44.5%) patients underwent chemotherapy, among whom 122 survived and 63 were deceased (OR: 4.193; 95% CI: 2.480–7.089; $p < 0.001$). Chemotherapy was associated with a statistically significant in the overall relative risk of mortality. (Table 2) Patients who received chemotherapy had a lower life expectancy. Concerning the patients with endometrial cancer, The proportion of patients receiving chemotherapy for this disease was 28.4% ($n = 63$). These patients

Table 2. Preoperative features of the patients.

	Surviving patients Number/ percentage (n/%) 325/78.1	Exitus patients Number/ percentage (n/%) 91/21.9	Total	Odds Ratio (Mortality/Survival) (95% Confidence Interval)	p
Chemotherapy due to other malignancies					
Present	16 (4.9)	2 (2.2)	18 (4.3)	0.304 (0.069–1.343)	.116**
Absent	309 (95.1)	89 (97.8)	398 (95.7)		
Chemotherapy due to the present malignancy					
Present	122 (37.5)	63 (69.2)	185 (44.5)	4.193 (2.480–7.089)	<.001**
Absent	203 (62.5)	28 (3.8)	231 (55.5)		
Radiotherapy					
Present	99 (3.6)	23 (25.3)	121 (29.2)	1.180 (0.662–2.105)	.575**
Absent	226 (69.4)	68 (74.7)	294 (70.8)		
Preoperative Anemia					
Present	26 (8.0)	10 (11.0)	36 (8.7)	1.540 (0.534–4.438)	.424**
Absent	299 (92.0)	81 (89.0)	380 (91.3)		
Preoperative Blood Transfusion					
Present	12(3.7)	4 (4.4)	16 (3.8)	0.705 (0.145–3.423)	.665**
Absent	313 (96.3)	87 (95.6)	400 (96.2)		
Preoperative Plasma Albumin (g/dL)	3.65±.65	3.40±.80	3.59 ± 0.69	N/A	<.001*
Preoperative Plasma Total Protein (g/dL)	6.37±.96	6.07 ± 1.14	6.30 ± 1.01	N/A	.003*

Note: *t-test; **Binary logistic regression, N/A: Not available.

had a 5-year survival rate of 81.0%, while the rate was 91.2% among patients who did not receive chemotherapy (OR: 2.437, 95% CI: 1.058–5.614, $p = 0.036$). The difference was statistically significant. For ovarian cancer, chemotherapy was also increasing the risk of mortality; but the difference was not statistically significant (OR: 2.065, 95% CI: 0.857–4.977, $p = 0.106$). On the other hand, the relative risk for mortality was significantly higher for patients with cervical cancer receiving chemotherapy (OR:14.444, 95% CI:2.238–93.222; $p = 0.005$).

The most common regimen was the combination of carboplatin and paclitaxel (77.1%). No significant differences were observed in chemotherapy agents between those who survived and those who were deceased.

In the conducted study, 29.2% of patients, equating to 121 individuals, underwent radiotherapy. Of these, 30.6% ($n = 99$) were among the survivors, and 25.3% ($n = 23$) were among the deceased. The OR calculated was 1.180, with a 95 CI of 0.662 to 2.105. The p-value obtained was 0.5785. A statistically significant increase in the relative risk of mortality associated with radiotherapy was not detected.

3.5. Surgical technique

Within the institution, both laparoscopic and laparotomic surgeries were performed. Of the 10 patients who underwent laparoscopic surgery, most had endometrial cancer, with one case each of cervical cancer, ovarian cancer, and gastrointestinal stromal tumor. The five-year survival rate was 80.0% for patients who had laparoscopic surgery, compared to 78.1% for those who underwent laparotomic surgery. Despite the slight difference in survival rates, the statistical analysis showed no significant difference ($p = 0.885$).

3.6. Intraoperative and postoperative medication

All patients received intraoperative opioids, and the most commonly used opioid was remifentanil. The mean fasting duration was 9.00 ± 2.07 hours, and all patients received thrombosis prophylaxis and intestinal preparation. Regarding surgery, most patients ($n = 406$, 97.6%) underwent laparotomy, and a nasogastric (NG) or an orogastric (OG) tube was inserted in 371 (89.2%) of them. Additionally, the mean surgical duration was 180.00 ± 78.82 min, the mean anesthesia duration was 200.00 ± 83.37 min, the most common anesthesia method was inhalation anesthesia ($n = 220$, 52.9%), and the second most common method was RA + inhalation ($n = 197$, 46.4%). No significant differences were observed in these parameters between the surviving and deceased patients.

In the early postoperative period, the incidence of nausea and vomiting was 35.8% ($n = 149$), affecting 35.7% of the surviving patients and 36.3% of the deceased patients ($p = 0.920$). The mean time to postoperative oral intake was 2.13 ± 2.19 days. Early oral intake seemed to be associated with increased overall survival ($p = 0.046$). Regarding postoperative analgesia in the ward, diclofenac sodium and opioids were used together (69.7%), followed by diclofenac sodium (16.6%), and patient-controlled analgesia (PCA) (13.7%). However, the use of PCA devices was discontinued in 2012 due to unresolved technical problems with the devices. No significant correlation was found between the form of postoperative analgesia administration and survival ($p = 0.612$).

3.7. Hypothermia

Rate of intraoperative hypothermia was 38.6% ($n = 116$) in the study cohort. The increased relative risk of mortality was significantly higher in patients, who experienced hypothermia (OR:1.768, 95% CI: 1.080–2.894, $p = 0.024$).

3.8. Postoperative morbidities and hospital stay

Postoperative morbidity features of the patients are given in Table 3. Parameters other than postoperative wound site infection and blood transfusion demonstrated no statistically significant differences among the survivor and exitus patients. Overall wound site infection rate was 7.0% ($n = 29$), while it was 5.5% ($n = 18$) among the surviving patients and 6.3.0% ($n = 11$) among the deceased. The OR was 1.21 (95% CI: 0.47–3.13); indicating a potential increase in mortality rate associated with wound site infection. However, the statistical insignificance of this finding was underscored by a p-value of 0.692, suggesting the difference in mortality rates was not statistically meaningful. Overall postoperative blood transfusion rate was 18.0% ($n = 75$); surviving patients had a significantly lower transfusion rate of 14.5%, whereas the rate in the excitus patients was 30.8% (OR for mortality 2.15, 95% CI: 1.20–3.86; $p = 0.010$).

Table 4 presents an analysis of postoperative hospital stays and admissions to the Post-Anesthesia Care Unit (PACU) and Anesthesia Intensive Care Unit (AICU). The sole statistically significant difference observed pertained to the total hospital stay durations between surviving and deceased patients. Notably, no statistically significant differences were found regarding admissions to PACU or AICU. Moreover, planned and unplanned admissions to PACU or AICU did not demonstrate a statistically significant increase in the relative risk of mortality. However, both the duration of stay in PACU/AICU and the overall hospital stay were significantly longer for the deceased group.

4. Discussion

A total of 416 patients undergoing gynecological cancer surgery in a seven-year period were assessed. The overall 5-year survival rate was 79.4%. The most common cancer was endometrial cancer, followed by ovarian cancer and cervical cancer (53.36%, 34.37%, and 8.89%, respectively) [7,8]. Number of other gynecological cancers were significantly lower. American Cancer Society (ACS) also reports endometrial cancers as the most common gynecologic cancer among American women. The overall 5-year survival rates of endometrial cancer is reported as 84%; similar to the rate in our cohort [9]. Meanwhile the 5-year survival rate of ovarian cancer (65%) was higher in our cohort than it is reported by ACS (50%) and also higher for cervical cancer (78%) than it is reported by ACS (67%) [10,11].

In our study, while the overall albumin values were not excessively low, the preoperative albumin values in the

Table 3. Postoperative morbidity characteristics.

	Surviving patients Number/percentage (n/%) 325/78.1	Exitus patients Number/percentage (n/%) 91/21.9	Total	Odds Ratio (Mortality/Survival) (95% Confidence Interval)	p
Wound site infection					
Present	18 (5.5)	11 (6.3)	29 (7.0)	1.21 (0.47–3.13)	0.692**
Absent	307 (94.5)	80 (84.7)	387 (93.0)		
Pneumonia					
Present	1 (0.3)	1 (1.2)	2 (0.5)	1.47 (0.61–35.35)	0.813**
Absent	324 (99.7)	90 (98.9)	414 (99.5)		
Atelectasis					
Present	4 (1.2)	3 (3.3)	7 (1.7)	1.51 (0.23–9.67)	0.661**
Absent	321 (98.8)	88 (96.7)	409 (98.3)		
Other pulmonary complications					
Present	15 (4.6)	10 (11.0)	25 (6.0)	1.54 (0.60–4.12)	0.385**
Absent	310 (95.4)	81 (89.0)	391 (94.0)		
Sepsis					
Present	1 (0.3)	6(6.6)	7 (1.7)	9.77 (1.01–94.30)	0.049**
Absent	324 (99.7)	85 (93.4)	409 (98.3)		
Intraabdominal abscess					
Present	1 (0.3)	3 (3.3)	4 (1.0)	4.80 (0.31–74.46)	0.262**
Absent	324 (99.7)	88 (96.7)	412 (99.0)		
Arrhythmia					
Present	19 (5.8)	9 (9.9)	28 (6.7)	1.24 (0.49–3.19)	0.651**
Absent	306 (94.2)	82 (90.1)	388 (93.3)		
Renal failure					
Present	9 (2.8)	9 (9.9)	18 (4.3)	1.81 (0.59–5.56)	0.303**
Absent	316 (97.2)	82 (90.1)	398 (95.7)		
Delirium					
Present	8 (2.5)	2 (2.2)	10 (2.4)	0.94 (0.19–4.61)	0.937**
Absent	317 (97.5)	89 (97.8)	406 (97.6)		
Postoperative blood transfusion					
Present	47 (14.5)	28 (30.8)	75%18)	2.15 (1.20–3.86)	0.010**
Absent	278 (85.5)	63 (69.2)	341%82.0)		

Note: ** Binary logistic regression.

Table 4. Postoperative PACU/AICU admission features.

	Surviving patients Number/ percentage (n/%) 325/78.1	Exitus patients Number/ percentage (n/%) 91/21.9	Total	Odds Ratio (Mortality/Survival) (95% Confidence Interval)	p
Admission to PACU/AICU					
Present	9 (2.8)	11 (12.1)	20(4.8)	4.969 (0.232–106.507)	0.305**
Absent	316 (97.2)	80 (87.9)	396(95.1)		
Unplanned PACU/AICU admission					
Present	1 (0.3)	4 (4.4)	5(1.2)	2.609 (0.036–190.592)	0.661**
Absent	324 (99.7)	87 (95.6)	411(98.8)		
Planned PACU/AICU admission					
Present	8 (2.5)	7 (7.7)	15(3.6)	0.383 (0.005–28.006)	0.661**
Absent	317 (97.5)	84 (92.3)	411(96.4)		
PACU/AICU admission duration (days)	0.16 ± 1.8	1.51 ± 7.10	0.46 ± 3.72	N/A	0.002*
Hospital admission duration (days)	11.03 ± 8.40	16.35 ± 12.45	12.19 ± 9.67	N/A	<0.001*
Postoperative mechanical ventilator (recovery/ PACU/AICU)					
Present	9 (2.8)	11 (12.1)	20 (4.8)	1.905 (0.094–38.619)	0.675**
Absent	316 (97.2)	80 (87.9)	396 (95.2)		

Note: **AICU**: anesthesia intensive care unit, **PACU**: Post anesthesia care unit *t-test; **Binary logistic regression, N/A: Not available.

deceased patients were lower than those in the surviving patients. Thus, the mortality rate increased with decreased albumin levels. Albumin levels are an indirect marker of organ function (e.g. the liver) as it is an acute-phase reactant, showing the patient's metabolic status and providing information about the patient's general status [12]. In a retrospective cohort study of 533 patients who underwent elective gynecologic cancer surgery between 2005 and 2015 [13], 97 patients (18.2%) experienced complications in the postoperative 30-day period. They reported that age,

operative duration, and serum albumin levels were valuable predictors of 30-day morbidity. The association of low preoperative albumin levels with mortality has been reported in several studies [12,14–16]. Whether elevating serum albumin levels in the short-term with albumin solution infusion in the preoperative period is beneficial for patients with hypoalbuminemia is currently under debate. Nevertheless, preventing situations that predispose patients to hypoalbuminemia-like malnutrition earlier in the process is important. Conditions that cause hypoalbuminemia should be targeted, water and sodium loading should be avoided, surgical and medical treatments for inflammation and sepsis should begin early, and the patient should be given appropriate nutritional support.

Mortality was associated with the amount of colloid used. Specifically, an increase in colloid use was associated with reduced survival rates in patients with endometrial cancer and ovarian cancer. However, this association was not significant with cervical cancer. Currently, the fluid types and administration strategies that should be used and the outcomes of these methods are debatable [17]. Studies on the type of fluid treatment required during surgery have focused on liberal, restrictive, and targeted fluid treatment methods [18] and have shown differences in preoperative and postoperative definitions, fluid types, additional fluid administration situations, and assessment criteria for the efficacy of the method, hindering accurate interpretation of the results of these studies [19]. A meta-analysis concluded that during elective surgery, the group with restrictive fluid treatment experienced fewer complications than the group with liberal treatment, and restrictive fluid treatment in elective surgery reduced morbidity by 35%, making it the recommended fluid management method [20]. A study by Jia et al. [21] compared restrictive and liberal fluid treatment outcomes and found that they were associated with both general and cardiopulmonary complication rates. However, restrictive fluid treatment was associated with more rapid healing and a shorter hospital stay. Our study was observational and performed by investigating routine implementation records; therefore, it only encompassed the total amount of fluid administered during the intraoperative period. Additionally, fluid treatment was administered when deemed appropriate by the clinician responsible for overseeing patients in the ward or intensive care unit during both the intraoperative and postoperative periods. Although generally restricted during the intraoperative period, its administration at other time points is unknown.

In our study, the postoperative transfusion rates were higher in deceased patients. Geist et al. [22] assessed the correlation between perioperative erythrocyte transfusion, morbidity, and oncologic outcomes in a study that included patients with stage IIIC-IV epithelial ovarian cancer receiving neoadjuvant chemotherapy and interval debulking surgery. They reported that perioperative blood transfusions were administered to 50.4% of the patients. They administered more perioperative blood transfusions to patients with preoperative anemia and predicted high blood loss. More transfusions were performed in patients who underwent moderate and highly complicated surgeries than in those who underwent surgery with minor complications. While a correlation was observed between preoperative erythrocyte transfusion and intraabdominal infection, no correlations were observed with wound site complications or venous/pulmonary thromboembolism. When investigated according to age and stage, no significant difference was observed in terms of survival between patients who received preoperative erythrocyte transfusions and those who did not. A differential diagnosis of anemia should be made for patients with preoperative anemia, and elective surgery should be delayed until the anemia is treated. In our study, the preoperative anemia rate was 8.7%, and the preoperative blood transfusion rate was 3.8%. Our hospital does not have a protocol for patients with preoperative anemia, and the patients often undergo transfusion to increase their hemoglobin levels. Although our preoperative transfusion rate was low, the transfusion rate before elective surgery should be zero. The transfusion of blood or blood products reduces the rate of assisting cytotoxic T cells (transfusion-related immune modulation) [23,24], and patients undergoing blood transfusions may have increased rates of tumor recurrence, perioperative infection, and mortality. In our hospital, anesthesiologists decide whether to perform transfusions according to the amount of hemorrhage, hypotension, and intraoperative hemoglobin levels. However, the records used in this study lacked data regarding the reasons for blood transfusion. Moreover, standard monitoring, rather than advanced hemodynamic monitoring, was performed for patients during anesthesia. Perioperative hypothermia, which is frequently encountered in patients under general anesthesia and often neglected despite its preventable role in perioperative hemorrhage, is a primary risk factor of morbidity and mortality [3]. In the present study, the incidence of hypothermia was 38.6% and was associated with reduced survival.The Turkish Society of Anesthesia and Reanimation performed studies on this topic in Turkey and attempted to increase awareness during a 'Meeting for Patient Blood Management Awareness' in Izmir, Turkey in 2017.

In recent years, wound site infection rates for gynecological surgeries have been reported to be 11% in Europe [25], 2–5% in America [26], and 10.5% in India [27]. Similarly, in our study, this rate was 7%. We found that the wound site infection rate was higher in deceased patients. Surgical site infection continues to be a serious problem in modern surgery despite aseptic and antiseptic implementations, sterilization methods, operating room conditions and surgical techniques, advances and developments in intensive care facilities, and prophylactic antibiotic administration. For example, the incidence of wound site infection after hysterectomy has been reported to range from 2.0–9.9% [22]. Moreover, many studies have evaluated wound site infection and mortality and morbidity rates [28,29]. However, more studies are needed to better assess the incidence rates and effective countermeasures for wound site infections according to the cancer type. Most surgical site infections can be avoided with simple precautions such as using appropriate antibiotics, selecting appropriate surgical technique, consistently complying with asepsis – antisepsis rules, shaving hairs in the surgical region, using an electric razor rather than a cutting implement, using appropriate antimicrobial prophylaxis, administering additional doses for long surgeries involving hemorrhage, ensuring appropriate hydration, ensuring continuation

of nutrition, ensuring that the patient is normothermic in the perioperative period with a variety of heating methods, ensuring sufficient oxygenation of the patient in the perioperative period, keeping patients oligemic in the perioperative period, and achieving multidisciplinary cooperation. In the cases evaluated in this study, surgical site infection prevention strategies were as per those recommended in the literature. Although electric razors were used, antibiotic administration generally occurred immediately before or after the incision.

The mean hospital stay duration was 12.19 ± 9.67 days for our patients and longer in deceased patients. In a study implementing the Enhanced Recovery after Surgery (ERAS) program, Bergstrom et al. [30] retrospectively reviewed gynecologic oncology patients who underwent elective laparotomy. They investigated the patients' demographic characteristics, surgical variables, postoperative outcomes, antimicrobial use, and venous thromboembolism prophylaxis. ERAS patients were found to use fewer opioids and less PCA. Along with this significant reduction in opioid use, these patients reported less pain and had a hospital stay of 3–5 days. Bisch et al. [31] compared the outcomes before and after implementing the ERAS guidelines in two centers performing gynecologic oncology surgery in Canada. The clinical outcomes and compliance rates were obtained using the ERAS interactive control system, and the patients were monitored for 30 days after discharge. After implementation, the mean compliance rate with the ERAS care team increased from 56% to 77%. For all surgeries, the mean admission duration decreased from 4.0 days to 3.0 days after ERAS. When assessed according to the magnitude of the surgery, patients in the moderate-to-large surgical class had a reduction in the mean hospital stay of two days, and the rate of complications before discharge decreased from 53.3% to 36.2% after ERAS. They concluded that the systematic implementation of the ERAS gynecologic oncology guidelines in a health system generally improves patient outcomes and preserves resources. Moreover, the ERAS protocols may be applicable to gynecologic oncology abdominal surgeries. The institution had not implemented ERAS protocol during the period the study was concerned, and therefore, a comparison could not be made. Nevertheless, we attach significant importance to ERAS protocol and want to emphasize it. Owing to modern anesthesia, analgesia, and supportive administration, the ERAS protocol targeting a reduced metabolic response to major gynecologic oncology surgery requires collaboration between the surgeon, anesthesiologist, and nurses. Although anesthesiologists partially abide by the ERAS guidelines perioperatively, surgeons and nurses implement methods that contradict these guidelines. Awareness of this topic among anesthesiologists, surgeons, and nurses should be increased by communicating information about the ERAS guidelines.

Currently, although effective postoperative pain control is an important part of postoperative care, 30–80% of patients complain of a moderate to severe degree of pain after surgery. The results of insufficient postoperative pain control include activation of the sympathoneural and neuroendocrine systems, tachycardia, hypertension, hyperglycemia, immunosuppression, and reduced regional perfusion, which delay healing, lengthen hospital stays, and increase medical costs [32]. Thoracic epidural anesthesia (TEA) is a common technique for postoperative analgesia. However, even if patients are normovolemic, the sympathetic block induced by TEA may cause hypotension, requiring treatment with vasopressors. Moreover, difficulties may be experienced in ensuring fluid balance in patients receiving large volumes of acid during surgeries, such as those for ovarian cancer, which require acute fluid resuscitation. Consequently, epidural catheters may be used less often [33]. Additionally, TEA causes delays in mobilization and urinary catheter removal, which may increase the duration of hospitalization and complication rates in patients undergoing gynecologic cancer surgery [34]. Low-dose intrathecal morphine and spinal anesthesia are alternatives to TEA. Because they allow earlier removal of the urinary catheter and mobilization, they are superior to TEA in ensuring early discharge from the hospital [34]. Intrathecal morphine was commonly used in our study cohort. Patient controlled analgesia (PCA) is also another commonly used option but we could not effectively assess PCA due to the lack of devices during the study period.

Intraperitoneal local anesthetics reduce postoperative pain. This technique has been tested for laparoscopic surgery [35]. However, the benefit was limited to a few hours postoperatively and was not linked to the dose of analgesia. We have not presented specific data regarding the subject; however, our experience is similar and our opinion is that it brings limited benefit. In conclusion, patient status should be individually assessed, and the implemented analgesia plan should be multimodal.

This study has several limitations. First, the number of ovarian and endometrial cancer cases were significantly higher than other (cervical, vulvar) gynecologic cancers and that made it impossible to deeply assess the data from cancer cases apart from ovarian and endometrial origin. Cervical cancer cases were also more detailed examined; however the number of cases were limited. Second, because this was a single-center study, we were unable to assess different approaches by different surgical teams. Third, due to the retrospective nature of this study, we were limited to archived records. A prospective study would enable us to determine the parameters more freely and reach a greater number of patients. We could not assess presence of ascites and the success of cytoreduction (optimal or not). During the period that had been included in the study, the institution was in transition to a new digital archiving system. Therefore, it was sometimes impossible to retrieve all required information about the patient, which limited the number of cases. Lastly, the number of laparoscopic cases were low to present a comparison with a sufficient number of cases. Nevertheless, our institution has noteworthy experience in oncologic surgery as a tertiary center. Our anesthesiology and gynecologic oncology departments have been working in collaboration for more than 35 years. Mutual understanding contributes to the success of teamwork; therefore, we believe that our data significantly reflect the expected outcomes of gynecologic oncology surgery.

5. Conclusion

Perioperative patient management for gynecologic oncology surgery requires a multidisciplinary approach, primarily

involving an anesthesiologist and a surgeon. Preoperative planning reduces the risks of perioperative and postoperative complications. Inadequate preoperative preparation has been observed to increase the necessity for interventions, such as blood transfusion and colloid infusion, which have been shown to correlate with suboptimal outcomes. Enhancing a multidisciplinary approach can contribute to the optimization of postoperative management and surveillance, including the monitoring of serum albumin levels. This strategy is likely to expedite patient recovery, decrease the length of hospital stays, and reduce both morbidity and mortality rates.

Abbreviations

AICU	Anesthesia intensive care unit
ASA	American Society of Anesthesiologists
ERAS	Enhanced Recovery after Surgery
IFA	International Fluid Academy
LA	Local anesthetic
NK	Natural killer
PACU	Post-anesthesia care unit
PCA	Patient-controlled analgesia
SSI	Surgical site infection
TAP	Transversus abdominis plane
TEA	Thoracic epidural analgesia
VAS	Visual analogue scale

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Author contributions

Hicret Yeniay: conducted the study and wrote the manuscript as the first author; Bahar Kuvaki: supervisor and critical contributions; Sule Ozbilgin: conducted the study and wrote the manuscript as the corresponding author; Hasan Bahadır Saatli: conducted the study and collected the data; Hikmet Tunç Timur: conducted the study, data collection, and statistical analysis.

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