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ORIGINAL INVESTIGATION

Perioperative goal-directed fluid management using noninvasive hemodynamic monitoring in gynecologic oncology

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Abstract

Background: Intraoperative fluid management is important for the prevention of perioperative morbidity and mortality. Our study aimed to investigate the perioperative feasibility and benefits of Goal-Directed Fluid Management (GDFM) using noninvasive hemodynamic monitoring in gynecologic oncology patients with acute blood loss and severe fluid loss. We assessed the effects of GDFM on hemodynamics, organ perfusion, complications, and mortality outcomes.

Methods: This randomized prospective study included 104 patients over the age of 18 years, including 56 patients with endometrial cancer and 48 patients with ovarian cancer who had open surgery. The anesthetic approach was standardized for all patients. We compared the perioperative results of the subjects who were randomized into GDFM (n = 51) and Liberal Fluid Management (LFM) (n = 53) groups using a computer program.

Results: The median perioperative crystalloid replacement (2000 vs. 2700; $p < 0.001$) and total volume of fluid (2260 vs. 3200; $p < 0.001$) were lower in the GDFM group compared to the LFM group. The hemodynamic findings and the HCO_3 and lactate levels of the GDFM group did not significantly change perioperatively. The heart rate, mean arterial pressure, and HCO_3 levels of the LFM group decreased and serum lactate levels increased perioperatively. The hospitalization rate in ICU (7.8% vs. 28.3%; $p = 0.010$), rate of patients with comorbidity conditions indicated in ICU (2% vs. 17%; $p = 0.024$), and rate of complications (17.6% vs. 35.8%; $p = 0.047$) were lower in the GDFM group compared to the LFM group.

Conclusion: The amount of intraoperatively administered crystalloid solution and complication rates were significantly lower in gynecologic oncologic surgery patients who received GDFM.

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Besides, hemodynamic findings, and lactate levels of the GDFM group did not change significantly during the perioperative period.

Introduction

Intraoperative fluid management is important for the prevention of peri- and postoperative complications, morbidity, and mortality, particularly in gynecologic oncological operations involving multi-organ resection for tumors. Surgery can lead to significant fluid loss due to prolonged peritoneal air exposure, significant blood loss, and acute drainage of tumor-associated ascites. Intraoperative drainage of ascites is followed by reduced fluids in vessels, which may require the administration of large volumes of fluid for replacement.[1] While planning fluid management, the anesthesiologist needs to ensure adequate blood flow for adequate and safe tissue oxygenation and the capacity of the cardiac output to meet metabolic requirements.

Goal-Directed Fluid Management (GDFM) includes the evaluation of fluid sensitivity and cardiac functions using dynamic and static parameters to measure cardiac output in order to optimize oxygen supply to tissues during surgery. Randomized controlled trials and meta-analyses have reported superior outcomes for GDFM in terms of organ damage, mortality, wound healing, length of hospital stay, and length of ICU stay compared to Liberal Fluid Management (LFM).[2,3] The established advantages of GDFM compared to LFM and the subsequent financial benefits have led to GDFM being recommended as the standard of care by a large number of scientific communities and being included in treatment guidelines.[4,5]

Patients undergoing gynecologic oncologic surgery are prone to significant fluid shift and blood loss and therefore are at risk for hypovolemia, end-organ hypoperfusion, and adverse postoperative outcomes.[6] Although GDFM has been frequently investigated in patients undergoing major abdominal surgery, it has been rarely investigated in patients undergoing major gynecologic surgery. In addition, intravascular volume depletion and acute hemorrhage are important problems in gynecological oncology cases. In these cases, management of perioperative GDFM with minimal therapeutic procedures is essential. Therefore, in this study, we investigated the effects of GDFM on hemodynamic morbidity using PVI and investigated the effects of GDFM on mortality.

Methods

Study design and population

This prospective study was conducted between May 2019 and December 2019 at the Gynecological Oncology Clinic of the Health Sciences University Istanbul Bakirkoy Dr. Sadi Konuk Training and Research Hospital. One hundred and twenty seven adult patients with an American Society of Anesthesiologists (ASA) physical status of II—III presenting for major abdominal oncologic surgery (expected duration $\geq$ 2 h) were evaluated. The exclusion criterias were as follows: patients younger than 18 years, Body Mass Index (BMI) $\geq$ 35 kg.m^{-2}, laparoscopic surgery, peripheral artery disease, chronic obstructive pulmonary disease, obstructive sleep apnea syndrome, arrhythmia, advanced kidney or liver failure, decompensated heart failure (ejection fraction of $<$ 30%), and not being able to tolerate a tidal volume of 8 mL.kg^{-1} in mechanical ventilation (for accuracy of the Pleth Variability Index). Twenty three patients who met the exclusion criteria were excluded from the study. A total of 104 patients, including 56 patients with endometrial cancer and 48 patients with ovarian cancer, who met the inclusion criteria were included in the study (Figure 1).

The study was planned as per the 2013 Brazil revision of the Helsinki Declaration. All patients signed informed consent forms. The study was granted ethical approval by the local ethics committee (2019\152) and was registered as a clinical trial (NCT03956901).

Assuming an alpha of 0.05, a power of 0.80, and consistent with previous reports[7] with 10% lower complication rate in the GDFM group, the estimated sample size was at least 50 patients in both protocol groups. Age and body mass index were evaluated as potential confounders. According to this, patients were single-blindly assigned to the targeted fluid therapy or liberal fluid therapy branches by computer stratified randomization analysis with a ratio of 1:1 in the STATA program (StataCorp LLC, Texas, USA). Anesthesiologists were not blinded to group assignments. However, patients, surgeons, PACU and surgical nurses, and those who provided the data analysis were blinded. The data of the patients were obtained by saving them on the memory card of the monitor at the end of the case.

Anesthesia initiation

The anesthetic approach was standardized for all patients. Patients were allowed clear fluid intake up to 2 hours and solid food intake up to 6 hours before the operation. In the operating room, heart rate, oxygen saturation, Central Venous Pressure (CVP), and invasive and noninvasive arterial pressure measurements were made with a Datex S/5 monitor (Datex Ohmeda®, GE Healthcare, Chicago, IL, USA). In the GDFM group, hemodynamic fluid responsiveness was achieved by Pleth Variability Index (PVI) monitoring with a finger sensor (in the arm without invasive arterial cannulation, using the finger probe from the 4th finger and covered in an opaque manner) (Masimo Corporation, Radikal 7, USA). Vascular access was opened with a 16—18G catheter for all patients. Before anesthesia induction, 0.03 mg.kg^{-1} midazolam was administered, and epidural catheter was inserted for postoperative analgesia. No medication was administered to the patients through the intraoperative epidural

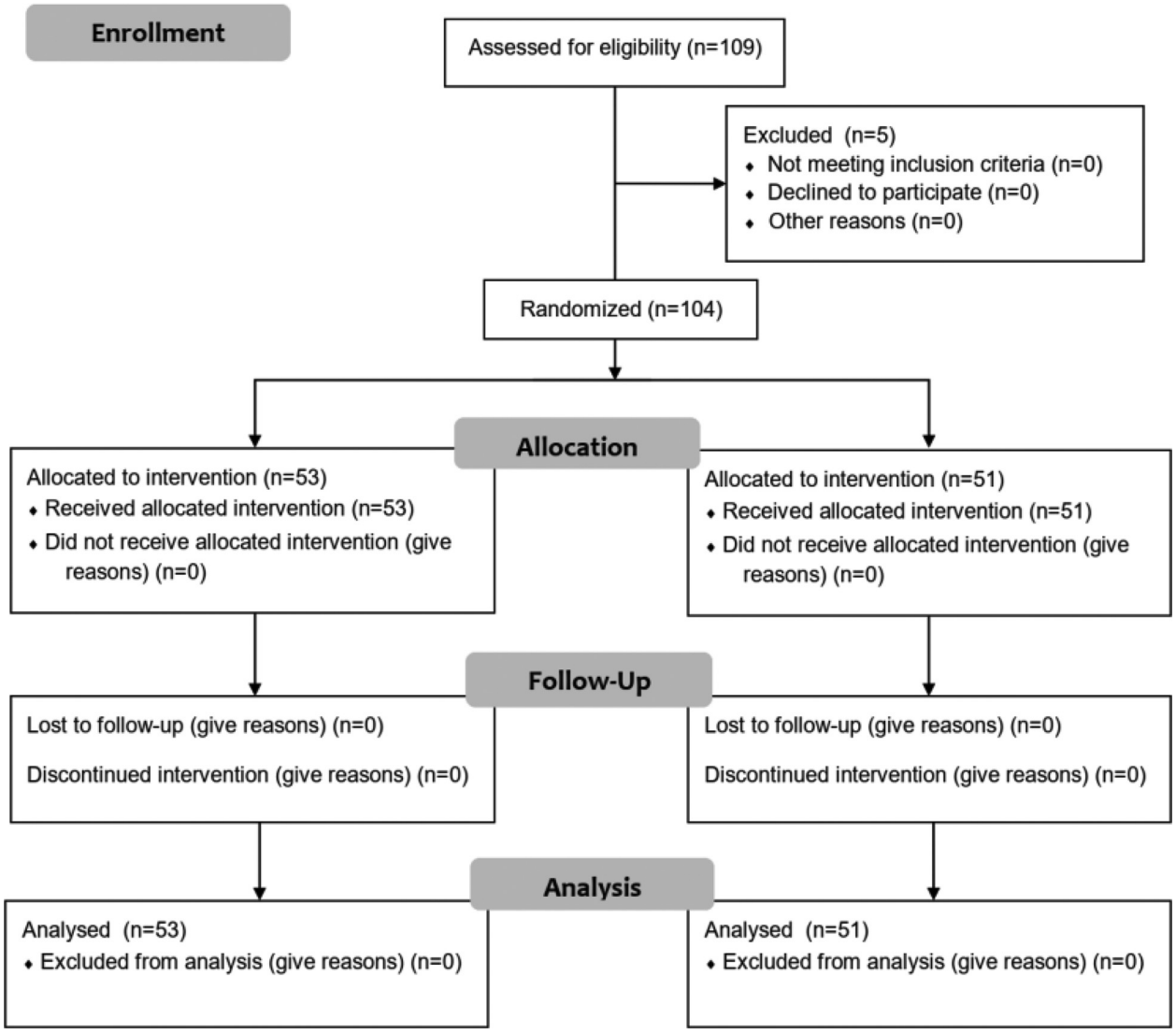

Figure 1 Trial profile. (GDFM, Goal-Directed Fluid Management; LFM, Liberal Fluid Management; MAP, Mean Arterial Pressure; NE, Norepinephrine, PVI, Pleth Variability Index).

catheter. All patients had an arterial line for arterial blood gas monitoring.

After anesthesia induction with 1 $\mu g.kg^{-1}$ fentanyl and 2–3 $mg.kg^{-1}$ propofol, the patient was curarized with 0.6 $mg.kg^{-1}$ rocuronium and connected to a ventilator. Mechanical ventilation was set to the volume-controlled mode with I:E 1:2, tidal volume 8 $mL.kg^{-1}$ of ideal body weight, and respiratory frequency adjusted according to end-tidal CO_2 (ECO_2 35–45 mmHg). Mechanical ventilation was maintained with a fresh gas flow rate of 3 $L.min^{-1}$ with 40% oxygen. Anesthesia was maintained with 1 MAC sevoflurane, 0.01–0.2 $\mu g.kg^{-1}.min^{-1}$ remifentanil infusion, and rocuronium as needed.

Perioperative fluid management

LFM application

A crystalloid fluid bolus (Ringer's lactate solution) of 500 mL was infused together with the induction of anesthesia, followed by a maintenance infusion of 4–8 $mL.kg^{-1}.h^{-1}$. Maintenance fluid therapy was continued in patients with MAP > 65 mmHg. If Mean Arterial Pressure (MAP) was < 65 mmHg, the patient was administered a 250 mL bolus of crystalloid solution and 1–2 μg bolus Norepinephrine (NE). Afterwards, MAP was followed at 5-minute intervals. If MAP was still < 65 mmHg after subsequent measurements, the patient was given 250 mL of crystalloid solution. In continuing hemodynamic follow-ups, if MAP < 65 mmHg despite mini fluid challenge, NE 0.1–1 $\mu g.kg^{-1}.min^{-1}$ (from a solution at a concentration of 0.08 $mg.mL^{-1}$) infusion was started and MAP adjusted to > 65 mmHg.

GDFM application

A crystalloid fluid bolus (Ringer's lactate solution) of 500 mL was infused together with the induction of anesthesia, followed by 2 $mL.kg^{-1}$ crystalloid fluid infusion. If the PVI was < 13% and MAP > 65 mmHg, the fluid infusion of the patients was continued at the adjusted dose. If PVI was < 13% and MAP was < 65 mmHg, fluid infusion was continued, and a 1–2 μg bolus NE was administered. Similar to the LFM

Table 1 Preoperative demographic, clinical, and laboratory findings.

Variables	All population n = 104	GDFM n = 51	LFM n = 53	*p*
Age, years	57.1±12.3	55.5±12.5	58.6±12.1	0.191
BMI, $kg.m^{-2}$	31.4±9.0	30.3±6.0	32.4±11.1	0.245
ASA, n (%)				
II	69 (66.3)	35 (68.6)	34 (64.2)	0.681
III	35 (33.7)	16 (31.4)	19 (35.8)	
Surgery time, minutes	307.5 (120–550)	300 (120–550)	350 (145–510)	0.098
Diagnosis, n (%)				
Endometrial	57 (54.8)	27 (52.9)	30 (56.6)	0.844
Ovarian	47 (45.2)	24 (47.1)	23 (43.4)	
Types of procedures, n (%)				
Endometrial	n = 57	n = 27	n = 30	
Hysterectomy	57 (100)	27 (100)	30 (100)	-
Bilateral BSO	57 (100)	27 (100)	30 (100)	-
PPALND	57 (100)	27 (100)	30 (100)	-
Ovarian	n = 47	n = 24	n = 23	
PPALND	44 (93.6)	22 (91.7)	22 (95.7)	
DPS/R	13 (27.7)	8 (33.3)	5 (21.7)	0.574
Bowel resection	8 (17.0)	5 (20.8)	3 (13.0)	0.747
LWR	4 (8.5)	2 (8.3)	2 (8.7)	0.999
Splenectomy	4 (8.5)	2 (8.3)	2 (8.7)	0.999
VATS	2 (4.3)	–	2 (8.7)	0.451
Ascites fluid, n (%)				
No	83 (79.8)	41 (80.4)	42 (79.2)	0.999
Yes	21 (20.2)	10 (19.6)	11 (20.8)	
Hemoglobin, $g.dL^{-1}$	11.4±1.6	11.4±1.5	11.5±1.7	0.724
Albumine, $mg.dL^{-1}$	37.6±4.6	37.1±4.9	38.0±4.2	0.349
Creatinine, $mg.dL^{-1}$	0.6 (0.3−9.4)	0.6 (0.3−9.4)	0.6 (0.3−1.7)	0.554

Numerical variables with normal distribution were shown as mean ± standard deviation. Numerical variables that do not show normal distribution are shown as median (min−max). Categorical variables were shown as numbers (%).
ASA, American Society of Anesthesiologists physical status; BMI, Body Mass Index; Ca, Cancer; GDFM, Goal-Directed Fluid Management; LFM, Liberal Fluid Management; ICU, Intensive Care Unit; PPALND, Pelvic Paraaortic Lymph Node Dissection; DPS/R, Diaphragmatic Peritoneal Stripping/Resection; LWR, Liver Wedge Resection; VATS, Video-Assisted Thoracoscopic Surgery.

group, MAP was followed at 5-minute intervals. If PVI was < 13% and MAP was < 65 mmHg after subsequent measurements, a repeat dose of NE bolus was administered. In repeated measurements, NE infusion of 0.1−1 $\mu g.kg^{-1}.min^{-1}$ (from a solution with a concentration of 0.08 $mg.mL^{-1}$) was started in patients with MAP < 65 mmHg. If PVI was > 13% and MAP was < 65 mmHg, the patient was administered a 250 mL crystalloid fluid bolus. If MAP < 65 mmHg persisted, 1−2 μg bolus NE was administered. If the PVI was > 13% and MAP was < 65 mmHg in subsequent measurements, a 250 mL crystalloid bolus was repeated for the last time. NE infusion of 0.1−1 $\mu g.kg^{-1}.min^{-1}$ (0.08 $mg.mL^{-1}$ solution) was started in patients with MAP < 65 mmHg on repeated measurements, and fluid infusion was continued until PVI was < 13%. The total fluid administered was recorded.

In patients with bleeding, if arterial blood gas, a target hemoglobin concentration within the target range (7−9 $g.dL^{-1}$), and PVI > 13%, they received erythrocyte suspension.[8] If more than 1,000 mL of ascitic fluid was aspirated in patients with ascites in the GDFM group, to maintain oncotic pressure, 1−2 units of Fresh Frozen Plasma (FFP) or 20% human albumin at 3 $mL.kg^{-1}$ were used targeting PVI < 13%.[9] In the LFM group, the amount of FFP and albumin were determined according to MAP, presence of tachycardia, and urine output findings. In these groups, the choice between using balanced crystalloids or colloids (albumin 100 mL) was left to the attending anesthesiologist.

Following perioperative hemodynamic stabilization, we recorded PVI, blood gas values, perioperative blood loss, and the amount of administered fluids at T0 (15 minutes after anesthesia induction), T1 (hour 1), T2 (hour 2), and after extubation. At the end of the operation, the patients were assessed to decide between extubation or admission to the ICU according to hemodynamic findings. NE infusion was evaluated and decided considering ongoing hemodynamic instability, respiratory distress, massive blood transfusion, and additional comorbidities (uncontrolled diabetes, uncontrolled hypertension) for ICU admission.

On the postoperative 24th hour, we recorded fever, creatinine, length of ICU stay, and length of hospital stay (the length of hospital stay was defined as the postoperative follow-up in bed until discharge). The patients were reached by phone on postoperative day 30 to confirm survival.

Statistical analysis

Data were analyzed using SPSS 20 for Windows (IBM Corp., Armonk, NY, USA). The normal distribution of the data was evaluated by the Kolmogorov-Smirnov test. The normally distributed variables were presented as mean ± standard deviation while the non-normally distributed variables were presented as median (min–max). Categorical variables were presented as numbers and percentages. We used Student's *t*-test for the intergroup comparison of normally distributed variables and the Mann-Whitney U test for the intergroup comparison of non-normally distributed variables. Chi-Square and Fisher's exact tests were used for the intergroup comparison of categorical variables. The changes in laboratory findings before and after the operation were evaluated using the Generalized Linear Mixed Model (GLMM) for the analysis of longitudinal data with repeated measures for all patients and the two groups (GDFM and LFM). Values of $p < 0.05$ were considered statistically significant.

Results

The mean age of the subjects was 57.1 ± 12.3 years, and 66.3% (n = 69) were ASA II. There was no significant difference between the groups in terms of demographic characteristics and preoperative clinical and laboratory findings. Table 1 presents the relevant data in detail.

The median amount of crystalloid solution (2000 vs. 2700; $p < 0.001$) and median total volume of fluid (2260 vs. 3200; $p < 0.001$) were lower in the GDFM group compared to the LFM group. Other perioperative clinical findings were not significantly different for the GDFM and LFM groups (Table 2).

The mean Heart Rate (HR), mean MAP, and median serum lactate levels were similar for the two groups at T0 and T1, whereas they were higher in the LFM group at T2. Other perioperative laboratory findings were not significantly different for the two groups (Table 3).

The decrease in mean HR and mean MAP and the increase in median lactate levels and median base excess were significantly higher in the LFM group. The changes in other perioperative laboratory parameters were not significantly different (Table 3).

When preoperative and postoperative mean hemoglobin, mean albumin, and median creatinine levels were compared, and the changes observed were similar in the GDFM and LFM groups (Table 4).

The postoperative findings are shown in detail in Table 5. The hospitalization rate in ICU (7.8% vs. 28.3%; $p = 0.010$), rate of patients with comorbidities in ICU (2% vs. 17%; $p = 0.024$), and rate of complications (17.6% vs. 35.8%; $p = 0.047$) were lower in the GDFM group compared to the LFM group. Other postoperative events and mortality outcomes were not statistically different (Table 5).

Discussion

In this cohort of gynecologic oncologic surgery patients, we applied a pulse contour analysis-guided hemodynamic and static management protocol. We found that GDFM provides

Table 2 Perioperative clinical findings.

Variables	All population n = 104	GDFM n = 51	LFM n = 53	*p*
Blood loss, mL	400 (50–3000)	350 (50–3000)	500 (50–2000)	0.484
Urine output, mL	150 (25–1500)	150 (25–1500)	175 (50–1100)	0.169
Administered NE infusion, n (%)	9 (8.7)	2 (3.9)	7 (13.2)	0.182
Intravenous fluid replacement				
Crystalloid solution, n (%)	104 (100.0)	51 (100.0)	53 (100.0)	–
Volume, mL	2500 (812–6000)	2000 (812–5000)	2700 (1000–6000)	< 0.001[a]
Colloid solution, n (%)	49(47.1)	20(39.2)	29(54.7)	0.122
Volume, mL	500 (500–1000)	500 (500–1000)	500 (500–1000)	0.204
Total fluid volume, mL	2750 (812–8400)	2260 (812–7400)	3200 (1500–8400)	< 0.001[a]
Erythrocyte replacement, n (%)				0.074
None	74 (71.2)	39 (76.5)	35 (66.0)	
1 unit	8 (7.7)	6 (11.8)	2 (3.8)	
2 units	13 (12.5)	3 (5.9)	10 (18.9)	
3 units	9 (8.7)	3 (5.9)	6 (11.3)	
Fresh Frozen Plasma, n (%)				0.335
None	67 (64.4)	35 (68.6)	32 (60.4)	
1 unit	5 (4.8)	4 (7.8)	1 (1.9)	
2 units	19 (18.3)	8 (15.7)	11 (20.8)	
3 units	6 (5.8)	3 (5.9)	3 (5.7)	
4 units	5 (4.8)	1 (2.0)	4 (7.5)	
5 units	2 (1.9)	–	2 (3.8)	

Numerical variables with normal distribution were shown as mean ± standard deviation. Numerical variables that do not show normal distribution are shown as median (min–max). Categorical variables were shown as numbers (%).
GDFM, Goal-Directed Fluid Management; LFM, Liberal Fluid Management.
[a] $p < 0.05$ shows statistical significance.

Table 3 Perioperative laboratory findings.

Variables	All population n = 104	GDFM n = 51	LFM n = 53	*p*
Hemoglobin, g.dL^{-1}				
T0	10.8±1.5	11.0±1.5	10.7±1.6	0.356
T1	10.8±1.6	10.9±1.5	10.6±1.7	0.333
T2	10.7±1.7	10.9±2.0	10.6±1.4	0.322
Postextubation	11.0±1.3	11.1±1.4	11.0±1.2	0.808
p_r	0.140	0.845	0.102	
p_d		0.805		
Hearth rate, beats.min^{-1}				
T0	**78.4±15.4**	**79.6±17.6**	77.3±13.1	0.444
T1	68.9±12.2	71.9±14.3	**66.0±9.1**	0.014[a]
T2	69.1±12.5	72.3±13.3	**66.2±10.9**	0.012[a]
Postextubation	**84.1±14.3**	**89.3±15.7**	79.2±10.8	<0.001[a]
p_r	< 0.001[a]	< 0.001[a]	< 0.001[a]	
p_d		0.016[a]		
Mean arterial pressure, mmHg				
T0	79.2±14.2	82.7±18.0	75.8±8.0	<0.001[a]
T1	77.8±14.4	83.5±15.1	**69.3±6.6**	<0.001[a]
T2	75.9±13.9	82.6±15.5	**69.4±8.1**	<0.001[a]
Postextubation	**85.1±14.9**	**93.2±14.3**	77.3±10.9	<0.001[a]
p_r	< 0.001[a]	0.003[a]	< 0.001[a]	
p_d		0.003[a]		
pH				
T0	**7.5±0.1**	**7.5±0.1**	**7.5±0.1**	0.777
T1	7.4±0.1	7.4±0.1	7.4±0.1	0.279
T2	7.4±0.1	7.4±0.1	7.4±0.1	0.107
Postextubation	7.4±0.1	7.4±0.1	7.4±0.1	0.198
p_r	< 0.001[a]	< 0.001[a]	< 0.001[a]	
p_d		0.138		
HCO_3, mmoL.L^{-1}				
T0	24.5±2.3	24.7±2.5	**24.3±2.1**	0.335
T1	24.0±3.6	24.9±4.2	23.2±2.6	0.013[a]
T2	23.9±3.3	24.8±3.9	23.2±2.4	0.013[a]
Postextubation	23.4±3.0	24.0±3.2	23.0±2.7	0.070
p_r	0.004[a]	0.361	< 0.001[a]	
p_d		0.048[a]		
Lactate, mEq.L^{-1}				
T0	1.1 (0.1–3.2)	1.1 (0.5–2.8)	1.1 (0.1–3.2)	0.698
T1	1.1 (0.5–3.5)	1.1 (0.5–3.3)	1.1 (0.5–3.5)	0.573
T2	1.2 (0.4–6.3)	1.2 (0.4–3.8)	**1.4 (0.6–6.3)**	0.042[a]
Postextubation	1.7 (0.7–6.5)	**1.8 (0.7–6.4)**	**1.8 (0.7–6.5)**	0.665
p_r	< 0.001[a]	< 0.001[a]	< 0.001[a]	
p_d		0.047[a]		
Base excess, mEq.L^{-1}				
T0	**-0.1((-8.9)–(6.9))**	-0.1((-4.1)–(5.3))	**0.1((-8.9)–(6.9))**	0.610
T1	-0.9((-14)–(6.9))	-0.3((-4.9)–(5.4))	-1.3((-14)–(6.9))	0.107
T2	-0.5((-11)–(4.5))	-0.3((-6.7)–(4.5))	-0.6((-11)–(3.6))	0.105
Postextubation	-1.3((-13)–(7.5))	-0.4((-5.1)–(5.9))	-1.7((-13.0)–(7.5))	0.192
p_r	< 0.001[a]	0.121	< 0.001[a]	
p_d		0.032[a]		

Numerical variables with normal distribution were shown as mean ± standard deviation. Numerical variables that do not show normal distribution are shown as median (min−max). Categorical variables were shown as numbers (%).
HCO_3, Bicarbonate; GDFM, Goal-Directed Fluid Management; LFM, Liberal Fluid Management; pH, power of Hydrogen, T0, perioperative baseline, T1, 1-hour later; T2, 2-hour later.
[a] $p < 0.05$ shows statistical significance. p_r, Statistical difference of changes in laboratory findings in the group. p_d, Statistical difference of changes in laboratory findings between groups.

Table 4 Preoperative vs. postoperative laboratory findings.

Variables	GDFM (n = 51)	p_r	LFM (n = 53)	p_r	Δp
Hemoglobin, g.dL^{-1}					
Preoperative	11.4±1.5	< 0.001[a]	11.5±1.7	< 0.001[a]	0.818
Postoperative	10.5±1.3		10.6±1.3		
Albumin, mg.dL^{-1}					
Preoperative	37.1±4.9	< 0.001[a]	38.0±4.2	< 0.001[a]	0.230
Postoperative	28.8±3.5		28.6±4.5		
Creatinine, mg.dL^{-1}					
Preoperative	0.6 (0.3–9.4)	0.989	0.6 (0.3–1.7)	0.101	0.605
Postoperative	0.7 (0.3–8.6)		0.7 (0.4–2.3)		

Numerical variables with normal distribution were shown as mean ± standard deviation. Numerical variables that do not show normal distribution are shown as median (min–max). Categorical variables were shown as numbers (%).
GDFM, Goal-Directed Fluid Management; LFM, Liberal Fluid Management; pH, power of Hydrogen; WBC, White Blood Cell; CRP, C-Reactive Protein.
[a] $p < 0.05$ shows statistical significance. p_r, Statistical difference of changes in laboratory findings in the group. Δp, Statistical difference of changes in laboratory findings between groups.

favorable tissue oxygenation (such as stable serum lactate values) and reduces the amount of perioperative fluid administration due to its hemodynamic effects (such as stable MAP) compared to LFM, and GDFM was associated with reduced ICU admissions and postoperative complications.

Excess preoperative fluid administration in major abdominal and thoracic surgeries is associated with postoperative complications. Liberal and restrictive fluid management have been shown to be hazardous for high-risk surgical patients due to the risk of hypovolemia.[10] Therefore, for the possibility of safely limiting and personalizing fluid administration in high-risk surgical patients, GDFM is being recommended as the standard of care in relevant guidelines.[4,5]

Goal-directed fluid therapy suggests that reducing fluid administration when hemodynamic targets are met can help avoid inadequate fluid replacement.[11] Our results are consistent with the literature. In our study, we administered a crystalloid solution to all patients, but the amount of administered crystalloid solution was lower in the GDFM group compared to the LFM group. The use of crystalloid solutions alone may result in inadequate intravenous fluid replacement and iatrogenic fluid loading,[12] which may place patients at risk. Moreover, the GDFM method can reduce the risk of tissue edema that may result from excessive crystalloid fluid administration.[13] At the same time, the proportion of patients given both colloid solution and FFP in the LFM

Table 5 Event and mortality findings after the operation.

Variables	All population (n = 104)	GDFM (n = 51)	LFM (n = 53)	p
Hospitalization in ICU, n (%)	19 (18.3)	4 (7.8)	15 (28.3)	0.010[a]
Duration of stay in ICU, days	1 (1–10)	2 (1–10)	1 (1–9)	0.242
Indications of ICU, n (%)				
Comorbidity	10 (9.6)	1 (2.0)	9 (17.0)	0.024[a]
Closer hemodynamic monitoring	5 (4.8)	1 (2.0)	4 (7.5)	0.383
Inotropic therapy	11 (10.6)	2 (3.9)	9 (17.0)	0.065
Hemodynamic instability	3 (2.9)	2 (3.9)	1 (1.9)	0.973
Duration of stay in hospital, days	8 (0–30)	7 (2–30)	9 (2–28)	0.078
Fever, n (%)	8 (7.7)	4 (7.8)	4 (7.5)	0.999
Complication, n (%)	28 (26.9)	9 (17.6)	19 (35.8)	0.047[a]
Wound infection	15 (14.4)	6 (11.8)	9 (17.0)	0.579
Pulmonary edema	4 (3.8)	–	4 (7.5)	0.136
Evisceration	3 (2.9)	2 (3.9)	1 (1.9)	0.973
Acute renal failure	2 (1.9)	1 (2.0)	1 (1.9)	0.999
Retroperitoneal hematoma	2 (1.9)	1 (2.0)	1 (1.9)	0.999
Postoperative ileus	2 (1.9)	1 (2.0)	1 (1.9)	0.999
Urethral stricture	1 (1.0)	–	1 (1.9)	0.999
Anastomotic leak	1 (1.0)	–	1 (1.9)	0.999
Mortality, n (%)	1 (1.0)	–	1(1.9)	0.999

Numerical variables that do not show normal distribution are shown as median (min–max). Categorical variables were shown as numbers (%).
GDFM, Goal-Directed Fluid Management; LFM, Liberal Fluid Management; ICU, Intensive Care Unit.
[a] $p < 0.05$ shows statistical significance.

group was partially higher than the GDFM group. This situation supports the need for more fluid replacement to provide hemodynamic stability in the LFM group, in line with the literature.[7,9] In addition, although the proportion of patients with ascitic fluid was similar in both groups, these patients corresponded to half of the patients given colloid solution and FFP. It has been suggested that FFP transfusion in patients with malignant ascites may help restore hemodynamic stability.[14]

Dynamic variables based on ventilation-induced changes in cardiac output help predict fluid response. Timely interventions based on the individual needs of the patient can prevent hypotension and hemodynamic imbalance.[15,16] Arterial pulse pressure variation is cited as one of the most useful dynamic variables in guiding volume replacement.[15,17] In our study, perioperative decreases in MAP and HR were significantly higher in the LFM group compared to the GDFM group. The benefits of GDFM may be associated with the administration of fluids at the right time, helping avoid hypovolemia and hypoperfusion. Another advantage of the GDFM protocol is using NE as the first-line intervention for hypotension, independently of stroke volume variation.[18]

In our study, the comparative norepinephrine usage rate was approximately 1:3 for the GDFM and LFM groups, even though this finding was not statistically significant. These findings support the idea that the risk of hypotension is lower for GDFM, and the patient is less likely to require NE intervention.

The perioperative tissue perfusion outcomes of GDFM are superior to those of LFM approaches. When oxygen supply is insufficient, pyruvate cannot enter the Krebs cycle and is shunted to lactate. Therefore, serum lactate levels reflect anaerobic cellular metabolism that results from tissue hypoxia.[19] Serum lactate levels increase when oxygen supply is insufficient to meet tissue metabolism requirements. Latent hypoperfusion without clinical symptoms of shock elevates serum lactate levels.[20] These are solid parameters for the assessment of inadequate oxygen perfusion. In our study, serum lactate levels did not change in the GDFM group but increased in the LFM group. Forget et al.[16] demonstrated that GDFM with PVI applied during major abdominal surgery was associated with lower lactate levels and that these patients required significantly less crystalloid fluid administration. The results of our cohort of patients undergoing gynecologic oncological surgery suggest that GDFM is superior to LFM as demonstrated by more stable serum lactate levels and reduced fluid replacement.

Morbidity and mortality are significantly higher in patients who undergo high-risk surgeries. Most of these patients have clinically significant dehydration preoperatively, and patients lose varying volumes of fluid intraoperatively. Insufficient intravascular volume reduces pulse volume and cardiac output, resulting in inadequate tissue and organ perfusion. This can result in the development of serious complications, longer-term hospitalization, and, without the appropriate interventions, even death. For this reason, intraoperative fluid therapy is important both for surveillance and for preventing postoperative complications. In our study, ICU admission and complication rates were lower in the GDFM group, consistent with the literature.[2,10,12,21] Also, the complication rate of the LFM group was almost double that of the GDFM group. In our study, the distribution of patients with wound infection in the LFM and GDFM groups was similar. This is consistent with the conclusion in a meta-analysis that complementary hydration alone does not affect wound infection rate, regardless of any specific hemodynamic goal.[22] However, when the amount of perioperatively applied fluids is aimed at increasing subcutaneous oxygen tension, a greater amount of collagen in wound healing has been observed.[23] In particular, anastomotic leak, pulmonary edema, and urethral stricture were observed only in the LFM group. A recent study has shown that patients treated with a non-guided restrictive fluid administration protocol had a higher risk of postoperatively developing acute kidney injury and that this was associated with lower intraoperative urine output.[24] Large amounts of IV fluid replacement can exacerbate capillary leakage associated with the systemic inflammatory response to surgery and may contribute to the development of intestinal anastomotic edema.[25] Therefore, the complications that were observed only in the LFM group may have been due to the unsteady mucosal perfusion that resulted from unstable fluid therapy.[26,27] However, in our study, the distribution of complication types determined in both groups did not differ significantly. In our study, the complication rates in the GDFM group were consistent with GDFM applications presented in similar gynecologic surgery cohorts.[12,28] One patient died during the 30-day follow-up. This patient was in the LFM group and died due to a postoperative ileus complication. Postoperative ileus is a common complication of intra-abdominal surgeries. However, it is suggested that targeted fluid therapy may not be an effective strategy in reducing the risk of postoperative ileus.[29] Also, a longer-term follow-up would possibly change the postoperative mortality rate.

The major limitations of the present study are the relatively small number of patients and the results are based on a single center experience. In addition, we evaluated only 30-day short term survival outcomes. Another important limitation is the intensive care indications due to the preoperative comorbidities of the patients. The higher ICU hospitalization rate observed especially in the LFM group may be due to comorbidity including ICU indication. On the other hand, the BMI level was slightly higher in the LFM group. In our study, calculating the tidal volume based on ideal body weight, is appropriate to exclude patients with very high BMI. Various metabolic and neurohormonal changes commonly associated with overweight or obesity may have contributed to abnormalities in cardiac morphology and function.[30] One of the important limitations of our study is that muscle relaxation was not monitored. We used rocuronium as a muscle relaxant in our patients. Monitoring and maintenance of a constant level of muscle paralysis could have minimized the possibility that muscular contraction influenced on lung mechanics.

We conclude that the clinical use of GDFM in gynecologic oncological surgery is beneficial for limiting the amount of intraoperatively administered crystalloid solution without causing hypovolemia, hypotension, or serum lactate elevation. This may be associated with rapid recovery of bowel function, wound healing, and reduced ICU admission, length of hospital stay, and complication rates.

Conflicts of interest

The authors declare no conflicts of interest.

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