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Original Research

Restrictive Fluid Therapy for High-Complexity Advanced Ovarian Cancer Surgery: A Single-Center Retrospective Cohort Study

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Abstract

Background: Postoperative fluid management is vital for preventing perioperative morbidity and mortality in high-complexity advanced ovarian cancer surgery. We investigated the feasibility and benefits of restrictive fluid therapy on postoperative recovery. **Methods**: Patients with advanced ovarian cancer who underwent open radical surgery were randomized into the restrictive or liberal fluid group. The endpoints were the length of hospital stay post-surgery and the incidence of complications within 30 days. **Results**: The restrictive and liberal fluid regimen groups included 30 and 41 patients, respectively. The length of hospital stay was 16.5-days and 21.0-days for the restrictive and liberal group, respectively (p = 0.035). Multiple linear regression analysis showed that length of hospital stay was 2.971-days shorter in the restrictive group than in the liberal group (95% confidence interval (CI): –5.818~–0.124, p = 0.04). The incidence of complications at the end of 30 days was significantly lower in the restrictive group than in the liberal intravenous group (26.7% versus 51.2%; p = 0.032). Adjusted logistic regression demonstrated that restrictive group could significantly reduce the risk of postoperative complications by 68% (Odds Ratio 0.32, 95% CI: 0.11–0.91, p = 0.033). **Conclusions**: Restrictive fluid management after high-complexity advanced ovarian cancer surgery can significantly decrease the risk of major postoperative complications and facilitate postoperative recovery.

Keywords: restrictive fluid therapy; ovarian cancer; high-complexity; complication; postoperative recovery

1. Introduction

Ovarian cancer is a common malignancy in women with a high mortality rate. Unfortunately, the patients usually were diagnosed with an advanced stage with metastatic diseases. The routine therapeutic option for advanced ovarian cancer includes surgical removal of all the visible lesions followed by postoperative adjuvant chemo- and molecularly-targeted-therapies [1]. These complicated surgical procedures involve multiple organ resections and extensive resection of the peritoneum. The extent to which complete tumor resection should be attempted, however, has been subject to debate of late [2]. Postoperative complications remain to be leading causes of high perioperative mortality and medical costs. A longer interval between surgery and follow-up chemotherapy may predict worse survival, arguing the prognostic importance of minimizing postoperative complications [3,4].

Ensure euvolemia and adequate tissue perfusion can significantly reduce the incidence of perioperative complications, and consequently, result in superior prognosis in patients. In fact, acute kidney injury (AKI) is associated with insufficient fluid rehydration. In contrast, pulmonary complications, tissue edema and anastomotic leakage are generally coupled with excessive fluid rehydration [5,6]. Therefore, fluid management is of particularly importance for ovarian cancer patients undergoing cytoreductive surgery. Practically, fluid management in ovarian cancer is complicated due to the following issues: preoperative hypoproteinemia, massive ascites, large amount of peritoneal resection causing fluid loss during operation, hypotension induced by perioperative anaesthesia [7,8].

Restrictive fluid therapy was first proposed by Moore *et al*. [9]. It is based on the principle of ensuring adequate circulating blood volume, tissue perfusion, and oxygenation of vital organs by limiting the total amount of fluid input, so as to reduce postoperative complications and mortality. Since 2019, the gynecologic oncology team of Zhongda Hospital Affiliated to Southeast University, have attempted to implement modified restrictive fluid therapy for a small cohort of patients with highly-complicity advanced ovarian cancer undergoing extensive surgery. The objective of this study was to explore the correlation between postoperative complications and the recovery of patients undergoing high-complexity radical surgery for ovarian cancer treated with modified restrictive fluid therapy, to identify a more effective and safer postoperative fluid treatment plan

for such patients. Our hypothesis is that restrictive fluid management can decrease the risk of major postoperative complications and improve recovery after surgery.

2. Methods

2.1 Data Source

This retrospective study was approved by the Ethics Committee of the Ethics Committee of Zhongda Hospital. Informed consent was waived. Patients with International Federation of Gynaecology and Obstetrics (FIGO) stage III and IV ovarian cancer or recurrent ovarian cancer treated at Zhongda Hospital Affiliated to Southeast University from January 2019 to December 2021 were enrolled in this study. Data from all participants were retrieved from the hospital's medical records.

2.2 Study Design

The inclusion criteria were as follows: (1) patients undergoning cytoreductive surgery, including primary debulking surgery, IDS (interval debulking surgery, after chemotherapy), and secondary cytoreduction; (2) patients with an American Society of Anesthesiology (ASA-PS) score of 1–3; (3) patients aged 18–75 years and body mass index (BMI) <40; (4) patient who had undergone laparotomy that took longer than 120 minutes and were hospitalized for at least 3 days; (4) R0 surgical resection; (5) availability of complete medical records.

The exclusion criteria were as follows: patients who (1) had undergone urgent or acute surgery, (2) had undergone palliative or unresectable surgery, (3) were aged >75 years with BMI >40, (4) showed signs of renal dysfunction, defined by serum creatinine levels >176 μmol/L and/or blood urea nitrogen (BUN) >7.1 mmol/L, (5) showed signs of cardiac dysfunction, defined by Brain natriuretic peptide precursor (NT-proBNP) levels >300 ng/L, (6) showed signs of pulmonary insufficiency, defined by Forced Expiratory Volume In one second (FEV1) $<50\%$, (7) showed signs of sepsis or systemic inflammatory response syndrome, (8) had undergone laparoscopic surgery, (9) had incomplete medical history.

Preoperative management of all patients followed the concept of enhanced postoperative rehabilitation (ERAS) as listed below: no preoperative bowel preparation; no prophylactic use of antibiotics element; no drink clear liquid 2 hours before operation. General anesthesia was performed in all patients. Oxygen inhalation, electrocardiogram (ECG), pulse, blood oxygen saturation (SpO2), heart rate (HR) and depth of anesthesia blood pressure (BP) and other vital signs were monitored.

The anesthesia plan of the two groups was the same. During operation, the routine fluid replacement plan was applied in all the patients with parameters including intraoperative physiological requirement, vasodilation volume, loss of third space, and intraoperative blood loss. The infusion dripping rate was around 10–25 mL/kg/h.

The daily infusion volume, blood transfusion volume, urine volume, drainage fluid volume, and gastrointestinal decompression fluid volume were recorded three days after operation. Postoperative fluid balance was defined as the sum of fluid administered, i.e., crystalloid, colloid, blood, oral intake and fluid lost, i.e., surgical drain, gastric retention and urine production in the ward each day. Consequently, the average value of the three days of fluid administered and the average value of the three days of liquid balance were calculated.

Patients were divided into two cohorts: restrictive fluid therapy group (R) and the liberal fluid replacement group (L). If the daily average sum of infused fluid was below 2500 mL and the average fluid balance three days after the surgery was equal to or below zero, the patients were enrolled in the restrictive fluid therapy group; for the rest, patients were included in the liberal fluid replacement group.

All the relevant parameters presented in the study were retrieved from the hospital database with complete electronic medical record. Age, BMI, ASA score, albumin level, hemoglobin level, creatinine level, and comorbid conditions were recorded as preoperative data. The duration of surgery, the Aletti score for surgical complexity, intraoperative fluid administration, operation time, blood loss, and urine volume were recorded as operative details. The use of vasopressors, serum creatinine, albumin, c-reactive protein levels, postoperative complications, duration of hospital stay, postoperative chemotherapy interval and duration of recovery were recorded as postoperative recovery indicators.

2.3 Outcomes

The primary outcome variables were the following postoperative recovery indicators:

1. Postoperative length of hospital stay: calculated the from day of surgery until the day of discharge.
2. Postoperative chemotherapy interval: calculated as the number of days from the postoperative period to the first day of chemotherapy.
3. Return of bowel function.
4. Postoperative mobilization time.
5. Recovery rate of albumin level.

The secondary endpoint was the incidence of the following major postoperative complications within 30 days of surgery:

1. AKI (acute kidney injury): Acute kidney injury can be diagnosed if one of following three points is met: (1) increase of serum creatinine level to be higher than 0.3 mg/dL (26.5 umol/L) within 48 hours; (2) increase of serum creatinine level to be higher than 1.5 folds that of the baseline and the upregulation lasting for 7 days; and (3) urine volume to be less than 0.5 mL/kg*h for more than 6 hours.
2. Fistula (intestinal fistula, urinary fistula).
3. Septic complications (sepsis, surgical site infection,

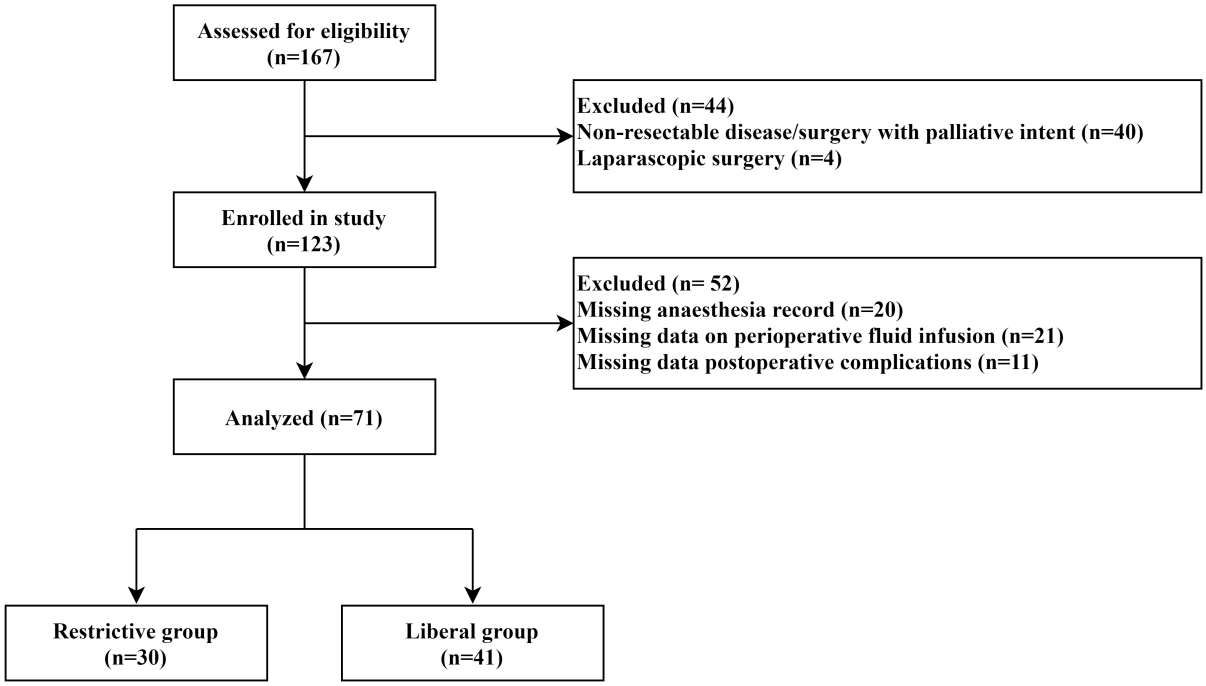

Fig. 1. Selection of patients from the Zhongda Hospital Ovarian Cancer Database.

and pneumonia).

4. Pulmonary edema: clinical observation of respiratory distress, impaired oxygenation and radiological evidence of pulmonary oedema.

5. Cardiac insufficiency: symptoms of typical heart failure, diagnosis by color Doppler ultrasound and the elevation of heart failure serological markers such as brain natriuretic peptide.

6. Others: thrombosis, unplanned operation, and postoperative death.

2.4 Statistical Analysis

Normal distribution of measurement data was expressed as mean $\pm$ standard deviation (SD), and the independent sample *t*-test was used for comparing groups. Non-normal distribution was represented by medians (quartile spacing). The Mann-Whitney U non-parametric test was used for comparing the groups. Stepwise multiple linear regression analysis was performed to determine factors influencing the duration of hospital stay. A χ^2 test or Fisher's exact probability test was performed for complications in two groups. The association between postoperative fluid administration and complications, was assessed by means of a multivariate logistic regression analysis and was expressed as odds ratios (OR) with corresponding 95% confidence interval (CI). For all analyses, a two-sided $p < 0.05$ was considered significant. Data were analyzed using SPSS software version 22.0 (IBM Corp., Armonk, NY, USA).

3. Results

3.1 Patient Enrollment and Follow-Up

Between 2019 and 2021, a total of 167 patients with stage III and IV epithelial ovarian cancer who underwent cytoreductive surgery were recorded in internal institutional database. 44 patients were excluded due to unresectable tumors, palliative surgery or laparoscopic surgery. An additional 52 patients were excluded because of incomplete parameters (anesthesia records, perioperative fluids, or complications). In the end, a total of 71 patients were included in the analysis (see Fig. 1).

3.2 Trial Results

Seventy-one patients were initially enrolled in this study, of which 30 patients were in the restrictive group and 41 patients in the liberal group. There were no significant differences in the demographic characteristics, underlying comorbidities, or operational characteristics between the two groups ($p < 0.05$) (Table 1).

There was no significant difference in intraoperative information between the two groups, including the operative duration, blood loss, urine volume, colloidal and crystalloid volume, and usage of vasopressor see Table 2. Daily postoperative fluid volume was 2461 $\pm$ 246 mL in the restrictive group and 3221 $\pm$ 438 mL in the liberal group ($p < 0.001$). Moreover, the amount of crystalloid input in the restrictive group was reduced after the operation, and the difference was significant when compared with that in the liberal group ($p < 0.001$). Meanwhile, more patients in the restrictive group than in the liberal group received vasopressors postoperatively (56.7% versus 24.4%, $p = 0.006$).

Table 1. Demographic and perioperative characteristics of the patients at baseline.

	Restrictive fluid (n = 30)	Liberal fluid (n = 41)	*p*
Age, mean ± SD, yr	58.97 ± 10.89	58.15 ± 10.32	0.747
BMI, mean ± SD, kg/m^2	24.25 ± 3.14	23.29 ± 2.63	0.167
ASA score, no. (%)			0.281
1	1 (2.4%)	3 (10%)	
2	39 (95.1%)	27 (90%)	
3	1 (2.4%)	0 (0%)	
Total comorbid conditions, no. (%)	11 (36.7%)	15 (37.5%)	0.943
Hypertension	7 (23.3%)	5 (12.2%)	
Diabetes mellitus	3 (10%)	6 (14.6%)	
Cardiac disease	1 (3.3%)	1 (2.4%)	
Cerebrovascular disease	3 (10%)	2 (4.9%)	
Chronic renal failure	1 (3.3%)	1 (2.4%)	
Thrombosis	1 (3.3%)	0 (0%)	
Aletti score, no. (%)			0.697
<8	7 (23.3%)	8 (19.5%)	
≥ 8	23 (76.7%)	33 (80.5%)	

Values are presented as mean ± SD, median [inter-quartiles] or n (%).

Abbreviations: ASA, American society of anesthesiologists; BMI, body mass index; SD, standard deviation.

Table 2. Blood loss and administered intravenous-fluid volumes.

	Restrictive Fluid (N = 30)	Liberal Fluid (N = 41)	*p* value
Intraoperative data			
Duration, mean ± SD, min	290.5 ± 83.1	316.3 ± 90.7	0.224
Blood loss (P25, P75), mL	800 (575, 1125)	800 (500, 1650)	0.243
Crystalloid (P25, P75), mL	1500 (1187, 2000)	2000 (1500, 2500)	0.103
Colloid, mean ± SD, mL	1258 ± 574	1287 ± 776	0.964
Use of vasopressor, no. (%)	20 (66.7%)	28 (70%)	0.767
Urine volume (P25, P75), mL	500 (275, 800)	500 (200, 875)	0.971
Albumin administered, mean ± SD, g	33.3 ± 24.4	43.9 ± 24.5	0.076
After surgery			
Total fluid administered, mean ± SD, mL	2461 ± 246	3221 ± 438	<0.001
Crystalloid (P25, P75), mL	1000 (825, 1100)	1500 (1000, 2000)	<0.001
Colloid (P25, P75), mL	1500 (1275, 1650)	1700 (1300, 2000)	0.058
Use of vasopressor, no. (%)	17 (56.7%)	10 (24.4%)	0.006

Values are presented as median [inter-quartiles] or mean ± SD.

3.3 Primary Outcome

The median length of postoperative hospital stay was 16.5 days in the restrictive group and 21.0 days in the liberal group, with a significant difference ($p = 0.035$). Significant differences in the length of hospital stay and chemotherapy interval were found between patients in the two groups ($p = 0.035$ and $p = 0.008$, respectively), as shown in Table 3 and Fig. 2. There was no significant difference in the time taken to regain bowel function (passage of flatus) between the two groups (median: 4.5 versus 4 days; $p = 0.578$). Meanwhile, the ratio of lactate-to-albumin was significantly different between the two groups (0.054 ± 0.037 versus 0.093 ± 0.047, respectively, $p = 0.028$).

Age, comorbidity, groups, operation time, albumin recovery rate, surgical complexity (Aletti score), and incidence of postoperative complications were used as independent variables. Postoperative duration of hospital stay was considered as the dependent variable. The equation entered into the model included three independent variables: age, Aletti score, group as shown in Table 4 ($R^2 = 0.322$). According to the absolute value of the regression coefficient, age and Aletti score were positive predictors of hospital stay. With increasing age and Aletti score, hospital stay was found to be extended. After controlling for age and Aletti scores, the hospital stay in the restrictive group was 2.971 days shorter than that in the liberal group.

3.4 Secondary Outcomes

Complications were observed in eight patients (26.7%) in the restrictive group and 21 patients (51.2%) in the liberal group ($p = 0.032$) (Table 5). There were

Table 3. Primary outcomes.

	Restrictive fluid (N = 30)	Liberal fluid (N = 41)	*p* value
Primary outcome			
Hospital stay, (P25, P75), d	16.5 (15, 21.75)	21.0 (17.5, 24.5)	0.035
Chemotherapy interval, mean ± SD, d	13.4 ± 4.1	16.7 ± 5.4	0.008
Mobilization time (P25, P75), d	3.5 (2, 4)	4 (3, 5)	0.018
Bowel function return (P25, P75), d	4.5 (3, 5)	4 (3, 6)	0.578
Recovery of serum albumin concentration, mean ± SD, d	2.3 ± 1.4	2.9 ± 2.1	0.142
Ratio of lactate-to-albumin	0.054 ± 0.037	0.093 ± 0.047	0.028
Unplanned admission to ICU, no. (%)	1 (33.3%)	4 (9.8%)	0.296

Values are presented as median [inter-quartiles] or mean ± SD.
ICU, intensive care unit.

Table 4. Multiple linear regression analysis of hospital stay after radical surgery for advanced ovarian cancer.

Independent variables	B (95% CI)	Std. Error	*t*	*p*
Constant	1.428	4.41	0.324	0.747
Aletti score	0.817 (0.396∼1.238)	0.211	3.936	0.000
Age	0.197 (0.063∼0.331)	0.067	2.961	0.004
groups	–2.971 (–5.818∼–0.124)	1.426	–2.095	0.040

Postoperative hospital stay is the dependent variable.

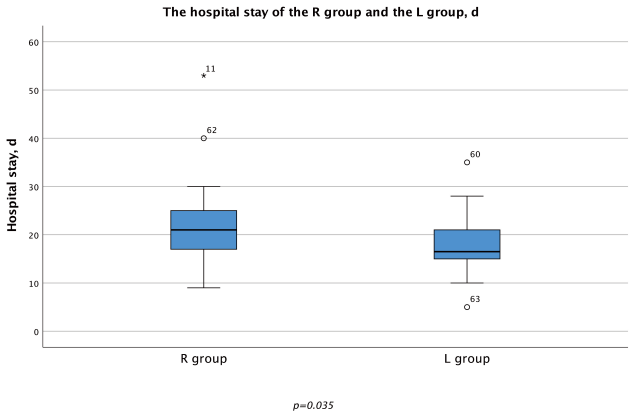

Fig. 2. Box plot comparing hospital stay between the restrictive group and the liberal group.

greater instances of thrombosis in the liberal group than the restrictive group (0% versus 14.6%; $p = 0.031$). Fewer instances of sepsis were observed in the restrictive group than the liberal group (0% versus 12.2%), but the difference was not significant ($p = 0.058$). Other complications and postoperative death were not different among the two groups. The results of the multivariable regression analysis are presented in Table 5. In the adjusted analysis, the risk of total complications decreased by 68% in restrictive group (OR 0.32, 95% CI: 0.11–0.91, $p = 0.033$).

4. Discussion

4.1 Main Findings

Fluid therapy to maintain tissue perfusion is the standard practice for patients undergoing surgery. However, excessive fluid resuscitation can lead to edema, increased pulmonary morbidity, impaired coagulation, sepsis, and poor wound healing [10]. Enhanced recovery after surgery (ERAS) optimizes perioperative interventions to decrease postoperative complications and facilitate postoperative recovery [11]. With advances in ERAS pathways, fluid management for major abdominal surgery is becoming more and more restrictive. Nonetheless, being too restrictive can be harmful, particularly to the renal function [5].

Studies comparing restrictive and liberal fluid therapy have had controversial results. The most widely known study supporting restrictive fluid management is that by Brandstrup *et al*. [12]. They reported higher rates of anastomotic leakage and infections in the liberal group, both of which may actively lead to sepsis and impaired wound healing [12]. This is in line with the findings of McArdle *et al*. [13], Peng *et al*. [14], and Nisanevich *et al*. [15], who argued that tissue edema may be due to the liberal fluid regimen. Nevertheless, a meta-analysis of randomized controlled trials assessing the effect of intravenous fluid therapy during major elective open abdominal surgery on postoperative complications reported no difference between the restrictive or liberal fluid therapy [16]. Interestingly, when repeating the meta-analysis in another clinical set, restrictive fluid administration was superior to liberal fluid administration in reducing the infectious, pulmonary, and cardiac complications after major abdominal surgeries [17].

These contradictory observations might come from the imprecise definitions of the terms “restrictive” and “liberal”. Comparisons are not well-controlled given the vague definition of restrictive measurements. In a past study, Myles RELIEF [5] defined the restrictive intravenous fluid regimen as a net zero fluid balance, with a 5 mL/kg bolus at induction of anesthesia followed by an intraopera-

Table 5. Secondary outcomes.

	Restrictive fluid (n = 30)	Liberal fluid (n = 41)	OR (95% CI)	*p* value
AKI	2 (6.7%)	8 (19.5%)		0.170
Intestinal obstruction	2 (6.7%)	4 (9.8%)		0.640
Intestinal fistula	1 (3.3%)	6 (14.6%)		0.118
Urinary fistula	1 (3.3%)	1 (2.4%)		0.823
Anastomotic bleeding	1 (3.3%)	0 (0%)		0.187
Cardiac insufficiency	0 (0%)	3 (7.3%)		0.130
Thrombosis	0 (0%)	6 (14.6%)		0.031
Pneumonia	0 (0%)	2 (4.9%)		0.330
Surgical site infection	2 (6.7%)	3 (7.3%)		0.647
Sepsis	0 (0%)	5 (12.2%)		0.058
Arrhythmia	1 (3.3%)	0 (0%)		0.423
Unplanned operation	2 (6.7%)	4 (9.8%)		0.496
Postoperative death	0 (0%)	2 (4.9%)		0.330
Total no. of patients	8 (26.7%)	21 (51.2%)		0.032
			0.34 (0.13–0.95)[a]	0.041
			0.32 (0.11–0.91)[b]	0.033

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; AKI, acute kidney injury.

[a] Unadjusted OR.

[b] Adjusted OR Adjusted for: age, operation time, preoperative hemoglobin concentration, comorbid condition, Aletti score.

tive crystalloid infusion at a rate of 5 mL/kg/h, continued after surgery at 0.8 mL/kg/h for 24 h. The liberal group received a 10-mL/kg bolus on the induction of anesthesia followed by an intraoperative crystalloid infusion at a rate of 8 mL/kg/h, continued postoperatively at 1.5 mL/kg/h for 24 h. In this setting, the restrictive regimen was associated with a higher rate of AKI. The parameters in the restrictive group of the Brandstrup study more closely resembled the liberal group in Myles RELIEF, with a weight gain of around 1 kg post-operation at 1.5–2 mL/kg/h [12]. Due to the lack of a standardized definition of restrictive fluid, the results reported by Brandstrup were inconsistent with those by Myles RELIEF [12].

In clinical practice, physicians generally pay careful attention to postoperative fluid management. Due to our inability to intervene and control the amount of intraoperative blood loss and fluid replacement, we conducted a restricted fluid management study after surgery. The daily physiological fluid requirement for adults is about 25–30 mL/kg, and the daily fluid loss is approximately 1500–2500 mL [18]. According to the Brandstrup report, if the postoperative fluid administration rate is maintained at 1.5–2 mL/kg/h, the daily postoperative fluid intake is usually no more than 2500 mL based on the average weight of 50–60 kg in Chinese women. Therefore, we defined restrictive fluid management in this study as the daily postoperative fluid intake, no more than 2500 mL, maintaining zero or negative fluid balance.

Our study showed that restrictive therapy resulted in shorter length of hospital stay and chemotherapy interval, suggesting faster recovery after surgery in the restrictive fluid group. Furthermore, the ratio of lactate-to-albumin, which is also a useful biomarker of recovery, was also lower in the retrospective group [19]. Serum lactate and albumin levels fluctuate during critical illness, and an increased ratio of lactate-to-albumin correlates with the development of multiple organ dysfunction syndrome and mortality in severely septic and other critically ill patients [20,21]. A multiple linear regression analysis also confirmed that patients in the restrictive group spent 2.971-days lesser in the hospital than those in the liberal group, suggesting that restrictive therapy can effectively accelerate postoperative recovery.

In this study, we included advanced ovarian cancer patients with Aletti score of 4 or more during radical surgery, which is a highly complex operation with surgical resection of one or more organs, so the postoperative management is more challenging and the research is necessary. We demonstrated that restrictive fluid management decreased the total 30-day complications after surgery with a marginal difference in sepsis rate. This is consistent with the results of Peng *et al*. [22]. The cause may be a greater volume of extracellular fluids in the liberal group on the first two postoperative days [22]. Other reason may be that cellular swelling broadly impairs intracellular signaling mechanisms responsible for immune regulation [23]. In addition, instances of thrombosis were significantly lower in restrictive groups, probably due to the overloaded fluid impacting the coagulation function. Crystalloids have been shown to promote a hypercoagulation state, possibly predisposing to thromboembolic events. The detailed mechanisms underlying these observations remain unclear. Nonetheless,

it is tempting to speculate that the dilution of anticoagulants, such as antitrombin III and protein C, might facilitate thrombosis formation [24]. In multivariate regression analysis, the risk of postoperative complications decreased by 68% in the restrictive group. Taken together, our current analysis advocates for a restrictive approach.

The American Society for Enhanced Recovery recommends adopting Goal-directed fluid therapy (GDFT) in a critical surgical patient [25]. GDFT is a fluid management option based on specific hemodynamic indexes to intepretate the patient's volume status, aiming at reducing the postoperative mortality and complication rate and facilitating the early recovery of patients. Thus, it has been an emerging principle to guide the use of intravenous infusion components, quantities and vasoactive drugs. Current studies have suggested that GDFT regimen can effectively maintain hemodynamic stability, improve inflammatory responses and ensure proper tissue perfusion with physiological oxygenation. In addition to advanced ovarian cancer, the benefits of GDFT have been extensively confirmed by different surgeries in divergent tumor types [26]. Nonetheless, GDFT relies on complex parameters, which require invasive monitoring systems, Consequently, GDFT is more suitable for intraoperative monitoring instead of postoperative monitioring. Although GDFT monitoring machines are becoming more sophisticated, the application of GDFT in patient undergoing routine gynecologic tumor surgery is still challenging. Guan *et al*. [27] compared intraoperative GDFT with restrictive fluid therapy combined with an ERAS protocol and evaluated its effect on the incidence of AKI after a thoracoscopic lobectomy in high-risk patients. As per their report, although restrictive fluid therapy is non-inferior to GDFT in reducing the incidence of AKI, it is far more straightforward than GDFT in practice [27]. The updated ERAS guidelines on perioperative fluid management are primarily based on studies reporting on surgeries for other abdominal malignancies or general abdominal surgery [28]. Postoperative fluid management associated with radical surgery of ovarian cancer is rarely reported. Therefore, since 2019, postoperative restrictive fluid management regimen is being implemented in a few selected patients undergoing radical surgery for ovarian cancer. Combined with the results of this study and relevant clinical management experience, the concept of a "Dry Ward" has been proposed.

"Dry Ward" emphasizes adequate postoperative fluid management. To the best of our knowledge, the "Dry Ward" concept described in current study is introduced to the field for the first time. The key points are as follows: Firstly, fluid administration and balance should be managed within 3 days after surgery. It will be essential to calculate the sum of fluid administered and fluid lost in the ward every day. The recommended daily intake in total should be no more than 2500 mL, with a balance of zero or even negative. Organ perfusion, blood volume and tissue perfusion are monitored by non-invasive parameters (pulse, central venous pressure, blood pressure, urine volume, oxygen saturation, manually central venous pressure, CVP) and invasive parameters (hemoglobin, albumin, hematocrit, and blood gas analysis). The targets employ the following principles: blood pressure should not be lower than 20% of the normal value; heart rate should not be lower than 20% of normal value; CVP measured manually in the ward should be 5–12 cm H_2O; urine volume should be maintained above 0.5 mL/kg/h) and blood lactic acid should not exceed 2 mmol/L. Vasopressors should be used if hypotension occurs, and diuretics are administered when oliguria is observed or weight increase exceeds 1 kg.

Secondly, the choice of fluid type and individual treatment plan is crucial. In recent years, a series of comparative studies on the role of crystalloid and colloid in fluid and fluid resuscitation therapy have been investigated, yet, the conclusion of safety and effectiveness of these two options is still missing and even controversial. In clinical practice, fluid types and treatment programs should be selected in each patient according to various factors, such as different purposes of fluid therapy, types of diseases, functional hemodynamic status and different stages of perioperative period. When the patient has insufficient blood volume and needs a large amount of fluid replacement, it would be proper to supply with crystal fluid and simultaneous appropriate colloid to control infusion volume and reduce tissue edema. Meanwhile, blood product transfusion is decided according to the hematological status. If the patient has no hypovolemia, it is recommended to supplement physiological needs with crystal fluid.

Lastly, albumin supplementation is recommended for ovarian cancer patients during or after surgery. It is known that low levels of serum albumin, which are common in patients with critical illness, are associated with poor outcome. As such, restricted albumin-based fluid therapy is recommended for all critical illed patients who require extensive fluid resuscitation.

4.2 Strengths and Limitations

A strength of this study was that it analyzed the influence of postoperative fluid management on high-complexity advanced ovarian cancer surgery. Therefore it provides the evidence of "Dry Ward" management after advanced ovarian cancer surgery. To the best of our knowledge, this is the first retrospective study on the influence of postoperative fluid management on high-complexity advanced ovarian cancer surgery.

There are a few of limitations in the study. First, this study adopts a retrospective design. Inherent defects from the uncontrolled, regulatory and insufficient data are introduced. Second, we included only advanced ovarian cancer cases undergoing open radical surgeries from a single center but not mutlicenters. Our fluid recommendations thus may not be applicable to less invasive laparoscopic proce-

dures or other hospitals that use different patient care protocols. Third, our results reflect the current incidence of recent recovery and complications but not the long-term survival data (disability-free survival up to 1 year after surgery, overall survival, and progression free survival), which can be investigated by future prospective studies.

5. Conclusions

Our study demonstrates that restrictive fluid management in patients undergoing surgery for high-complexity advanced ovarian cancer can reduce the risks of major postoperative complications and promote postoperative recovery. The results are expected to provide a more direct fluid treatment strategy guidance for patients with advanced ovarian cancer after radical surgery. However, prospective studies with large sample sizes are still needed warranted to confirm our fluid management. Clinical management of fluid administration in ovarian cancer remains a challenge.

Abbreviations

AKI, acute kidney injury; FIGO, International Federation of Gynaecology and Obstetrics; BUN, blood urea nitrogen; NT-proBNP, Brain natriuretic peptide precursor; FEV1, Forced Expiratory Volume In one second; OR, odds ratios; ERAS, Enhanced recovery after surgery; GDFT, Goal-directed fluid therapy.

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

Q-FZ and YS conceived and designed the original study. Q-FZ, M-SC, Y-JZ was responsible for data collection, data management. Q-FZ, J-YX explained the data. Q-FZ and BD drafted the manuscript. YS revised the manuscript. All authors approved the final manuscript.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Zhongda Hospital (2022ZDSYLL105-P01).

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Conflict of Interest

The authors declare no conflict of interest.

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