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Observation on the Effects of Different Analgesic Depths on Perioperative Inflammatory Factor Levels in Patients Undergoing Gynecological Laparoscopic Tumor Surgery

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Abstract: *Objective:* To investigate the effects of different analgesic depths on perioperative inflammatory factor levels and immune function in patients undergoing laparoscopic surgery for gynecological tumors. *Methods:* A total of 104 patients scheduled for laparoscopic radical tumor resection were enrolled and randomly allocated to a deep analgesia group or a shallow analgesia group, with 52 patients in each group. Intraoperative analgesic depth was regulated by adjusting the target-controlled infusion concentration of remifentanil according to the analgesic depth index.The index was maintained at 30–50 in the deep analgesia group and 51–70 in the shallow analgesia group. Hemodynamic parameters, stress hormones, inflammatory factors, immune function, and postoperative recovery indicators were compared between the two groups. *Results:* Compared with the shallow analgesia group, the deep analgesia group exhibited smaller fluctuations in blood pressure and heart rate. Increases in serum cortisol and norepinephrine levels were significantly lower in the deep analgesia group. The levels of interleukin-6, tumor necrosis factor-α and C-reactive protein were significantly reduced, whereas the interleukin-10 level was higher. Reductions in CD3+ T lymphocytes, the CD4+/CD8+ ratio and natural killer cell activity were attenuated in the deep analgesia group. Postoperative pain scores, analgesic consumption and the incidence of nausea and vomiting were also lower, while postoperative recovery was accelerated (all $P < 0.05$). *Conclusion:* Deep analgesia management can attenuate perioperative stress and inflammatory responses, reduce postoperative immune suppression and promote early recovery in patients undergoing laparoscopic surgery for gynecological tumors.

Keywords: Analgesic depth; Gynecological laparoscopic surgery; Tumor; Inflammatory factors; Immune function

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1. Introduction

Previous evidence indicates that anesthetic depth may influence perioperative inflammatory responses and

hospitalization outcomes in patients undergoing laparoscopic radical tumor surgery [1]. Anesthetic depth has also been associated with changes in perioperative T-lymphocyte subsets [2]. In addition, perioperative anesthetic strategies can affect the release of IL-1, IL-6 and TNF-α during gynecological laparoscopic surgery [3]. These findings suggest that anesthetic and analgesic management may be important modifiable factors affecting perioperative inflammation and immune function.

Objective nociception monitoring provides a measurable basis for individualized analgesic management. Nociception level index-guided analgesia has been reported to improve postoperative recovery [4] and reduce intraoperative opioid consumption [5]. Systematic evidence also supports the validity of the analgesia nociception index and nociception level index for assessing nociceptive responses in anesthetized patients [6]. However, evidence regarding the influence of different analgesic depths on inflammatory responses in patients undergoing gynecological laparoscopic tumor surgery remains limited. Therefore, the present study established different analgesic depth ranges and investigated their effects on perioperative inflammatory factors, immune function and early postoperative recovery.

2. Materials and methods

2.1. Baseline characteristics

This prospective randomized controlled study was conducted from June 2023 to November 2024. Patients scheduled to undergo laparoscopic radical surgery for gynecological malignant tumors were recruited from the Department of Gynecology of our hospital.

A total of 104 patients were randomly allocated to a deep analgesia group or a shallow analgesia group using a computer-generated random number sequence, with 52 patients in each group. No statistically significant differences were observed in baseline characteristics between the two groups ($P > 0.05$).

Table 1. Comparison of baseline characteristics between the two groups

Variables	Deep analgesia group (n = 52)	Shallow analgesia group (n = 52)	Statistical value	*P*-value
Age (years)	50.2 ± 8.5	50.6 ± 8.9	t = 0.234	0.815
Body mass index (kg/m²)	22.9 ± 2.7	23.2 ± 2.9	t = 0.545	0.587
Radical resection of ovarian tumor, n	18	19	$\chi^2 = 0.286$	0.867
Radical surgery for endometrial cancer, n	18	17	—	—
Radical surgery for cervical cancer, n	16	16	—	—
ASA physical status (I/II, n)	20/32	18/34	$\chi^2 = 0.163$	0.686

2.2. Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) Patients diagnosed with gynecological malignant tumors based on pathological and imaging examinations and meeting the indications for laparoscopic radical surgery; (2) Patients aged 18–70 years; (3) Patients with an American Society of Anesthesiologists (ASA) physical status classification of grade I or II; (4) Patients with an estimated surgical duration of 1.5–3.5 h; and (5) Patients with normal preoperative cognitive function who were able to cooperate with postoperative assessments and provided written informed consent.

The exclusion criteria were as follows: (1) Patients with pre-existing dysfunction of major organs,

including the heart, liver or kidney; (2) Patients with active infection before surgery or those who had received immunomodulatory drugs or glucocorticoids within the previous 3 months; (3) Patients with coagulation disorders or hematological diseases; (4) Patients with a history of long-term opioid use or potential drug dependence; (5) Patients with previously diagnosed chronic pain disorders; (6) Patients with allergic reactions to anesthetic agents used in the study; (7) Patients who required conversion to open surgery due to intraoperative changes in clinical conditions; and (8) Patients with psychiatric disorders that affected communication and cooperation.

2.3. Anesthesia and analgesia management

After entering the operating room, peripheral venous access was established in all patients. Electrocardiography, non-invasive blood pressure, pulse oxygen saturation, analgesic depth index and bispectral index (BIS) were monitored.

Anesthesia was maintained using intravenous propofol combined with target-controlled infusion of remifentanil. Cisatracurium was intermittently administered to maintain adequate muscle relaxation. In the deep analgesia group, the target-controlled concentration of remifentanil was dynamically adjusted to maintain the analgesic depth index at 30–50. In the shallow analgesia group, the index was maintained at 51–70 using the same adjustment procedure.

Propofol infusion was adjusted to maintain BIS values between 40 and 60 in both groups, ensuring a comparable depth of sedation. Approximately 15 min before the end of surgery, remifentanil infusion was discontinued. After wound closure, an intravenous patient-controlled analgesia pump containing sufentanil and tropisetron hydrochloride was connected. The background infusion dose, bolus dose and lockout interval were identical between the two groups.

Analgesic depth index values were recorded by investigators who did not participate in anesthesia management. Postoperative pain and complications were assessed by designated evaluators blinded to group allocation. All patients were followed until discharge.

2.4. Observation indexes

(1) Hemodynamic parameters

Hemodynamic parameters were recorded at four time points: before anesthesia induction (T0), 10 min after establishment of pneumoperitoneum (T1), 1 h after initiation of surgery (T2), and at the end of surgery (T3). The mean arterial pressure (MAP) and heart rate (HR) were documented at each time point.

(2) Stress hormone levels

Venous blood samples were collected before anesthesia induction (T0), at the end of surgery (T3), and 24 h after surgery (T4). Serum cortisol (Cor), norepinephrine (NE) and fasting blood glucose levels were measured to evaluate the perioperative stress burden.

(3) Inflammatory factor levels

Serum IL-6 and TNF-α levels were measured before anesthesia induction (T0), at the end of surgery (T3), and at 24 h (T4) and 48 h (T5) after surgery.CRP levels were measured at 24 and 48 h after surgery.IL-10 levels were measured at the end of surgery and 24 h after surgery. Cytokine concentrations were determined using enzyme-linked immunosorbent assay.

(4) Immune function parameters

Peripheral blood samples were collected before anesthesia induction (T0) and 24 h after surgery (T4).

The proportions of CD3+, CD4+ and CD8+ T lymphocyte subsets, the CD4+/CD8+ ratio and natural killer (NK) cell activity were measured to evaluate postoperative cellular immune suppression.

(5) Postoperative recovery and complication-related parameters

Recovery time and extubation time were recorded. Postoperative pain was assessed using the numerical rating scale (NRS) at 2, 12, 24 and 48 h after surgery. Cumulative patient-controlled analgesia pump consumption within 48 h, nausea and vomiting, time to first ambulation, time to first postoperative anal evacuation, and total postoperative hospital stay were recorded.

2.5. Statistical analysis

Statistical analyses were performed using SPSS version 26.0. Continuous variables with a normal distribution were expressed as the mean ± standard deviation. Comparisons between groups were performed using the independent-samples t-test. Repeated measurements were analyzed using repeated-measures analysis of variance. Categorical variables were presented as numbers and percentages and compared using the χ^2 test or Fisher's exact test.$P < 0.05$ was considered statistically significant.

3. Results

No patients required conversion to open surgery, and no severe anesthesia-related adverse events occurred. Complete data from all 104 patients were included in the final analysis.

3.1. Comparison of perioperative hemodynamic parameters between the two groups

MAP and HR at T0 were comparable between the two groups ($P > 0.05$). At T1, T2 and T3, MAP and HR were significantly lower in the deep analgesia group than in the shallow analgesia group (all $P < 0.001$).

Table 2. Comparison of perioperative hemodynamic parameters between the two groups (mean ± SD)

Time point	Parameters	Deep analgesia group (n = 52)	Shallow analgesia group (n = 52)	t-value	P-value
T0	MAP (mmHg)	87.6 ± 6.4	88.2 ± 6.9	0.452	0.652
	HR (beats/min)	75.3 ± 6.8	74.9 ± 7.1	0.294	0.769
T1	MAP (mmHg)	84.9 ± 5.9	95.8 ± 8.2	7.756	< 0.001
	HR (beats/min)	77.2 ± 6.5	90.6 ± 8.7	8.874	< 0.001
T2	MAP (mmHg)	82.7 ± 5.6	92.9 ± 7.4	7.995	< 0.001
	HR (beats/min)	74.5 ± 6.1	87.3 ± 7.9	9.213	< 0.001
T3	MAP (mmHg)	81.3 ± 5.2	88.7 ± 6.6	6.363	< 0.001
	HR (beats/min)	72.6 ± 5.8	82.1 ± 7.2	7.462	< 0.001

3.2. Perioperative stress hormone levels

No significant between-group differences were detected in cortisol, norepinephrine, or blood glucose at T0 ($P > 0.05$). At T3 and T4, all three indicators were significantly lower in the deep analgesia group than in the shallow analgesia group (all $P < 0.001$).

Table 3. Comparison of perioperative stress hormone levels between the two groups (mean ± SD)

Parameters	Time point	Deep analgesia group (n = 52)	Shallow analgesia group (n = 52)	t-value	*P*-value
Cortisol (nmol/L)	T0	305.8 ± 40.3	309.4 ± 43.6	0.443	0.659
	T3	372.6 ± 46.9	498.3 ± 58.7	12.202	< 0.001
	T4	341.5 ± 39.8	447.2 ± 52.4	11.669	< 0.001
Norepinephrine (pg/mL)	T0	182.6 ± 24.7	185.3 ± 26.1	0.545	0.587
	T3	238.4 ± 31.5	316.7 ± 39.8	11.402	< 0.001
	T4	209.7 ± 27.6	267.8 ± 34.9	9.478	< 0.001
Blood glucose (mmol/L)	T0	5.1 ± 0.6	5.2 ± 0.7	0.775	0.44
	T3	6.2 ± 0.7	7.6 ± 1.0	8.348	< 0.001
	T4	5.6 ± 0.6	6.7 ± 0.8	7.998	< 0.001

3.3. Inflammatory factor levels

Baseline IL-6 and TNF-α levels were comparable between the two groups. Postoperative IL-6, TNF-α and CRP levels were significantly lower in the deep analgesia group, whereas IL-10 levels were significantly higher (all $P < 0.001$).

Table 4. Comparison of inflammatory factor levels between the two groups (mean ± SD)

Parameters	Time point	Deep analgesia group (n = 52)	Shallow analgesia group (n = 52)	t-value	P-value
IL-6 (pg/mL)	T0	8.3 ± 1.8	8.5 ± 2.0	0.541	0.59
	T3	39.6 ± 7.1	56.4 ± 9.5	10.278	< 0.001
	T4	33.2 ± 6.0	47.5 ± 7.9	10.457	< 0.001
	T5	19.8 ± 4.5	29.7 ± 5.8	9.809	< 0.001
TNF-α (ng/L)	T0	20.8 ± 3.4	21.2 ± 3.7	0.573	0.568
	T3	45.9 ± 6.5	60.8 ± 8.3	10.211	< 0.001
	T4	38.6 ± 5.4	51.9 ± 7.0	10.809	< 0.001
	T5	27.4 ± 4.2	36.5 ± 5.7	9.353	< 0.001
CRP (mg/L)	T4	26.4 ± 5.1	37.8 ± 6.9	9.502	< 0.001
	T5	16.9 ± 3.6	24.8 ± 4.8	9.417	< 0.001
IL-10 (pg/mL)	T3	17.6 ± 3.0	12.9 ± 2.6	8.549	< 0.001
	T4	21.3 ± 3.6	15.8 ± 2.9	8.633	< 0.001

3.4. Immune function parameters

Immune function parameters were comparable between the two groups at T0. At T4, the deep analgesia group had higher CD3+, CD4+, CD4+/CD8+ and NK cell activity values and a lower CD8+ value than the shallow analgesia group (all $P < 0.001$).

Table 5. Comparison of immune function parameters between the two groups (mean ± SD)

Parameters	Deep analgesia group T0	Deep analgesia group T4	Shallow analgesia group T0	Shallow analgesia group T4	Between-group t-value at T4	*P*-value
CD3+ (%)	67.9 ± 5.4	62.3 ± 5.0	68.3 ± 5.7	55.1 ± 5.6	6.542	< 0.001
CD4+ (%)	42.1 ± 4.1	39.0 ± 3.9	41.8 ± 4.3	33.5 ± 4.2	6.749	< 0.001

Parameters	Deep analgesia group T0	Deep analgesia group T4	Shallow analgesia group T0	Shallow analgesia group T4	Between-group t-value at T4	*P*-value
CD8+ (%)	26.6 ± 3.0	27.2 ± 3.2	26.4 ± 3.3	30.1 ± 3.5	4.328	< 0.001
CD4+/CD8+ ratio	1.59 ± 0.23	1.44 ± 0.20	1.61 ± 0.25	1.11 ± 0.18	8.834	< 0.001
NK cell activity (%)	24.3 ± 3.5	22.0 ± 3.2	24.6 ± 3.7	16.8 ± 3.0	8.657	< 0.001

3.5. Postoperative recovery outcomes and complications

The deep analgesia group had shorter recovery and extubation times, lower 24-h NRS scores, lower analgesic pump consumption, earlier ambulation and anal exhaust, a lower incidence of nausea and vomiting, and a shorter hospital stay than the shallow analgesia group (all $P < 0.05$).

Table 6. Comparison of postoperative recovery outcomes and complications between the two groups

Parameters	Deep analgesia group (n = 52)	Shallow analgesia group (n = 52)	Statistical value	*P*-value
Recovery time (min)	11.8 ± 2.9	15.2 ± 3.7	t = 5.267	< 0.001
Extubation time (min)	15.9 ± 3.5	20.6 ± 4.3	t = 6.180	< 0.001
NRS pain score (24 h)	2.4 ± 0.7	3.9 ± 1.1	t = 8.421	< 0.001
Cumulative analgesic pump consumption (mL)	62.3 ± 9.8	84.6 ± 12.5	t = 10.180	< 0.001
Time to first ambulation (h)	13.6 ± 3.0	18.9 ± 4.2	t = 7.508	< 0.001
Time to first postoperative anal exhaust (h)	21.4 ± 4.0	28.3 ± 5.3	t = 7.535	< 0.001
Nausea and vomiting, n (%)	5 (9.6)	16 (30.8)	$\chi^2 = 7.472$	0.006
Total length of hospital stay (days)	4.9 ± 1.0	6.5 ± 1.3	t = 7.081	< 0.001

4. Discussion

Surgical trauma induces the release of damage-associated molecular patterns, activates innate immune cells and promotes the production of pro-inflammatory cytokines.IL-6 is an important mediator of the acute inflammatory response and stimulates hepatic CRP synthesis. TNF-α can promote leukocyte activation and amplify inflammatory cascades. In the present study, postoperative IL-6, TNF-α and CRP levels were significantly lower in the deep analgesia group, whereas the anti-inflammatory cytokine IL-10 was higher. These findings suggest that deeper analgesia may reduce excessive pro-inflammatory activation and support compensatory anti-inflammatory regulation. Previous research has similarly shown that perioperative anesthesia and analgesia strategies influence IL-6 and TNF-α levels in patients undergoing laparoscopic hysterectomy.

NK cells and T lymphocytes are important components of antitumor immune surveillance. Their perioperative suppression may weaken the elimination of residual tumor cells. Although the present results suggest that deep analgesia provides short-term immune protection, no long-term oncological endpoints were evaluated. Therefore, the findings cannot establish that deep analgesia reduces tumor recurrence or metastasis. Long-term follow-up is required to determine whether preservation of cellular immune function translates into improved oncological outcomes.

The deep analgesia group also achieved better postoperative recovery outcomes, including lower NRS scores, reduced analgesic pump consumption, earlier ambulation, earlier anal exhaust and shorter

hospitalization. Improved intraoperative nociceptive control may reduce central sensitization and early postoperative pain. Lower postoperative opioid requirements may further decrease nausea, vomiting and gastrointestinal inhibition, facilitating earlier activity and functional recovery. Notably, adequate analgesia did not delay emergence. Recovery and extubation times were shorter in the deep analgesia group, suggesting that analgesic depth index-guided titration did not produce excessive postoperative sedation.

Several limitations should be acknowledged. First, this was a single-center study with a relatively small sample size, which may limit the generalizability of the findings. Second, inflammatory and immune indicators were evaluated only during the early postoperative period. Third, the total intraoperative remifentanil dosage and exposure-adjusted effects were not analyzed in detail. Fourth, the study did not assess long-term recurrence, metastasis or survival. Multicenter randomized controlled studies incorporating standardized nociception monitoring, opioid consumption, long-term immune indicators and oncological outcomes are required.

5. Conclusion

In conclusion, deep analgesia management guided by an objective analgesic depth index reduced perioperative hemodynamic fluctuations and stress hormone release in patients undergoing gynecological laparoscopic tumor surgery. It also suppressed pro-inflammatory responses, increased IL-10 levels, attenuated postoperative cellular immune suppression and promoted early postoperative recovery. Objective monitoring-guided analgesic management may therefore provide a useful approach for optimizing perioperative anesthesia in this patient population.

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Disclosure statement

The authors declare no conflict of interest.

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