

Quadratus Lumborum Block for Robotic Prostatectomy: Improved Early Recovery but Not Short-Term Event-Free Survival – A Randomized Trial

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Abstract

Objective: This randomized, double-blind trial investigated whether adding a quadratus lumborum block (QLB) to general anesthesia (GA) improves 6-month event-free survival (EFS) and recovery after robot-assisted laparoscopic radical prostatectomy (RALP).

Methods: Three hundred fifty patients were randomized; the modified intention-to-treat population comprised 299 patients (GA+QLB, n=148; GA alone, n=151). The primary outcome was 6-month EFS (composite of biochemical/radiographic recurrence or initiation of salvage/adjuvant therapy). Secondary outcomes included opioid consumption, pain scores, quality of recovery, and inflammatory markers.

Results: Baseline characteristics were available for the per-protocol population (n=286). Within the confines of this trial, we did not detect a statistically significant difference in 6-month EFS between the GA+QLB and GA groups (adjusted HR = 0.858, 95% CI: 0.572–1.285, P = 0.457). However, the GA+QLB group demonstrated clinically meaningful improvements in early recovery outcomes, including significantly lower intraoperative opioid consumption, lower postoperative pain scores, shorter time to first flatus, and higher QoR-40 scores on postoperative day 1 (all P < 0.05). Inflammatory and immune markers showed no significant intergroup differences.

Conclusion: In this randomized trial, adding QLB to GA did not improve the 6-month composite EFS endpoint for RALP. While the oncologic effect remains inconclusive and requires longer follow-up, the study provides robust evidence that QLB significantly enhances early recovery—reducing opioid use and improving patient-reported quality of recovery. These benefits support routine inclusion of QLB in multimodal analgesia for RALP within ERAS pathways.

Trial registration: Chinese Clinical Trial Registry (ChiCTR); Identifier: [ChiCTR-2200066968]; Date of registration: December 22, 2022; Prospectively registered.

Introduction

Prostate cancer is a prevalent malignancy, and robot-assisted laparoscopic radical prostatectomy (RALP) is a curative treatment. Established pathological factors such as Gleason score and surgical margin status are key prognostic determinants. However, interest is growing in whether modifiable perioperative factors might also influence oncological outcomes ^[1].

The surgical period induces a stress response that can cause transient immunosuppression, potentially facilitating micrometastasis growth ^[2, 3]. Regional anesthesia reduces opioid consumption and attenuates this response ^[4], and opioids have immunosuppressive properties ^[5, 6]; preclinical studies also suggest local anesthetics may have direct anti-tumor effects ^[7, 8]. Despite this biological rationale, high-quality clinical evidence from RCTs on regional anesthesia and cancer recurrence remains scarce and conflicting ^[9–12].

Among various regional anesthesia techniques—including epidural, paravertebral, transversus abdominis plane (TAP) block, and wound infiltration—the quadratus lumborum block (QLB) is particularly suitable for RALP for several reasons. First, QLB provides broader analgesic coverage than TAP block or wound infiltration, blocking both somatic and visceral afferent pathways and covering the dermatomes relevant to robotic prostatectomy (T10–L2). Second, unlike neuraxial techniques (epidural or spinal), QLB avoids hypotension and urinary retention, which are particularly undesirable in pelvic surgery and enhanced recovery protocols. Third, QLB is compatible with Enhanced Recovery After Surgery (ERAS) pathways, facilitating early mobilization and reducing opioid consumption without delaying discharge [3].

A key limitation of prior studies is reliance on biochemical recurrence (BCR) alone. In current practice, high-risk patients often receive immediate adjuvant therapy that suppresses PSA, preventing them from ever meeting BCR criteria and causing misclassification. We therefore adopted a composite event-free survival (EFS) endpoint that also captures initiation of salvage/adjuvant therapy, providing a less biased assessment of disease progression.

Knowledge gap and study contribution: Prior RCTs have not specifically evaluated QLB for oncologic outcomes in RALP, and most have relied on BCR alone. This study is the first sham-controlled, double-blind RCT of QLB in RALP using a composite EFS endpoint that incorporates adjuvant therapy initiation. We hypothesized that adding QLB to GA would improve 6-month EFS, but the primary contribution is to provide high-level evidence on both oncologic and recovery outcomes within a rigorous design.

Materials and Methods

1.1 Study Design and Ethical Approval

This was a single-center, prospective, randomized, double-blind, controlled trial. The study protocol was approved by the Institutional Review Board (Approval No. [2022]046 – 01) and registered prospectively with the Chinese Clinical Trial Registry (Registration No. ChiCTR-2200066968). Written informed consent was obtained from all participants. The study is reported according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines.

1.2 Sample Size Calculation

The sample size was calculated a priori using PASS software (Version 15.0, NCSS, LLC). Based on a review of earlier literature and preliminary data from our institution—which included a higher-risk patient population treated before the widespread adoption of contemporary adjuvant therapy protocols—we assumed a 6-month event rate of 50% in the control group. We hypothesized that the addition of QLB could reduce this rate to 35% (an absolute risk reduction of 15%). We acknowledge that these assumptions were optimistic and not well supported by contemporary RALP cohorts; no prior RCT data existed to guide more precise estimates at the time of study planning. To detect this difference with a two-sided alpha of 0.05 and a power of 80%, and accounting for an estimated 15% dropout rate, the calculation indicated that 350 patients (175 per group) were required.

1.3 Participants and Randomization

Patients scheduled for RALP between January 1, 2023, and December 31, 2024, were assessed for eligibility.

Inclusion criteria: pathological diagnosis of prostate cancer, planned for RALP; clinical stage I–IV; age ≤ 85 years; ASA physical status I–III.

Exclusion criteria: preoperative distant metastasis, history of other active malignancies, severe cardiac/pulmonary/hepatic/renal dysfunction, psychiatric disorders, perioperative complications affecting prognosis, death during the study, or loss to follow-up.

A computer-generated randomization sequence was created by an independent statistician. Allocation was concealed using sequentially numbered, opaque, sealed envelopes. An independent anesthesiologist not involved in the study opened the envelopes and prepared the QLB injections (active or sham) to maintain blinding.

1.4 Blinding

A double-blind design was implemented. Patients, surgeons, postoperative care providers, and outcome assessors were blinded to group assignment. The anesthesiologists performing the blocks and general anesthesia were not involved in any postoperative data collection or outcome assessment. To maintain blinding, the sham block procedure included identical skin preparation, ultrasound probe application, and probe holding time as the active block.

We acknowledge a limitation of the sham procedure: patients in the sham group could potentially infer group assignment due to the absence of needle insertion sensation. To minimize this risk, patients were informed before randomization that both techniques (with or without needle injection) are used in clinical practice and that they might not feel the needle in either group. No topical anesthetic was applied to the skin to preserve sensation as part of the sham design. However, this limitation likely biased patient-reported outcomes (e.g., QoR-40) but not the objective primary outcome (EFS based on PSA levels and treatment decisions made by blinded clinicians).

1.5 Interventions

Group GA + QLB: Before induction of general anesthesia, patients received an anterior quadratus lumborum block (QLB Type 3) with 25 mL of 0.2% ropivacaine per side, as previously described ^[3], and shown in Fig. 1

(A) Patient positioned in the lateral decubitus position with the operative side up. The ultrasound probe is placed transversely at the lumbar level, between the iliac crest and the costal margin, at the anterior axillary line. (B) Corresponding ultrasound image showing the needle trajectory and injection target. The needle is advanced from the anterior approach toward the fascial plane between the quadratus lumborum (QL) muscle and the psoas major (PM) muscle. The white arrows indicate the injection target

(the thoracolumbar fascia at the anterolateral aspect of QL), and the yellow dashed line outlines the QL muscle. Local anesthetic (0.2% ropivacaine, 25 mL) is deposited in this interfascial plane. ES, erector spinae muscle.

Group GA alone: Patients underwent an identical preparation, including skin disinfection and application of the ultrasound probe with gel. The probe was held in place for a duration similar to the active block, but no needle was inserted and no fluid was injected (sham block). A single group of certified, senior attending physicians performed all quadratus lumborum blocks after completing standardized ultrasound training.

General anesthesia: A standardized protocol was used for all patients. Induction was achieved with 0.7 µg/kg sufentanil, 0.05 mg/kg midazolam, 0.3 mg/kg etomidate, and 0.6 mg/kg rocuronium. After tracheal intubation, anesthesia was maintained with propofol and remifentanil infusions titrated to maintain BIS between 40 and 60. Rocuronium was supplemented as needed. Postoperative analgesia: All patients received intravenous patient-controlled analgesia (PCA) for pain management.

Surgery: All RALP procedures were performed by a single surgical team via a transperitoneal approach with a 30° head-down tilt. All procedures were primarily performed by a single, highly experienced attending surgeon (> 200 RALP procedures), with three other fixed faculty members rotating as assistants.

1.6 Outcome Measures

Data were collected prospectively by research personnel blinded to group allocation.

Primary outcome: 6-month event-free survival (EFS), defined as the first occurrence of either: (a) biochemical or radiographic recurrence (PSA $\geq$ 0.2 ng/mL on two consecutive measurements, or clinical/radiographic evidence of recurrence); or (b) initiation of salvage or adjuvant therapy (any radiotherapy or androgen deprivation therapy following surgery, regardless of PSA level). This composite endpoint was chosen to capture all forms of disease progression and to avoid bias from guideline-directed early intervention in high-risk patients. The 6-month time horizon was selected because it represents the earliest clinically meaningful window for adjuvant therapy decisions after RALP.

Secondary outcomes: analgesic efficacy and opioid consumption (VAS scores, PCA demands, opioid dosage); recovery quality (time to first flatus, urinary catheter duration, QoR-40 score^[13]); inflammatory and immune markers (WBC, neutrophil, lymphocyte, platelet counts, NLR, PLR, SII, CRP, IL-6, PCT, D-dimer, FDP). All analyses of inflammatory and immune markers were exploratory and not adjusted for multiple comparisons; findings should be interpreted as hypothesis-generating.

1.7 Safety Monitoring and Adverse Events

Specific vigilance was maintained for QLB-related complications: LAST (Local anesthetic systemic toxicity), hematoma, infection, or neurological injury. All AEs were documented. SAEs were reported to the IRB within 24 hours.

1.8 Handling of Missing Data and Loss to Follow-up

The primary efficacy analysis was based on the modified intention-to-treat (mITT) population, defined as all randomized patients who received at least one dose of the assigned intervention and had at least one evaluable primary outcome datum. Of 350 randomized patients (GA, n = 175; GA + QLB, n = 175), 51 were excluded due to major protocol deviations or missing key data, leaving 299 patients in the mITT population (GA + QLB, n = 148; GA, n = 151). Of these, 13 were lost to follow-up, leaving 286 patients in the per-protocol population (GA + QLB, n = 140; GA, n = 146). Exclusion rates were balanced between groups (GA: 13.7%; GA + QLB: 15.4%). Data for excluded patients (n = 51) were not systematically collected, as exclusions occurred due to unanticipated intraoperative or postoperative events (e.g., massive hemorrhage, anaphylaxis, intestinal obstruction) that interrupted standard data collection protocols. This limitation is acknowledged, and the balanced exclusion rates between groups partially mitigate concerns about selection bias. A detailed breakdown of exclusion reasons by group is provided in Supplementary Table 1, and the derivation of analysis populations is shown in Supplementary Table 2. For the primary endpoint, missing follow-up data were handled using right censoring (as shown in Fig. 2). Three pre-specified sensitivity analyses were conducted: (1) worst-case ITT (all lost to follow-up considered events); (2) per-protocol analysis; (3) extreme-case stress test (all excluded and lost GA + QLB patients assumed events; only lost GA patients assumed events). A post-hoc power analysis based on observed event rates is provided in Supplementary Table 3.

Figure 2 Patient inclusion process

CONSORT flow diagram showing the randomization, exclusions, loss to follow-up, and final analysis populations (mITT and per-protocol) for both groups.

1.9 Statistical Analysis

Data analysis was performed using SPSS version 25.0 (IBM Corp.). Continuous variables were compared using Student's t-test or Mann-Whitney U test. Categorical variables were compared using chi-square or Fisher's exact test. Time-to-event analysis used the Kaplan-Meier method with log-rank test. A multivariable Cox proportional hazards model was used to calculate adjusted HRs, including treatment group and pre-specified covariates. A two-sided $P < 0.05$ indicated statistical significance.

Results

2.1 Comparison of Baseline Characteristics and Surgical Parameters between Groups Baseline demographics, surgical parameters, and intraoperative vital signs were comparable between groups (all $P > 0.05$; Table 1, Fig. 3). Baseline characteristics were available for the per-protocol population.

Table 1
Comparison of general information between the two groups of patients (per-protocol population, n = 286)

Factor	Group GA(n = 146)	Group GA + QLB(n = 140)	Statistic	P
Age(year)	69.52 ± 6.14	68.15 ± 6.63	$t = 1.055$	0.294
BMI (kg/m ²)	23.72 ± 2.72	24.76 ± 2.61	$t = -1.929$	0.057
ASA classification(cases,%)				
II	95(65.1%)	93(66.4%)	$\chi^2 = 0.058$	0.809
III	51(34.9%)	47(33.6%)		
Length of the operation (min)	229.43 ± 28.81	229.39 ± 39.10	$F = 4.211$	0.995
Preoperative comorbidities(cases,%)				
Hypertension	27(18.5%)	22(15.7%)	$\chi^2 = 0.248$	0.619
Diabetes	22(15.1%)	17(12.1%)	$\chi^2 = 0.475$	0.491
Heart disease	11(7.5%)	16(11.4%)	$\chi^2 = 1.523$	0.217
Respiratory system diseases	16(11.0%)	19(13.6%)	$\chi^2 = 0.390$	0.532
Comorbidity	35(24.0%)	43(30.7%)	$\chi^2 = 1.634$	0.201
Blood loss (ml)	112.50 ± 63.91	131.48 ± 77.88	$F = 3.761$	0.197
Mechanical ventilation time(min)	316.80 ± 33.61	311.96 ± 50.48	$t = 0.544$	0.588
Infusion volume (ml)	2026.70 ± 406.32	2029.17 ± 483.64	$t = -0.027$	0.979
Crystal	1342.61 ± 311.25	1300.46 ± 407.84	$t = 0.564$	0.574
Colloid	675.00 ± 276.29	727.78 ± 308.48	$t = -0.882$	0.380
Urinary tract infection(cases,%)	15(9.6%)	21(15.0%)	$\chi^2 = 1.440$	0.230
Note: BMI, Body Mass Index; ASA, American Society of Anesthesiology.				

2.2 Pathological Characteristics Preoperative PSA,ISUP Grade Group, pathological stage (pT, pN), surgical margin status, extraprostatic extension, seminal vesicle invasion, nerve-sparing status, and

extent of lymph node dissection were well-balanced between groups (all $P > 0.05$; Table 2), indicating similar disease severity and prognosis.

Table 2

Comparison of disease severity and key surgical variables between the two groups of patients (per-protocol population, n = 286)

Factors	Group GA(n = 146)	Group GA + QLB(n = 140)	Statistical value	P value
Preoperative PSA (ng/ml)	Mdn: 12.42; IQR: 9.72–21.24	Mdn: 13.54; IQR: 8.27–31.18	<i>U</i> = 1169	0.895
ISUP Grade Group(cases, %)				
Group 1(Gleason score ≤ 6)	16(11.0%)	18(12.8%)	Z=-0.745	0.456
Group 2(Gleason 3 + 4=7)	30(20.5%)	32(22.9%)		
Group 3(Gleason 4 + 3=7)	30(20.5%)	28(20.0%)		
Group 4(Gleason 8)	30(20.5%)	27(19.3%)		
Group 5(Gleason 9–10)	40(27.4%)	35(25.0%)		
Pathological T stage (pT stage, (cases, %))				
pT2	81(55.5%)	79(56.4%)	Z=-0.321	0.748
pT3a	21(14.4%)	22(15.7%)		
pT3b	30(20.5%)	28(20.0%)		
pT4	14(9.6%)	11(7.9%)		
Pathological N stage(pN stage, (cases, %))				
pN0	123(84.2%)	125(89.3%)	χ^2 = 1.575	0.209
pN1	23(15.8%)	15(10.7%)		
Extraprostatic Extension(cases, %)	33(22.6%)	25(17.9%)	χ^2 = 0.999	0.317
Seminal Vesicle Invasion(cases, %)	28(19.2%)	24(17.1%)	χ^2 = 0.367	0.544
Margin status (cases, %)				
Positive	20(13.7%)	23(16.4%)	χ^2 = 0.230	0.631
Nerve-sparing status(cases, %)				
Bilateral-nerve-sparing	83(56.8%)	72(51.4%)	Z=-0.449	0.653
Unilateral-nerve-sparing	30(20.6%)	40(28.6%)		
Non-nerve-sparing	33(22.6%)	28(20.0%)		

Factors	Group GA(n = 146)	Group GA + QLB(n = 140)	Statistical value	P value
Lymph node dissection(cases, %)				
None	15(10.3%)	13(9.3%)	Z=-0.463	0.643
Limited,	85(58.2%)	79(56.4%)		
Extended	46(31.6%)	48(34.3%)		

2.3 Primary Outcome: Event-Free Survival and Sensitivity Analyses The primary analysis was based on the mITT population, and the adjusted HR from the Cox model was 0.858 (95% CI: 0.572–1.285, $P = 0.457$). In the per-protocol population, during the 6-month follow-up, 117 events (40.9%) occurred (GA + QLB: $n = 54$; GA: $n = 63$, Table 3). Kaplan-Meier analysis showed no significant difference in event-free survival between groups (log-rank $\chi^2 = 0.372$, $P = 0.542$, Fig. 4). Sensitivity analyses confirmed the robustness of this finding: both worst-case intention-to-treat (HR 0.91, 95% CI 0.68–1.23; $P = 0.419$) and per-protocol analyses (HR 0.88, 95% CI 0.62–1.25; $P = 0.463$) yielded consistent results. Only an extreme-case analysis—which assumed that all excluded and lost-to-follow-up patients in the GA + QLB group experienced an event, while only those lost to follow-up in the GA group experienced an event—showed a significant effect favoring the control group (HR 1.396, 95% CI 1.037–1.878; $P = 0.027$). This scenario is clinically implausible, as it assumes no events among excluded GA patients, as shown in Table 4.

Table 3

The frequency of the Primary Composite Endpoint at 6 Months (per-protocol population, $n = 286$)

Primary Outcome	Group GA(n = 146)	Group GA + QLB(n = 140)	Statistical value	P value
Event occurred	63(43.2%)	54(38.6%)	$\chi^2 = 0.615$	0.433
Event-Free	83(56.8%)	86(61.4%)		
Biochemical or clinical recurrence	19(13.0%)	15(10.7%)	$\chi^2 = 0.352$	0.553
Initiation of therapy	44(30.1%)	39(27.9%)	$\chi^2 = 0.178$	0.673

Table 4
Sensitivity Analyses Summary

Analysis Set	Population (n) (GA / GA + QLB)	Events / Total(n)		Event Rate (%)		HR (95% CI)	P-value
		GA	GA+ QLB	GA	GA+ QLB		
Primary Analysis (mITT)	299 (151 / 148)	63/151	54/148	41.7%	36.5%	0.858 (0.572–1.285)	0.457
Worst-Case ITT Analysis	350 (175 / 175)	68/175	62/175	38.9%	35.4%	0.912 (0.676–1.231)	0.419
Per-Protocol (PP) Analysis	286 (146 / 140)	63/146	54/140	43.2%	38.6%	0.876 (0.615–1.249)	0.463
Extreme-Case Analysis	350 (175 / 175)	68/175	89/175	38.9%	50.9%	1.396 (1.037–1.878)	0.027
Note:* indicate $P < 0.05$							

2.3.1 Component-Specific Analysis of the Composite Endpoint To assess whether any single component drove the composite outcome, we performed exploratory analyses for each component separately. The incidence of biochemical or clinical recurrence was 13.0% (19/146) in the GA group versus 10.7% (15/140) in the GA + QLB group ($\chi^2 = 0.352$, $P = 0.553$). The incidence of adjuvant/salvage therapy initiation was 30.1% (44/146) versus 27.9% (39/140), respectively ($\chi^2 = 0.178$, $P = 0.673$). No significant differences were observed for any individual component. These findings suggest that the null result for the composite endpoint was not driven by opposing effects on different components.

2.4 Analgesic Efficacy and Opioid Consumption The GA + QLB group required significantly less intraoperative sufentanil and remifentanil ($P < 0.001$; Fig. 5). Postoperatively, this group had significantly fewer PCA demands at all time points ($P < 0.05$; Fig. 6), although resting VAS pain scores were not significantly different.

2.5 Recovery Quality The GA + QLB group had a significantly shorter median time to first flatus and a higher QoR-40 score on postoperative day 1 (both $P < 0.05$). Postoperative hospital stay and urinary catheter duration were similar between groups (Fig. 7).

2.6 Inflammatory and Immune Response Trends for IL-6, CRP, D-dimer, FDP, NLR, PLR, and SII were similar between groups, with an initial postoperative rise followed by a decline. Although PCT showed a statistically different trend ($P < 0.05$), this was not deemed clinically significant (Fig. 8). These analyses were exploratory; no adjustments for multiple comparisons were applied.

Note

Repeated-measures data were compared using repeated-measures analysis of variance; * indicates a statistically significant difference ($P < 0.05$) between the two groups at the same time points, and $\square$ indicates $P < 0.05$ for the trend of change between the two groups of patients.

2.7 Multivariable Analysis of the Primary Outcome The Cox model confirmed that anesthetic technique was not an independent predictor of EFS (adjusted HR = 0.858, 95% CI: 0.572–1.285, $P = 0.457$). In contrast, pT3b (adjusted HR = 4.254, 95% CI: 1.042–17.375, $P = 0.044$), pT4 stage (adjusted HR = 6.565, 95% CI: 1.488–29.005, $P = 0.013$) and lymph node metastasis (pN1) (adjusted HR = 1.919, 95% CI: 1.075–3.427, $P = 0.027$) were significant predictors of an event (Table 5).

Table 5
Multivariable Cox Regression Analysis for Event-Free Survival

Factors	Adjusted HR	Lower 95% CI	Upper 95% CI	P value
GA + QLB vs GA	0.858	0.572	1.285	0.457
Age	1.005	0.963	1.049	0.814
Preoperative PSA	0.999	0.990	1.009	0.909
ISUP Grade Group	-	-	-	0.631
Group 2 vs Group 1	0.896	0.369	2.173	0.808
Group 3 vs Group 1	0.614	0.223	1.695	0.347
Group 4 vs Group 1	0.723	0.276	1.898	0.511
Group 5 vs Group 1	1.084	0.404	2.910	0.872
Pathological T stage	-	-	-	0.041
pT3a vs pT2	1.202	0.364	3.968	0.762
pT3b vs pT2	4.254	1.042	17.375	0.044*
pT4 vs pT2	6.565	1.488	29.005	0.013*
pN1 vs pN0	1.919	1.075	3.427	0.027*
Margin status Positive vs Negative	1.320	0.825	2.114	0.247
Nerve-sparing status	-	-	-	0.536
Unilateral-nerve-sparing vs Bilateral	1.152	0.394	3.373	0.796
Non-nerve-sparing vs Bilateral	1.608	0.475	5.447	0.445
Lymph node dissection	-	-	-	0.240
Limited vs None	0.541	0.264	1.107	0.092
Extended vs None	0.698	0.207	2.347	0.561
Note:* indicate $P < 0.05$				

2.8 Adverse events No cases of LAST, nerve injury, or puncture site infection occurred. Three patient in the GA + QLB group developed a small puncture site hematoma, managed conservatively with compression. The incidence of postoperative nausea and vomiting was similar between groups ($P > 0.05$; Table 6). No procedure-related SAEs occurred.

Table 6
Adverse Events Report

Adverse event	Group GA (cases, %, n = 146)	GroupGA + QLB (cases, %, n = 140)	Statistical value	P vaule
Local anesthetic systemic toxicity	-	0(0%)	-	-
Puncture site hematoma	-	3(2.1%)	-	-
Postoperative nausea and vomiting	28(19.2%)	32(22.9%)	0.584	0.445
Nerve injury	-	0(0%)		-
Puncture site infection	-	0(0%)		-

Discussion

This randomized, double-blind trial investigated the impact of adding QLB to GA on a composite oncologic outcome and recovery metrics following RALP. The principal finding is that we did not detect a significant improvement in 6-month EFS with the addition of QLB, but conferred significant benefits for early postoperative recovery, including superior analgesia, reduced opioid consumption, and enhanced quality of recovery.

Oncological Outcome: Interpretation of the Primary Finding

Our null finding aligns with the majority of existing high-quality evidence in prostate cancer surgery [14–16]. Several explanations warrant consideration. First, dominant prognostic determinants—particularly advanced pathological stage (pT4) and lymph node metastasis (pN1), which were strong independent predictors in our multivariable analysis—may override any modest effect from a perioperative nerve block. Second, the study was underpowered to detect a small-to-moderate effect. Our sample size assumed a 50% event rate and 15% absolute reduction; the observed event rate was 43.2% and the observed absolute risk reduction was only 4.6% in the per-protocol population. Post-hoc power analysis indicated only ~ 18% power to detect the observed effect (Supplementary Table 3). Third, the 6-month composite EFS endpoint is heavily influenced by early adjuvant therapy decisions rather than true oncologic recurrence. If QLB had reduced true disease progression, it might also have reduced the need for adjuvant therapy—yet we observed no significant difference in therapy initiation rates between groups (30.1% vs. 27.9%, $P = 0.673$). Fourth, it remains possible that perioperative immune modulation by QLB, if present, is too subtle to alter early disease trajectory, or that our chosen biomarkers were insufficiently sensitive to detect it.

Recovery Benefits: Analgesia, Opioid Sparing, and Quality of Recovery

The significant benefits of QLB on recovery parameters are consistent with its known pharmacodynamic effects and the literature on regional anesthesia for abdominal surgery [17–19]. The reduction in opioid requirements validates QLB as an effective component of multimodal analgesia for RALP. These advantages translated into faster return of gastrointestinal function and higher QoR-40 scores. The absence of a significant reduction in hospital stay or catheter duration suggests these outcomes are influenced by broader institutional protocols beyond pain management.

Inflammatory and Immune Markers: Exploratory Findings

We did not observe consistent modulation of measured systemic inflammatory markers (IL-6, CRP) or immune indices (NLR, PLR, SII). These null findings should be interpreted with caution. These analyses were exploratory, without multiple-comparison correction; the single significant difference for PCT is not considered clinically meaningful. Moreover, selected markers are nonspecific and may not adequately capture complex multimodal immune modulation. The short follow-up and limited sampling times may have missed peak or delayed responses. Thus, our null findings do not definitively exclude an immunomodulatory effect of QLB but suggest such effects, if present, are not reflected in these conventional markers.

Comparison with Existing RCTs and Meta-Analyses

Our findings add to evidence that regional anesthesia does not meaningfully reduce cancer recurrence. A recent meta-analysis by Li et al. including 15 RCTs across various cancer types found no significant benefit of regional anesthesia on recurrence or survival (HR 0.98, 95% CI 0.87–1.10) [12]. In radical prostatectomy, Marcon et al. also reported no association between anesthetic technique and biochemical recurrence [14]. Our study extends these findings by using a composite EFS endpoint that captures guideline-directed adjuvant therapy, addressing a key methodological limitation of prior studies that relied solely on BCR.

Limitations

Several limitations warrant attention. Follow-up duration: The 6-month follow-up is a major limitation for an oncologic endpoint. Most prostate cancer recurrences occur beyond 12–36 months. This limitation biases the study toward the null for long-term effects; longer follow-up (3–5 years) is essential. Sample size and power: The study was underpowered to detect modest but potentially clinically relevant differences (achieved power ~ 18% for observed effect). Composite endpoint heterogeneity: The EFS components differ in biological significance—adjuvant therapy initiation reflects physician judgment,

while recurrence reflects true progression. This heterogeneity could bias the composite outcome if treatment effects differ across components. Missing data and sensitivity analysis: The extreme-case analysis yielded a significant result favoring the control group under clinically implausible assumptions; however, the consistency of primary, worst-case ITT, and per-protocol analyses supports robustness. Immunologic markers: Null findings should be interpreted with caution given exploratory nature, no multiple-comparison correction, nonspecific markers, and limited sampling. Post-randomization exclusions and incomplete baseline data: Baseline characteristics were available only for the per-protocol population (n = 286), because the 51 excluded patients and the 13 lost to follow-up lacked systematically collected baseline data. Thus, baseline balance in the mITT population (n = 299), used for the primary analysis, could not be fully verified. Although exclusion rates were balanced between groups (GA: 13.7%; GA + QLB: 15.4%), and the primary, worst-case ITT, and per-protocol analyses were consistent, residual selection bias cannot be entirely excluded. Blinding: The sham block did not replicate needle insertion sensation, potentially compromising blinding for patient-reported outcomes, though the objective primary outcome (EFS) is less susceptible to this bias.

Clinical Implications

- Despite the null oncologic finding, our results have clear clinical implications. QLB significantly improves early recovery outcomes—reducing opioid consumption, shortening time to gastrointestinal recovery, and improving QoR-40 scores—without increasing adverse events. These benefits align well with ERAS goals. QLB can be routinely recommended as part of multimodal analgesia for RALP, particularly in patients at high risk for postoperative pain or opioid-related side effects.

Conclusion

In this randomized trial, adding QLB to GA did not improve 6-month event-free survival after RALP. However, this conclusion is limited to this short-term, management-sensitive endpoint; longer follow-up (3–5 years) is required to assess any potential effect on cancer-specific survival. In contrast, QLB significantly enhanced early postoperative recovery, reducing opioid consumption, shortening time to gastrointestinal recovery, and improving patient-reported quality of recovery. These benefits support the routine use of QLB as part of multimodal analgesia within ERAS pathways for RALP.

Declarations

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Conflict of interest: The authors declare that they have no conflicts of interest.

Funding: There was no funding source for this study.

Data availability statement: The datasets generated and/or analyzed during the current study are not publicly available due to patient privacy and institutional restrictions, but are available from the corresponding author on reasonable request.

Human ethics and consent to participate declarations: This study was approved by the Medical Ethics Committee of the General Hospital of the Central Theater Command of the PLA ([2022]046-01), and it is registered in the Chinese Clinical Trial Registry (Registration No ChiCTR-2200066968). All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Consent for publication: Not applicable.

Contributions of each author:

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Figures

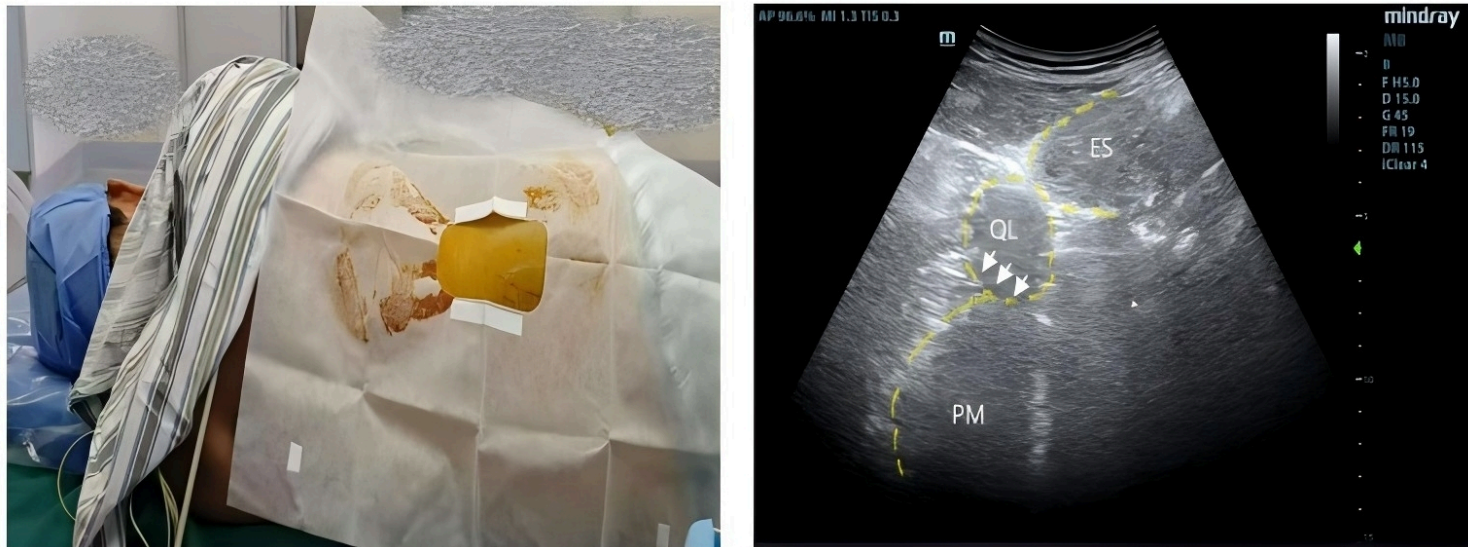


Figure 1

Anterior quadratus lumborum block (QLB Type 3) – patient positioning and ultrasound-guided injection.

(A) Patient positioned in the lateral decubitus position with the operative side up. The ultrasound probe is placed transversely at the lumbar level, between the iliac crest and the costal margin, at the anterior axillary line. (B) Corresponding ultrasound image showing the needle trajectory and injection target. The needle is advanced from the anterior approach toward the fascial plane between the quadratus lumborum (QL) muscle and the psoas major (PM) muscle. The white arrows indicate the injection target (the thoracolumbar fascia at the anterolateral aspect of QL), and the yellow dashed line outlines the QL muscle. Local anesthetic (0.2% ropivacaine, 25 mL) is deposited in this interfascial plane. ES, erector spinae muscle.

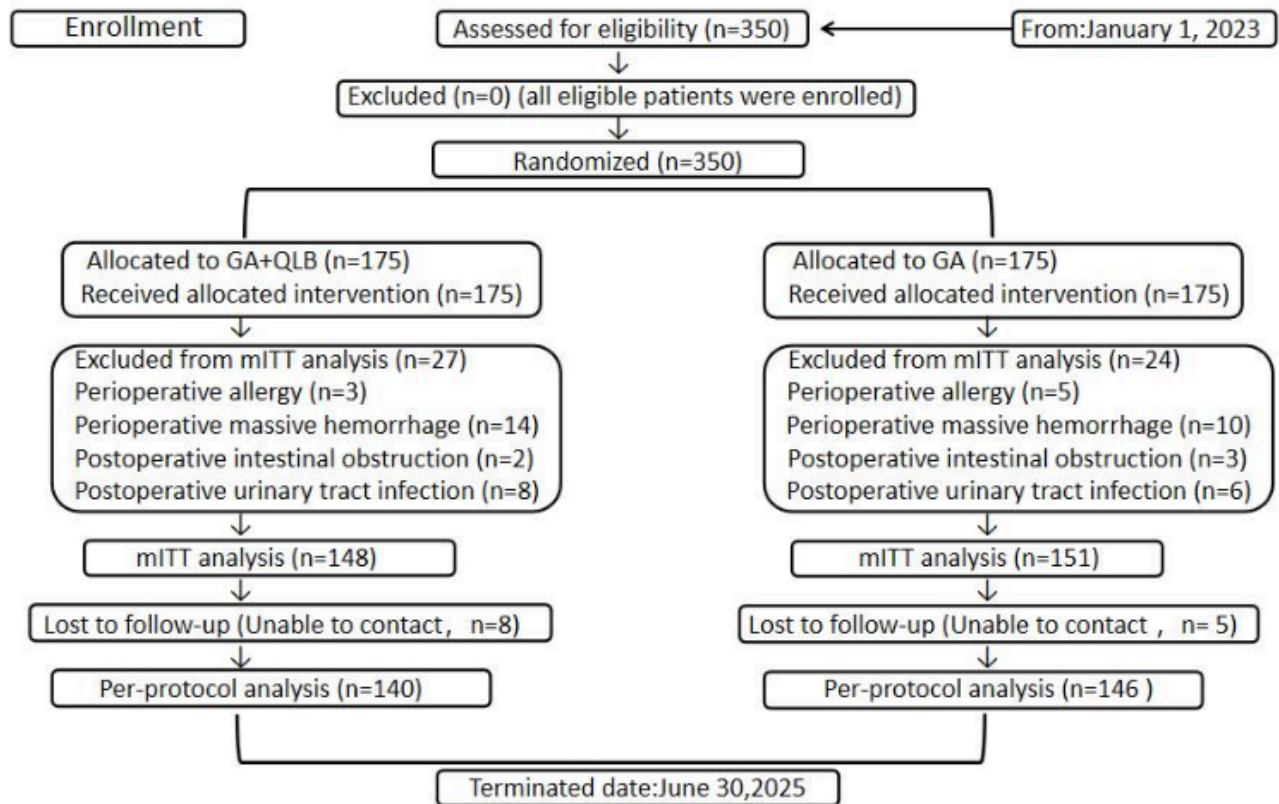


Figure 2

Patient inclusion process

CONSORT flow diagram showing the randomization, exclusions, loss to follow-up, and final analysis populations (mITT and per-protocol) for both groups.

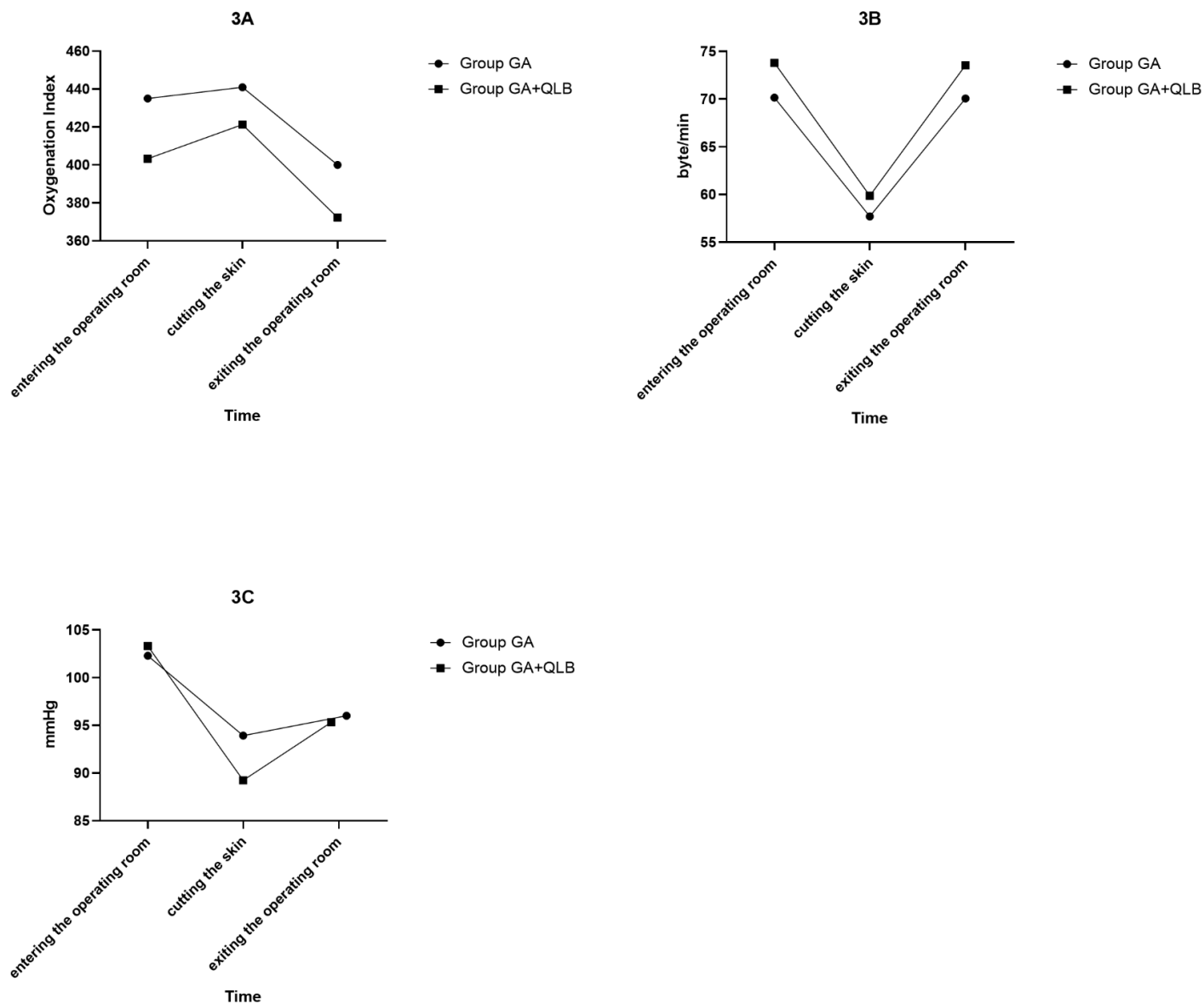


Figure 3

Comparison of oxygenation index, heart rate, and MAP values between the two groups at different time points.

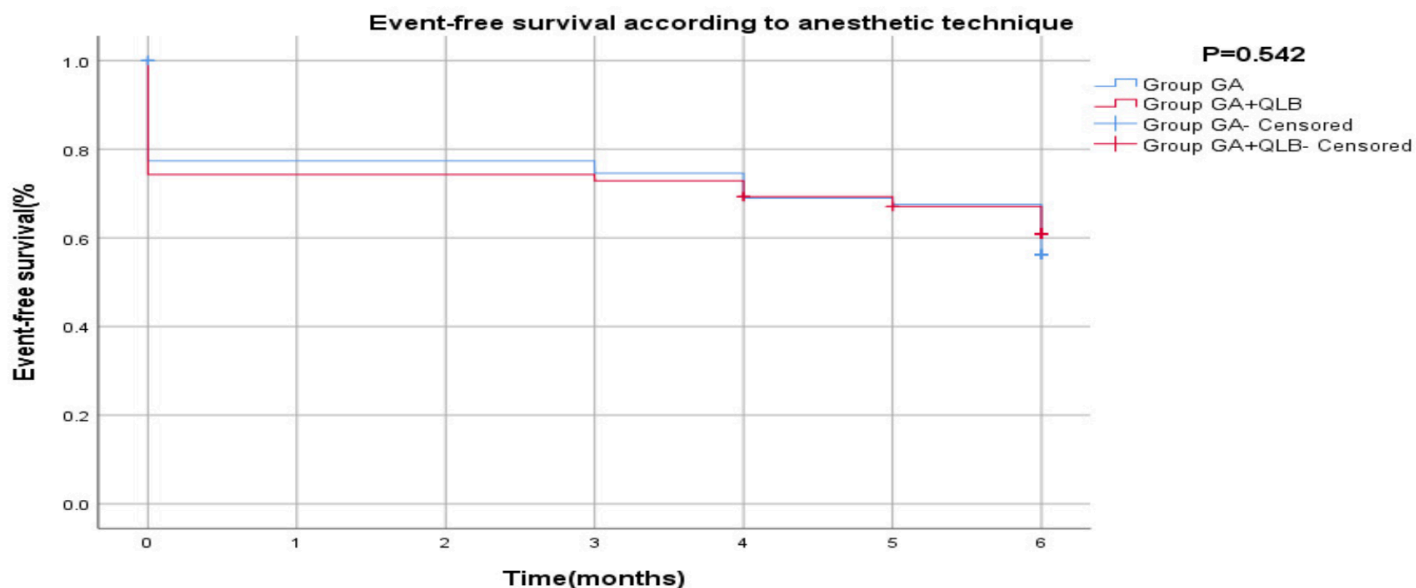


Figure 4

Event-free survival according to anesthetic technique(per-protocol population, n=286).

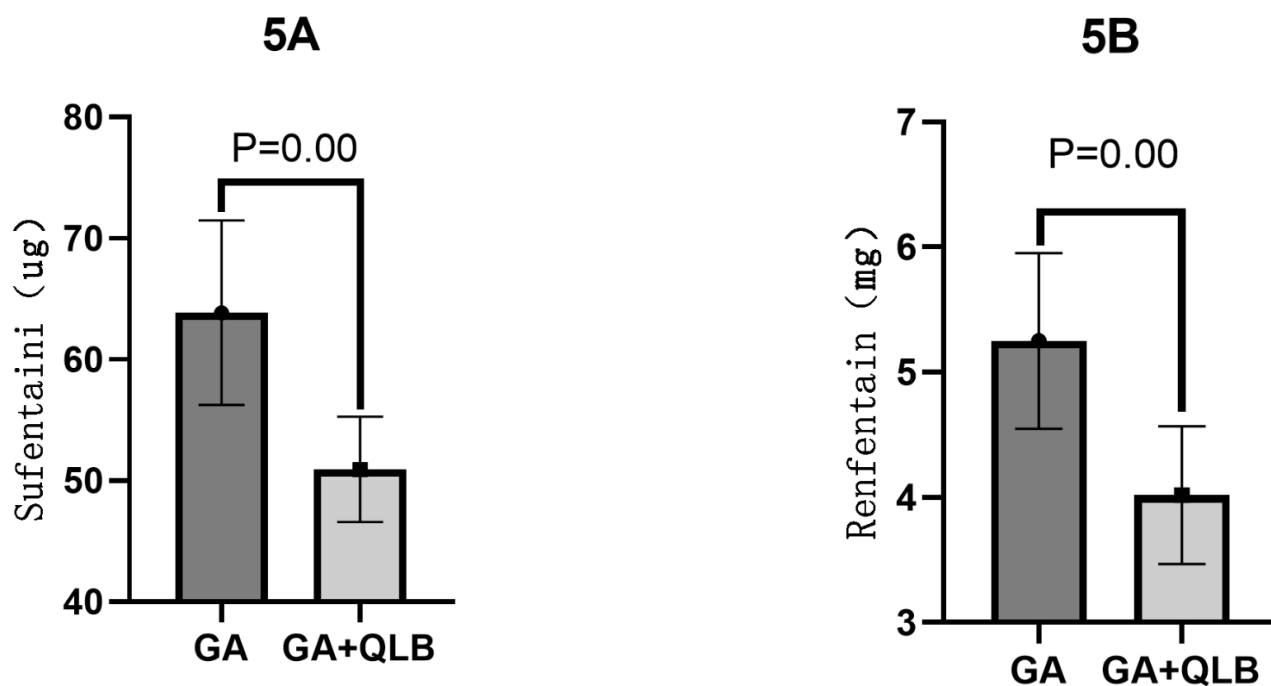


Figure 5

Comparison of the dosages of the sufentanil and remifentanyl between the two groups of patients(5A-B).

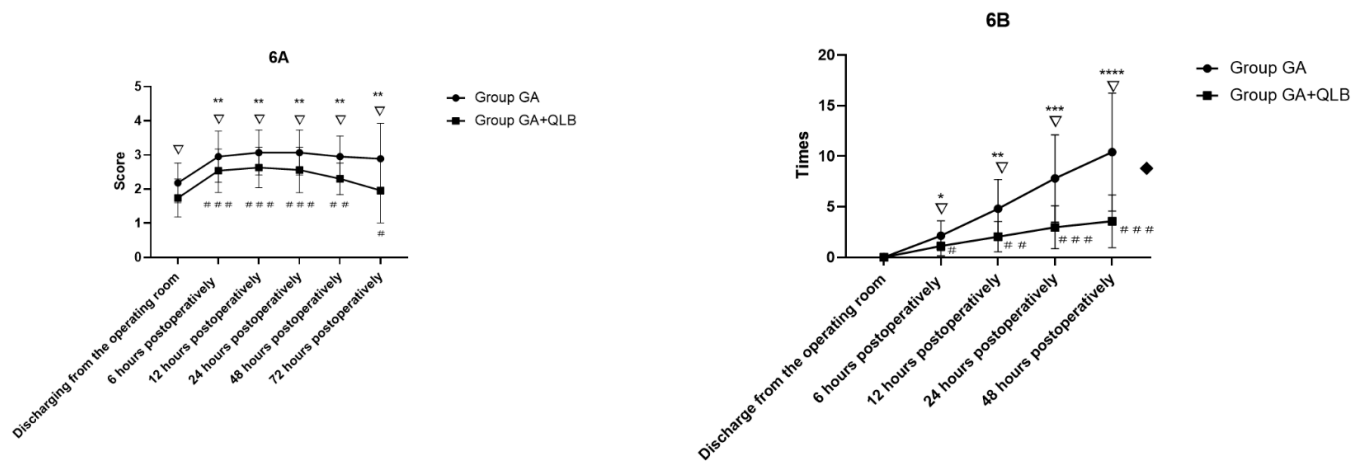


Figure 6

Comparison of VAS scores , the number of compressions of the analgesic pump between the two groups of patients at different time points(6A-B).

Note: Repeated-measures data were compared using repeated-measures analysis of variance; $\square$ $P < 0.05$, each time point after surgery vs. discharge from the operating room in the GA+QLBgroup; * $P < 0.05$, each time point after surgery vs. discharge from the operating room in the GA group; different numbers of $\square$ and * indicate $P < 0.05$ between each time point in a group; ∇ $P < 0.05$ between groups at the same time point; $\square$ $P < 0.05$ for the trend of changes between the two groups of patients.

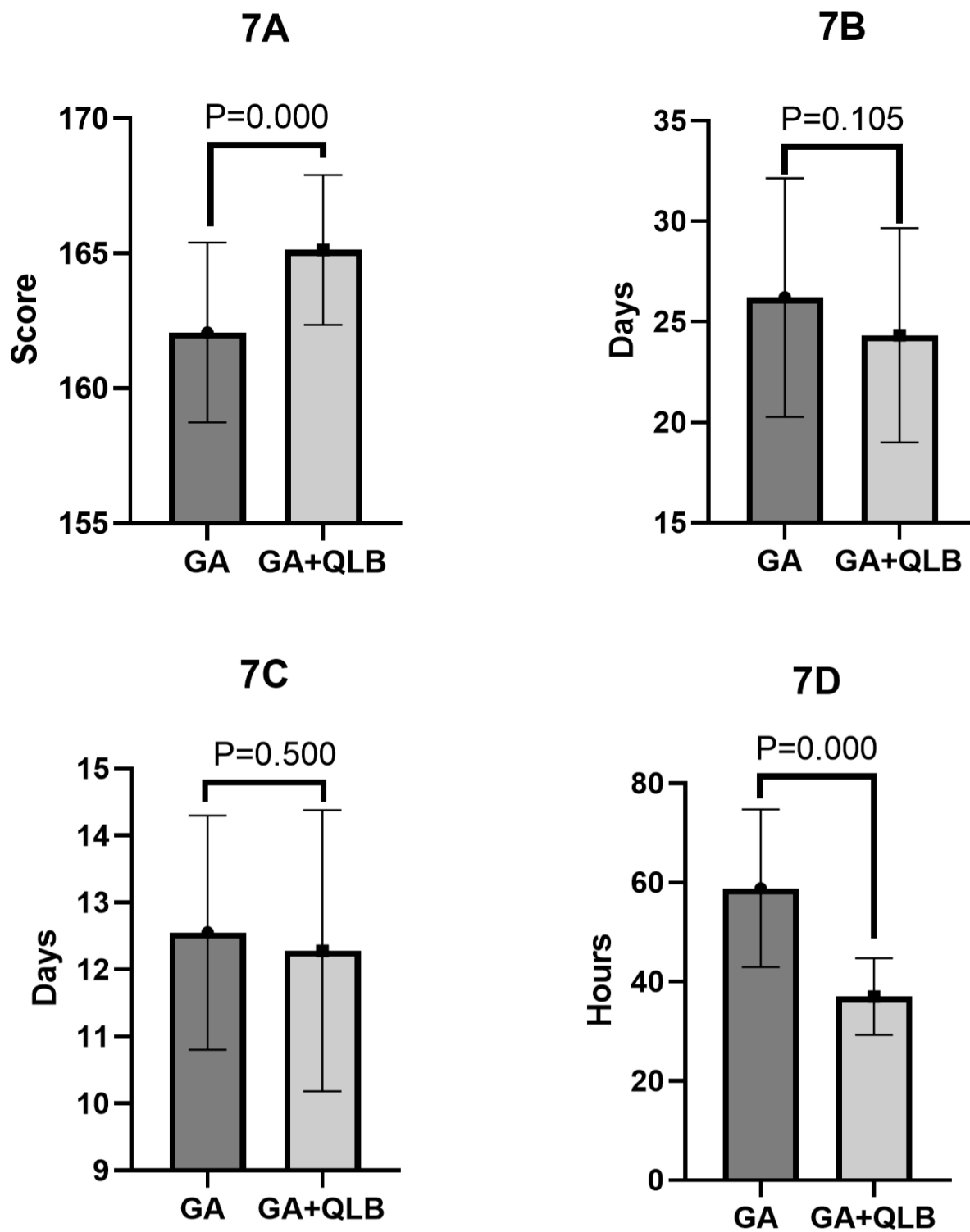


Figure 7

Comparison of postoperative QOR-40 scores, hospital stay, urinary catheter indwelling days, intestinal flatus between the two groups of patients(7A-D).

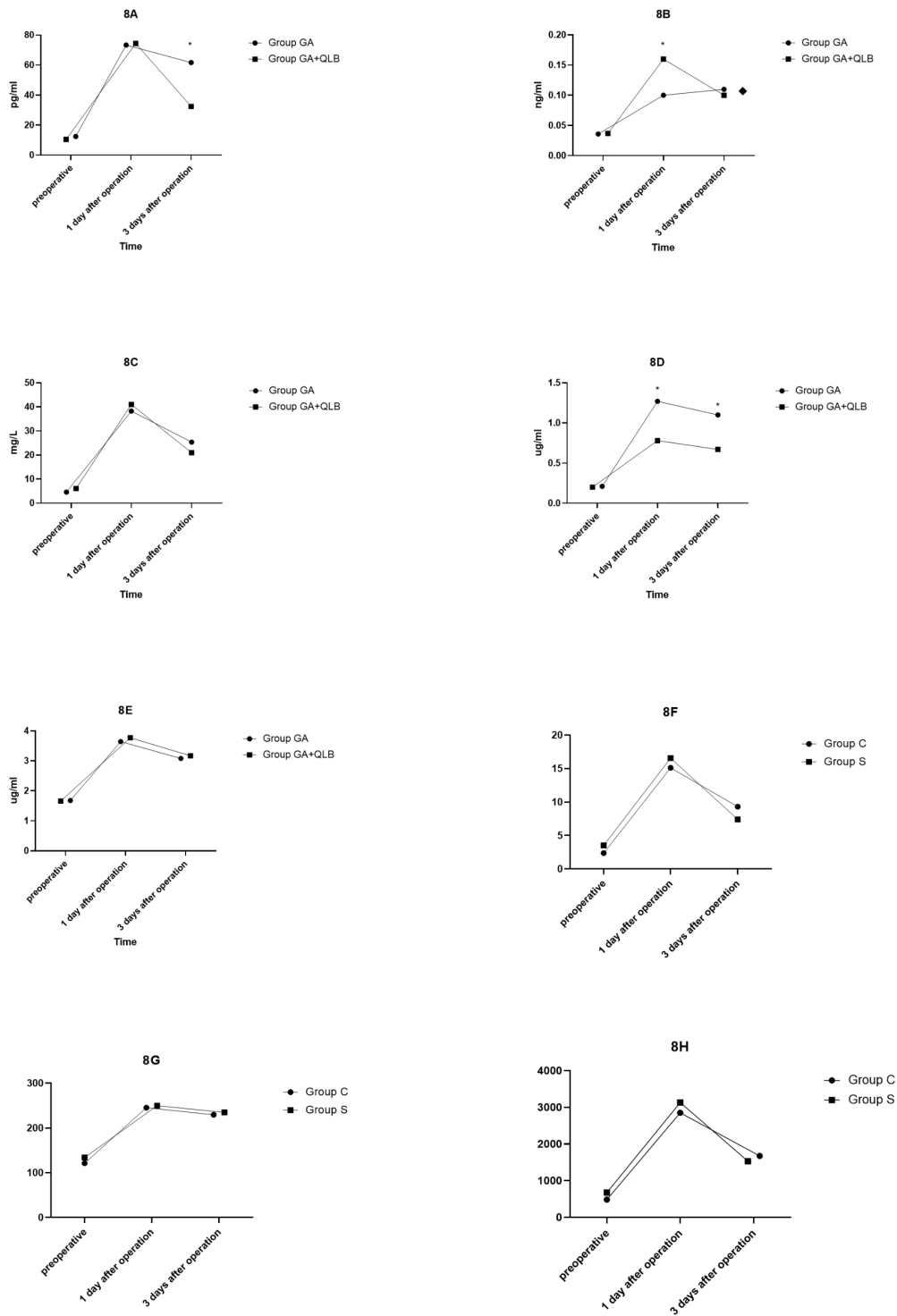


Figure 8

Comparison of the IL-6, PCT, CRP, D-dimer, FDP, NLR, PLR, SII at different time points between the two groups of patients(8A-H).

Note: Repeated-measures data were compared using repeated-measures analysis of variance; * indicates a statistically significant difference (P<0.05) between the two groups at the same time points,

and ¶ indicates $P < 0.05$ for the trend of change between the two groups of patients.

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