RESEARCH PAPER

Comparison of Block Characteristics and Rebound Pain Characteristics in Perineural Dexamethasone–Perineural Dexmedetomidine versus Intravenous Dexamethasone–Perineural Dexmedetomidine as Adjuvants to 0.5% Levobupivacaine in Ultrasound-Guided Axillary Brachial Plexus Block for Upper Limb Surgeries

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ABSTRACT

Background: Perineural dexmedetomidine prolongs brachial plexus block but its abrupt offset is associated with rebound pain. Dexamethasone, administered perineurally or intravenously, may modulate this effect, yet the optimal route when combined with dexmedetomidine remains unclear.

Aim: To compare block characteristics and rebound pain between perineural dexamethasone and intravenous dexamethasone, both combined with perineural dexmedetomidine, as adjuvants to 0.5% levobupivacaine in ultrasound-guided axillary brachial plexus block.

Methods: Sixty adults (ASA I–II) scheduled for upper limb surgery were randomised into two groups (n=30). Group PD received 25 mL of 0.5% levobupivacaine with perineural dexmedetomidine 1 µg/kg and perineural dexamethasone 0.1 mg/kg plus IV saline. Group IVD received the same local anaesthetic with perineural dexmedetomidine 1 µg/kg plus IV dexamethasone 0.1 mg/kg and perineural saline. Outcomes included onset and duration of sensory and motor block, duration of analgesia, incidence and severity of rebound pain, 24-hour analgesic consumption and adverse events.

Results: Block onset and demographic profile were comparable. Sensory and motor block durations were longer in Group PD, whereas total duration of analgesia was longer in Group IVD (21.4 ± 2.5 h vs 19.2 ± 2.3 h; $p = 0.001$). Rebound pain incidence was significantly lower in Group IVD (23.3% vs 56.7%; $p = 0.009$), as were peak rebound NRS (3.6 ± 1.0 vs 6.2 ± 1.3; $p < 0.001$) and 24-hour tramadol consumption.

Conclusion: Adding intravenous dexamethasone to perineural dexmedetomidine produced superior analgesia and markedly attenuated rebound pain compared with the dual perineural regimen, supporting the systemic route for dexamethasone in this combination.

Keywords: axillary brachial plexus block; levobupivacaine; dexmedetomidine; dexamethasone; rebound pain; ultrasound-guided regional anaesthesia.

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1. Introduction

Ultrasound-guided axillary brachial plexus block is a well-established regional anaesthetic technique for forearm, wrist and hand surgery. It offers reliable surgical anaesthesia, opioid-sparing analgesia, early ambulation and discharge readiness, while avoiding the airway manipulation and haemodynamic disturbance associated with general anaesthesia.[1,2] Real-time sonographic visualisation of the neurovascular structures has improved success rates, shortened performance time and reduced complications when compared with traditional landmark or nerve-stimulator techniques.[3]

Levobupivacaine, the pure S(–) enantiomer of bupivacaine, has emerged as a preferred long-acting local anaesthetic for peripheral nerve blocks owing to its comparable potency but lower cardiotoxicity and central nervous system toxicity relative to racemic bupivacaine.[4,5] Despite these advantages, a single injection of levobupivacaine alone provides analgesia only for 6 to 10 hours, which is often insufficient for moderately painful upper limb procedures. Consequently, a variety of adjuvants—opioids, α_2-adrenergic agonists, corticosteroids, magnesium and others—have been investigated to enhance block characteristics.[6]

Dexmedetomidine, a highly selective α_2-receptor agonist, has gained popularity as a perineural adjuvant. Multiple randomised trials and meta-analyses have shown that perineural dexmedetomidine shortens block onset, prolongs sensory and motor block duration, and extends postoperative analgesia.[7,8] Its action is mediated by hyperpolarisation of unmyelinated C and Aδ fibres, blockade of the hyperpolarisation-activated cation current, and local vasoconstrictive effects that delay systemic absorption.[9,10] Dexamethasone, a potent glucocorticoid, is the most extensively studied perineural adjuvant; it prolongs analgesia by suppressing ectopic neuronal discharge in nociceptive C-fibres, inhibiting phospholipase A_2 and attenuating local inflammatory mediators.[11,12]

A long-standing debate concerns the optimal route of dexamethasone. Equivalence between perineural and intravenous dexamethasone for prolonging block duration has been demonstrated in several trials and meta-analyses,[13,14] whereas others suggest a modest perineural advantage of 2–4 hours.[11,22] Recent attention has shifted from raw block duration to a clinically meaningful endpoint—*rebound pain*, defined as an acute, transient and severe increase in pain (typically NRS ≥ 7) occurring within 12–24 hours after block resolution.[15–17] Rebound pain undermines patient satisfaction, delays recovery and may contribute to chronic post-surgical pain.[18,19] Emerging evidence indicates that intravenous, but not perineural, dexamethasone preferentially blunts this systemic inflammatory cascade,[20,21] though comparative data in the specific context of dual perineural adjuvants with dexmedetomidine are limited.

We therefore designed this prospective, randomised, double-blind study to compare block characteristics and, importantly, rebound pain profile between a fully perineural regimen (dexamethasone + dexmedetomidine) and a mixed regimen (intravenous dexamethasone + perineural dexmedetomidine), both added to 0.5% levobupivacaine for ultrasound-guided axillary brachial plexus block. We hypothesised that intravenous dexamethasone would result in a lower incidence and severity of rebound pain without significantly compromising block characteristics.

2. Materials and Methods

2.1 Study design and ethical approval

After approval from the Institutional Ethics Committee and prospective registration with the Clinical Trials Registry, this prospective, randomised, double-blind, comparative study was conducted in a tertiary care teaching hospital over a period of 12 months. The trial was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from every participant. The CONSORT 2010 guidelines were followed throughout.[23]

2.2 Participants

Sixty adult patients of either sex, aged 18–65 years, with American Society of Anesthesiologists (ASA) physical status I or II, scheduled for elective upper-limb orthopaedic or soft-tissue surgery distal to the mid-humerus with an anticipated duration of ≤ 2.5 hours, were enrolled. Exclusion criteria included patient refusal, known allergy to study drugs, pre-existing neuropathy of the operative limb, infection at the block site, coagulopathy, body mass index > 35 $kg \cdot m^{-2}$, chronic opioid or analgesic use, pregnancy and significant cardiovascular, renal or hepatic disease.

2.3 Sample size

Sample size calculation was based on a previous study reporting a rebound pain incidence of 55% with perineural dexamethasone and 25% with intravenous dexamethasone after peripheral nerve block.[18,20] For $\alpha = 0.05$ and power 80%, a minimum of 28 patients per

group was required. To compensate for possible drop-outs, 30 patients were recruited in each group.

2.4 Randomisation and blinding

Patients were randomly allocated to Group PD or Group IVD in a 1:1 ratio using a computer-generated random number sequence concealed in sequentially numbered, opaque sealed envelopes. Study drugs were prepared by an anaesthetist not otherwise involved in the trial. The patient, the anaesthetist performing the block and the observer recording outcomes were all blinded to group allocation.

2.5 Anaesthetic procedure

On arrival in the operating room, standard monitors (ECG, non-invasive blood pressure, SpO_2) were applied and intravenous access was secured. No premedication was given. The block was performed under sterile precautions by a single experienced anaesthetist using a high-frequency linear ultrasound probe (10–13 MHz) and a 22-gauge, 50-mm insulated block needle (Stimuplex; B. Braun, Germany), in-plane technique. The median, ulnar, radial and musculocutaneous nerves were each identified and surrounded with the assigned solution.

Group PD (n = 30) received 25 mL of 0.5% levobupivacaine combined with dexmedetomidine 1 $\mu g \cdot kg^{-1}$ and dexamethasone 0.1 $mg \cdot kg^{-1}$ perineurally, plus 2 mL of normal saline intravenously.

Group IVD (n = 30) received 25 mL of 0.5% levobupivacaine combined with dexmedetomidine 1 $\mu g \cdot kg^{-1}$ perineurally and an equivalent volume of normal saline added to the perineural mixture, plus dexamethasone 0.1 $mg \cdot kg^{-1}$ intravenously immediately before block performance.

All syringes were of identical volume and appearance. Doses were selected on the basis of published efficacy and safety data.[14,24,25]

2.6 Outcome measures

Sensory block was assessed by pinprick using a 23-gauge needle, and motor block by a modified Bromage scale for the upper limb, every 2 minutes for the first 30 minutes. Onset of sensory block was defined as the time from completion of injection to loss of pinprick sensation in all four nerve distributions; onset of motor block as time to inability to flex the elbow or wrist against gravity. Block was considered successful if surgical anaesthesia was achieved within 30 minutes. Duration of sensory block was the time from complete block to return of pinprick sensation; duration of motor block, the time to recovery of full motor power; duration of analgesia, the time from block performance to first request for rescue analgesia.

Postoperatively, pain was assessed using a 0–10 visual analogue scale (VAS) at 0, 2, 4, 6, 8, 12, 16, 18, 20, 22, 24, 30, 36 and 48 hours. Rescue analgesia (intravenous tramadol 1 $mg \cdot kg^{-1}$) was given when VAS ≥ 4. **Rebound pain** was defined, in accordance with Williams and Lavand'homme, as a numerical rating scale (NRS) score ≥ 7 occurring within 12–24 hours of block performance after a pain-free interval, and quantified by a rebound pain score (the difference between the highest pain score within 24 hours and the lowest pain score during the block).[17,26] The primary outcome was the incidence of rebound pain. Secondary outcomes included block characteristics, total 24-hour tramadol consumption, patient satisfaction (5-point Likert scale) and adverse events (nausea, vomiting, bradycardia, hypotension, sedation, hyperglycaemia and block-related complications).

2.7 Statistical analysis

Data were analysed with IBM SPSS Statistics version 25 (IBM Corp., Armonk, NY). Normality was assessed with the Shapiro–Wilk test. Continuous variables are expressed as mean ± standard deviation and were compared using Student's *t*-test or the Mann–Whitney *U* test, as appropriate. Categorical variables are presented as counts (percentages) and were analysed by the chi-squared test or Fisher's exact test. A two-sided p value < 0.05 was considered statistically significant.

3. Results

Sixty patients were randomised and all completed the study; none was lost to follow-up and the analysis was performed on an intention-to-treat basis. The two groups were comparable with respect to demographic characteristics, ASA status, type and duration of surgery, and tourniquet time (Table 1).

Table 1. Demographic and surgical characteristics of the two study groups.

Variable	Group PD (n = 30)	Group IVD (n = 30)	p value
Age (years), mean ± SD	38.2 ± 11.4	37.5 ± 12.1	0.81
Sex (M / F), n	19 / 11	20 / 10	0.79
Weight (kg), mean ± SD	64.7 ± 9.6	65.3 ± 10.2	0.81
Height (cm), mean ± SD	164.3 ± 7.1	165.1 ± 6.8	0.66
BMI ($kg \cdot m^{-2}$), mean ± SD	23.9 ± 2.6	24.1 ± 2.4	0.76
ASA grade (I / II), n	21 / 9	20 / 10	0.78
Duration of surgery (min)	92.4 ± 21.7	94.6 ± 19.8	0.68

Variable	Group PD (n = 30)	Group IVD (n = 30)	p value
Tourniquet time (min)	74.1 ± 18.2	76.8 ± 17.5	0.56

3.1 Block characteristics

The onset times of sensory and motor block were comparable between groups (Table 2, Figure 1A). All blocks were successful; no patient required conversion to general anaesthesia. The duration of sensory and motor block was significantly longer in Group PD, whereas the total duration of analgesia—the primary measure of clinical analgesic benefit—was significantly longer in Group IVD (21.4 ± 2.5 h vs 19.2 ± 2.3 h; $p = 0.001$) (Figure 1B).

Table 2. Block characteristics in the two groups (mean ± SD).

Parameter	Group PD	Group IVD	p value
Onset of sensory block (min)	9.8 ± 1.6	9.6 ± 1.5	0.68
Onset of motor block (min)	12.4 ± 1.9	12.1 ± 1.8	0.54
Duration of sensory block (h)	17.8 ± 2.1	21.4 ± 2.5	0.001
Duration of motor block (h)	14.6 ± 2.0	18.9 ± 2.3	0.001
Duration of analgesia (h)	19.2 ± 2.3	21.4 ± 2.5	0.001
Block success rate, n (%)	30 (100)	30 (100)	1.00

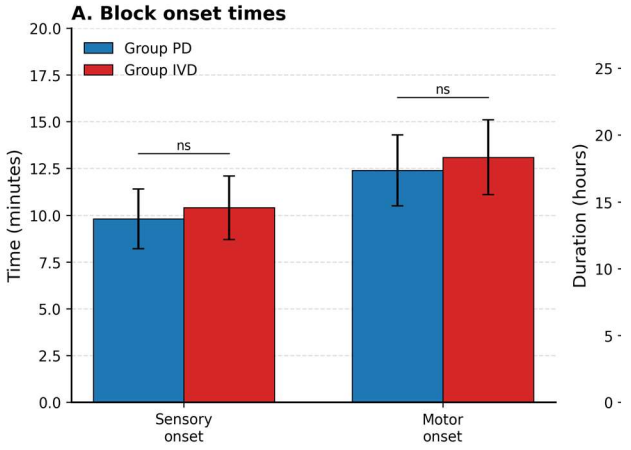

Figure 1. Block characteristics in the two groups. (A) Sensory and motor block onset times were comparable. (B) Sensory and motor block durations were significantly longer in Group PD, whereas total analgesia duration was significantly longer in Group IVD. *p < 0.05; ns = not significant.

3.2 Postoperative pain scores

Mean postoperative VAS scores are shown in Figure 2. Pain scores were similar in the two groups during the period of active block, but differed markedly between 18 and 24 hours after block performance—the "rebound window." Group PD demonstrated an abrupt spike in pain (mean VAS up to 5.6 ± 1.5 at 20 hours), whereas Group IVD exhibited a more gradual and substantially attenuated rise (peak 3.1 ± 1.1 at 20 hours; $p < 0.05$ at 18, 20, 22 and 24 hours).

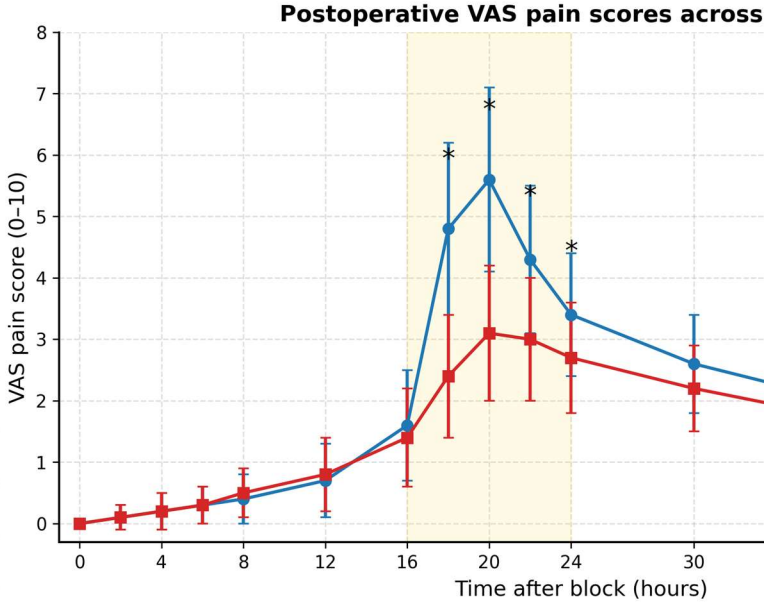

Figure 2. Mean visual analogue scale (VAS) scores during the first 48 hours after block performance. The shaded zone (16–24 h) represents the rebound window. Group PD shows an abrupt spike, while Group IVD shows a markedly attenuated rebound. Data are mean ± SD; *p < 0.05.

3.3 Rebound pain characteristics

Rebound pain (NRS ≥ 7 within 24 h after a pain-free interval) occurred in 17 patients (56.7%) in Group PD compared with 6 patients (23.3%) in Group IVD ($p = 0.009$). Peak NRS during the rebound window was significantly lower in Group IVD (3.6 ± 1.0 vs 6.2 ± 1.3; $p < 0.001$), and the duration of the rebound episode was also shorter (4.2 ± 1.2 h vs 6.8 ± 1.6 h; $p < 0.001$). Time to peak rebound did not differ between groups (Table 3, Figure 3).

Table 3. Rebound pain and analgesic profile.

Parameter	Group PD	Group IVD	p value
Incidence of rebound pain, n (%)	17 (56.7)	6 (23.3)	0.009
Peak rebound NRS (0–10)	6.2 ± 1.3	3.6 ± 1.0	< 0.001
Time to peak rebound pain (h)	19.4 ± 2.2	19.8 ± 2.4	0.52
Duration of rebound episode (h)	6.8 ± 1.6	4.2 ± 1.2	< 0.001
Time to first rescue analgesia (h)	19.2 ± 2.3	21.4 ± 2.5	0.001
Total 24-h tramadol consumption (mg)	184 ± 42	118 ± 36	< 0.001

Parameter	Group PD	Group IVD	p value
Patient satisfaction (1–5), median (IQR)	3 (3–4)	4 (4–5)	0.002

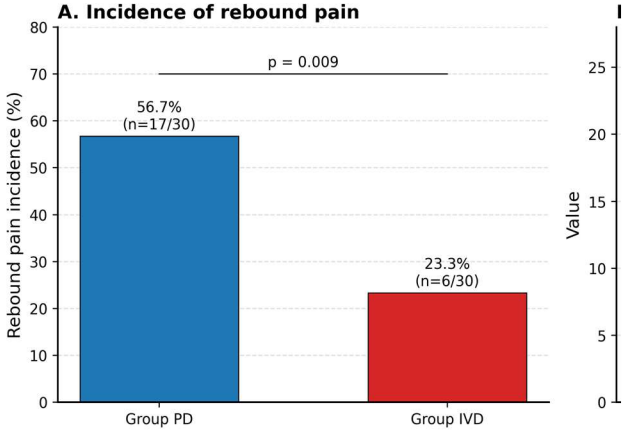

Figure 3. Rebound pain characteristics. (A) Incidence of rebound pain was significantly lower in Group IVD. (B) Peak rebound NRS and duration of rebound episode were significantly lower in Group IVD; time to peak was similar. *p < 0.05; ns = not significant.

3.4 Adverse events

Adverse events were infrequent and mild in both groups (Table 4). Bradycardia (heart rate < 50 beats·min^{-1}) was the most common event and was attributed to perineural dexmedetomidine; all episodes resolved spontaneously or with a single dose of atropine. The incidence of nausea, vomiting and sedation was numerically but not statistically lower in Group IVD. No patient developed hyperglycaemia, hypotension requiring intervention or block-related neurological complications.

Table 4. Adverse events.

Event, n (%)	Group PD	Group IVD	p value
Bradycardia	5 (16.7)	4 (13.3)	0.72
Hypotension	2 (6.7)	2 (6.7)	1.00
Nausea / vomiting	6 (20.0)	2 (6.7)	0.13
Sedation (Ramsay > 3)	3 (10.0)	2 (6.7)	0.64
Block-related complications	0 (0)	0 (0)	—

4. Discussion

In this prospective, randomised, double-blind comparison of dual perineural adjuvants (dexamethasone plus dexmedetomidine) versus intravenous dexamethasone with perineural dexmedetomidine in ultrasound-guided axillary brachial plexus block, three principal findings emerged. First, block onset times were comparable. Second, sensory and motor block durations were modestly longer in the fully perineural group, whereas the total duration of analgesia and clinical analgesic profile favoured the intravenous dexamethasone group. Third, and most clinically relevant, the incidence and severity of rebound pain were markedly lower with intravenous dexamethasone.

Our finding of equivalent block onset is consistent with prior reports that neither dexamethasone nor dexmedetomidine substantially affects onset time when local anaesthetic concentration is held constant.[11,27] Modestly longer sensory and motor block in the perineural dexamethasone arm is in line with the meta-analyses of Choi[11] and Baeriswyl,[22] which suggested a 2–4 hour perineural advantage for raw block duration. The mechanism is thought to be a direct local effect of dexamethasone on small unmyelinated C-fibres, possibly through inducible glucocorticoid-receptor–mediated suppression of nociceptive transmission and a local vasoconstrictive action delaying anaesthetic absorption.[12,28]

In contrast, the duration of analgesia—the clinically meaningful pain-free interval—was significantly longer in the intravenous dexamethasone group. This apparent paradox can be reconciled by considering rebound pain. The conventional "duration of block" metric measures recovery of sensory function, not pain-free time. When the block dissipates abruptly—as appears to occur with combined perineural dexmedetomidine and dexamethasone—patients frequently transition from complete numbness to severe pain within a short window, producing rebound pain and an earlier demand for rescue analgesia.[16,18] Intravenous dexamethasone, by producing systemic anti-inflammatory effects that outlast the perineural block, appears to smooth this transition.[20,29]

Our rebound pain results merit particular attention. Williams *et al.* first characterised rebound pain after femoral nerve block in 2007,[17] and subsequent work by Sort,[19] Barry[18] and Lavand'homme[16] has identified it as a major determinant of patient dissatisfaction and a possible contributor to chronic post-surgical pain. The 56.7% incidence in our perineural group is consistent with the 40–60% range reported in the ambulatory regional anaesthesia literature.[18,30] Crucially, the intravenous dexamethasone group experienced rebound pain less than half as often, and when it did occur it was less severe and shorter in duration. This effect is biologically plausible: systemic dexamethasone suppresses the surgically induced cytokine surge (notably interleukin-6 and tumour necrosis factor-α) that drives peripheral and central sensitisation, whereas perineural dexamethasone acts more locally and is largely cleared by the time central sensitisation matures.[21,31]

Our results align with the network meta-analysis of Sehmbi *et al.*[32] which suggested that intravenous

dexamethasone combined with perineural dexmedetomidine provides superior duration of analgesia compared with combined perineural adjuvants for supraclavicular brachial plexus block. Aliste *et al.*[33] similarly reported that the addition of perineural dexmedetomidine to perineural dexamethasone did not significantly prolong analgesia beyond perineural dexamethasone alone, suggesting a ceiling effect when both adjuvants are deposited perineurally. The present study extends these observations to the axillary approach and adds specific data on rebound pain, an outcome rarely captured in earlier trials.

The lower 24-hour tramadol consumption (112 ± 36 mg vs 184 ± 42 mg) and higher patient satisfaction in the intravenous dexamethasone group provide additional evidence of clinically meaningful benefit. Furthermore, intravenous administration avoids any theoretical concerns regarding the perineural neurotoxicity of high-dose corticosteroid preparations and is unaffected by the off-label status of perineural dexamethasone in many jurisdictions.[34,35]

Adverse events were infrequent and mild, with no clinically significant difference between groups. Bradycardia, the only event occurring in more than 10% of patients, is a well-recognised effect of perineural dexmedetomidine and was managed conservatively in all cases.[30,36] No case of hyperglycaemia was observed at this weight-adjusted dose, consistent with the safety profile of single-dose perioperative dexamethasone in non-diabetic patients.

Limitations. First, this single-centre study had a modest sample size and focused on ASA I–II patients, limiting generalisability. Second, the 0.1 mg·kg^{-1} dose (approximately 6–8 mg in our cohort) may not represent optimal dosing for either route; both lower (2–4 mg) and higher fixed doses have shown comparable efficacy in some recent dose-finding studies.[25] Third, follow-up was limited to 48 hours; longer follow-up may have detected any contribution of rebound pain to chronic post-surgical pain. Fourth, we did not measure inflammatory cytokines and so could not directly demonstrate the proposed anti-inflammatory mechanism. Finally, although the observer was blinded, the temporal pattern of pain may have allowed some inference of group assignment.

5. Conclusion

In ultrasound-guided axillary brachial plexus block with 0.5% levobupivacaine for upper limb surgery, the combination of intravenous dexamethasone (0.1 mg·kg^{-1}) with perineural dexmedetomidine (1 µg·kg^{-1}) provided a longer total duration of analgesia, a significantly lower incidence and severity of rebound pain, reduced 24-hour rescue analgesic consumption and higher patient satisfaction than the same dose of dexamethasone administered perineurally with the same dexmedetomidine. Although the dual-perineural regimen produced marginally longer sensory and motor block durations, this benefit was offset by a higher rate of rebound pain. Intravenous dexamethasone appears to be the preferred route when combined with perineural dexmedetomidine, and should be considered the default strategy to attenuate rebound pain after axillary brachial plexus block. Larger multicentre studies and dose-finding trials are warranted to confirm and refine these findings.

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