Does Spinal Anesthesia Result in a More Complete Sympathetic Block Than That from Epidural Anesthesia?

Rom A. Stevens, M.D.,* David Beardsley, M.D.,† J. Lee White, M.D.,‡ Tzu-Cheg Kao, Ph.D.,§
Rod Gantt, M.D.,† Stephen Holman, M.D.†

Background: Spinal and epidural injection of local anesthetics are used to produce sympathetic block to diagnose and treat certain chronic pain syndromes. It is not clear whether either form of regional anesthesia produces a complete sympathetic block. Spinal anesthesia using tetracaine has been reported to produce a decrease in plasma catecholamine concentrations. This has not been demonstrated for epidural anesthesia in humans with level of anesthesia below C8. One possible explanation is that spinal anesthesia results in a more complete sympathetic block than epidural anesthesia. To examine this question, a cross-over study was performed in young, healthy volunteers.

Methods: Ten subjects underwent both spinal and epidural anesthesia with lidocaine (plain) on the same day with complete recovery between blocks. By random assignment, spinal anesthesia and epidural anesthesia were induced *via* lumbar injection. Before and 30 min after local anesthetic injection, a cold pressor test (CPT) was performed. Blood was obtained to determine epinephrine and norepinephrine plasma concentrations at four stages: (1) 20 min after placing peripheral catheters, (2) at the end of a 2-min CPT (before conduction block), (3) 30 min after injection of epidural or spinal lidocaine, and (4) at the end of a second CPT (during anesthesia). Mean arterial pressure, heart rate, noninvasive cardiac index, and analgesia to pin-prick were monitored.

Results: Neither spinal nor epidural anesthesia changed baseline resting values of catecholamines or any hemodynamic variable, except heart rate, which was slightly decreased during spinal anesthesia. Median level of analgesia was T4 during spinal and T3 during epidural anesthesia. CPT before conduction block reliably increased heart rate, mean arterial pressure, cardiac index, epinephrine, and norepinephrine. Conduction block attenuated the increase in response to CPT only in mean arterial pressure (spinal and epidural) and cardiac index (spinal only). Neither technique blocked the increase in heart rate, norepinephrine, or epinephrine to CPT.

Conclusions: Spinal anesthesia did not result in a more complete attenuation of the sympathetic response to a CPT than did epidural anesthesia. In response to the CPT, spinal anesthesia blocked the increase in cardiac index, and epidural anesthesia resulted in a decrease in total peripheral resistance compared to the pre-anesthesia state. The differences between the techniques are not significant and are of uncertain clinical implications. (Key words: Anesthesia techniques: epidural; spinal. Anesthetics, local: lidocaine. Sympathetic nervous system. Sympathetic block.)

* Associate Professor of Anesthesiology, Loyola University of Chicago.

† Assistant Professor of Anesthesiology, Uniformed Services University.

‡ Assistant Professor of Anesthesiology, Georgetown University Medical Center.

§ Associate Professor of Preventive Medicine and Biometrics, Uniformed Services University.

EPIDURAL and spinal anesthesia are presumed to cause a complete sympathetic block of the anesthetized segments. For this reason, epidurally administered local anesthetics have been used to treat sympathetically mediated pain syndromes.[1] Additionally, diagnostic spinal or epidural blocks are used to confirm sympathetically mediated pain of the lower extremity.[2] However, few data exist supporting the concept of a "complete sympathetic block" during either spinal or epidural anesthesia.

Recently, we compared the abilities of epidural anesthesia using 2% lidocaine, 0.75% bupivacaine, and 3% 2-chloroprocaine to attenuate the sympathetic response to a cold pressor test (CPT).[3] When the sympathetic nervous system was stimulated using a CPT, lidocaine,

unlike bupivacaine and 2-chloroprocaine, did not attenuate heart rate (HR) and catecholamine response. Spinal anesthesia using tetracaine has been shown to decrease resting plasma catecholamine concentrations.[4] This is not the case for epidural anesthesia using lidocaine, bupivacaine, and 2-chloroprocaine (see above), despite comparably high level of block. Thus, it is possible that spinal anesthesia results in a more profound sympathetic block than does epidural anesthesia. Were this true, the reliability of epidurally administered local anesthetics to either diagnose or treat sympathetically mediated pain syndromes must be questioned. To test this possibility, we performed a cross-over study using healthy volunteers in whom effects of surgical stress and blood loss could be minimized. A CPT was used as a sympathetic stress, as in our previous study.

Methods

After approval from the Institutional Review Board at the National Naval Medical Center and written informed consent were obtained, 12 healthy subjects, ASA physical status 1, were enrolled. Each fasted overnight but had free access to caffeine-free clear liquids. On the day of the experiment, each subject received both epidural and spinal anesthesia, the order determined using a table of random numbers. Between trials, the neural blockade was allowed to fully dissipate, as evidenced by full return of motor and sensory function, ability to ambulate, and ability to void. Time from complete dissipation of anesthesia to beginning the second part of the experiment was at least 2 h and no more than 4 h.

Monitoring

Catheters were placed in a peripheral vein and radial artery (for blood sampling and blood pressure monitoring) using a total of 5 ml 1% lidocaine for local anesthesia. Subjects were monitored with an electrocardiogram for HR, an arterial blood pressure transducer attached to a Hewlett Packard monitor 78341 A (Hewlett Packard, Waltham, MA) for mean arterial pressure, and a CIC-1000 computer-interfaced transthoracic impedance cardiac output monitor (Sorba Medical Systems, Milwaukee, WI). Cardiac output measurements were averaged and updated every 10 s during four stages of the study (see below) using the CIC-1000. This system generates a 50-Hz, 500-μA signal

that is applied *via* patch electrodes located on the forehead and proximal left thigh. Two sensing electrodes, at the left base of the neck and left midaxillary line at the level of the xiphoid, measured changes in impedance over time (dZ/dt). CI and total peripheral resistance (TPR) were calculated by the CIC-1000. Although the absolute accuracy of this method for measuring cardiac output has been questioned, the accuracy of changes in cardiac output detected by the CIC-1000 in normal healthy subjects have been shown to correlate well with the same changes detected by thermodilution.[5]

Centroneuraxis Blockade

With the subjects in the lateral decubitus position, spinal and epidural local anesthetic injections were performed at the second or third lumbar interspace, after local anesthesia using a total of 5 ml 1% lidocaine. For epidural anesthesia, after obtaining a loss of resistance to air using a 17-G Tuohy needle and a negative aspiration test, a test dose of 5 ml 2% lidocaine (plain) was given. If no signs of intravascular or intrathecal injection were noted, an additional 25 ml of the same solution was incrementally injected over 5 min, with frequent aspiration tests. For spinal anesthesia, 2 ml 5% lidocaine in 7.5% dextrose was given *via* a 27- or 25-G Whitacre needle after aspiration of cerebrospinal fluid. The doses of lidocaine for epidural and spinal anesthesia were selected to provide a comparably high thoracic level of analgesia. The subjects were turned supine immediately after injection of lidocaine.

Level of sensory analgesia was determined by response to pin-prick by an individual unaware of whether the subject had received spinal or epidural lidocaine. After confirming a sharp sensation at the shoulder (C4 dermatome), the pin was moved up the trunk in a cephalad direction from anesthetized to unanesthetized dermatomes until the pin again felt as sharp as at the shoulder. The dermatome caudad to that level was considered to be the level of analgesia. Level of analgesia was tested bilaterally in the midclavicular line; if a difference was found, the lower level was recorded. The level was first tested 20 min after local anesthetic injection and then every 5 min until the second CPT was completed.

To grade motor block during anesthesia, a modified Bromage score was used[6]: no demonstrable motor block was scored as 0, inability to flex the hip as 1, inability to flex the knee as 2, and inability to move the ankle (complete motor block of the lower extremity) as 3.

Cold Pressor Test

A CPT was performed on two separate occasions during each experiment (before and during epidural or spinal block). Each subject immersed one hand up to the wrist into an ice-water bucket (4°C) for 120 s. Maximum HR, mean arterial pressure, and CI measured during the last 60 s of the CPT were recorded. A blood sample for measuring catecholamine concentrations was drawn at the completion of the 120-s CPT. The maximum catecholamine response to the CPT has been shown to occur at 2 min.[7]

Experimental Protocol

After catheters were inserted and monitoring devices attached, a 20-min equilibration period allowed the subjects to relax. Cardiovascular variables (HR, mean arterial pressure, CI, and TPR) were recorded and blood samples for catecholamine measurement were taken at four stages: (1) resting baseline; (2) immediately after stage 1, at the end of the first CPT; (3) 30 min after spinal or epidural local anesthetic injection, which was performed immediately after stage 2; and (4) immediately after stage 3, at the end of the second CPT. Plasma lidocaine concentrations were measured at stage 3. Blood drawn for samples (approximately 50 ml per experiment) was replaced with intravenous lactated Ringer's solution in a 3:1 ratio. Total intravenous fluid given during each part of the experiment (epidural or spinal anesthesia) was approximately 150 ml.

Catecholamine and Lidocaine Analysis

Whole blood for analysis was drawn from the arterial catheter. Blood was placed into chilled heparinized tubes and immediately cooled on ice for 10 min. Samples were centrifuged (3,000 rpm × 10 min) in a refrigerated centrifuge; plasma was frozen and stored at −70°C until assay. Catecholamine analysis was performed using single-isotope radioenzymatic method[8] with a lower limit sensitivity of 10 ng/l for epinephrine and norepinephrine. Specificity of this assay is greater than 0.98.

Plasma lidocaine concentrations were measured using fluorescence polarization method (Therapeutic Drug Monitoring System "TDX," Abbott, North Chicago, IL) with a sensitivity of 0.1 μg/ml.

Data Analysis

Data are presented as mean ± SEM, except that level of analgesia and motor block scores (discontinuous variables) are presented as median (minimum − max-

imum). For CPT 1, data are presented as change (stage 2 − stage 1); for CPT 2, data are presented as change (stage 4 − stage 3). Two-tailed paired *t* test was used to detect any difference in a variable of interest between epidural and spinal anesthesia, between any two stages, and between CPT 1 and CPT 2. Level of analgesia was coded as 1–20 for S1–C7, respectively. Two-sided Wilcoxon's signed-rank test was used to test for differences in analgesia level and motor block scores between spinal and epidural anesthesia. Because there was some variation among subjects in actual extent of neural blockade (level of analgesia), we attempted to relate level of analgesia with changes in hemodynamic and catecholamine concentrations during the second CPT. A Kendall tau b correlation coefficient was calculated,[9] and probability of correlation is reported. "Means, univariate, and correlation procedures" in SAS software was used for calculations (SAS Institute, Cary, NC). A $P < 0.05$ is considered significant.

Results

Two of the 12 volunteers developed no motor block after spinal lidocaine despite easily aspirated CSF. Anesthesia was restricted to sacral dermatomes, therefore a restricted spread of lidocaine within the intrathecal space was suspected. Data from both phases of the study for these subjects were removed from analysis because they did not develop sufficient block to meet the primary criterion for evaluation, *e.g.*, thoracolumbar sensory anesthesia. Of the remaining volunteers, three were women and seven were men. Mean age was 35.2 ± 0.9 yr, height 173 ± 3 cm, and weight 72.5 ± 3.3 kg.

Centroneuraxis Anesthesia

Median levels of analgesia at stages 3 and 4 (analgesia levels at these two stages did not differ for any subject) were T4 (range T5–T3) for epidural anesthesia and T3 (range T6–C8) for spinal anesthesia. There was no difference between level of analgesia for epidural *versus* spinal anesthesia. Median motor block scores were less for epidural (median 2, range 1–2) than for spinal anesthesia (median 3, range 3–3; $P < 0.05$. There were no differences in catecholamine concentrations or in any hemodynamic variable between stages 1 and 3 (resting stages before and after anesthesia) or between anesthetic techniques, except that HR was less during stage 3 after spinal anesthesia compared to stage 1 (ta-

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Table 1. Hemodynamic and Catecholamine Data for Resting Baseline (Stage I) and Resting Centro-Neuraxis Block (Stage III)

Treatment	MAP (mmHg)	Heart Rate (beats/min)	CI ($L \cdot min^{-1} \cdot m^{-2}$)	TPR ($dyne \cdot s^{-1} \cdot cm^{-5}$)	NE (ng/L)	E (ng/L)
Epidural stage I	95 ± 2	67 ± 3	4.2 ± 0.4	1,092 ± 127	258 ± 14	35 ± 7
Epidural stage III	92 ± 6	72 ± 3	3.8 ± 0.5	1,136 ± 125	242 ± 27	40 ± 8
Spinal stage I	90 ± 3	66 ± 3	4.0 ± 0.4	1,060 ± 134	302 ± 35	41 ± 9
Spinal stage III	86 ± 4	58 ± 2*	3.9 ± 0.4	1,012 ± 108	323 ± 45	55 ± 11

MAP = mean arterial pressure; CI = cardiac index; TPR = total peripheral resistance; NE = norepinephrine; E = epinephrine.

There were no differences in stage between epidural and spinal anesthesia, except for heart rate.

* $P < 0.05$ *versus* stage I (resting baseline).

ble 1). Mean plasma lidocaine concentrations at stage 3 were 3.6 ± 0.7 μg/ml and 1.0 ± 0.3 μg/ml for epidural and spinal anesthesia, respectively ($P < 0.05$).

Cold Pressor Tests

During the CPT 1 before either anesthetic technique, all hemodynamic and catecholamine variables, with the exception of TPR, significantly increased (table 2). Both spinal and epidural anesthesia attenuated the increase in mean arterial pressure during the second CPT ($P < 0.05$). Spinal but not epidural anesthesia attenuated the increase in CI. During the second CPT, increases in HR and plasma norepinephrine and epinephrine concentrations were not attenuated by either spinal or epidural anesthesia (table 2).

TPR with epidural but not spinal anesthesia significantly decreased during the second CPT. There were no significant differences between spinal and epidural anesthesia for any hemodynamic (including CI) or catecholamine variable during either the baseline (CPT 1) or postanesthetic (CPT 2) CPTs (table 2).

Because there was some variation in extent of analgesia level among individuals, relationships between level of analgesia and changes in plasma catecholamine concentrations and/or hemodynamic variables were sought. However, no correlations between level of analgesia and sympathetic response to the second CPT for either epidural or spinal anesthesia were found (table 3).

Discussion

Spinal anesthesia did not result in a more profound attenuation of the sympathetic response than did epidural anesthesia. The blood pressure response to a CPT was attenuated by both spinal and epidural anesthesia, as was the increase in CI in response to CPT by spinal but not by epidural anesthesia. In this study, despite midthoracic levels of analgesia and evidence of moderate to profound motor block, neither spinal nor epidural anesthesia attenuated increases in plasma catecholamine concentrations and HR in response to CPT. There were no important differences between these two forms of centroneuraxis blockade in their ability or lack of ability to blunt the sympathetic response to stress applied to an unblocked area of the body. Neither

Table 2. Changes from Baseline in Hemodynamic Variables and Catecholamine Concentrations Induced by a CPT before and during Block

Treatment	MAP (mmHg)	Heart Rate (beats/min)	CI ($L \cdot min^{-1} \cdot m^{-2}$)	TPR ($dyne \cdot s^{-1} \cdot cm^{-5}$)	NE (ng/L)	E (ng/L)
CPT 1 (preepidural)	25 ± 4*	12 ± 3*	0.7 ± 0.2*	70 ± 66	199 ± 67*	71 ± 16*
CPT 2 (epidural)	11 ± 3*†	15 ± 3*	1.0 ± 0.2*	−166 ± 68*†	257 ± 86*	62 ± 19*
CPT 1 (prespinal)	31 ± 3*	13 ± 2*	0.9 ± 0.2*	144 ± 83	136 ± 37*	72 ± 20*
CPT 2 (spinal)	8 ± 2*†	10 ± 2*	0.6 ± 0.1*†	−48 ± 27	103 ± 33*	38 ± 13*

CPT 1 = stage II–stage I; CPT 2 = stage IV–stage III; MAP = mean arterial pressure; CI = cardiac index; TPR = total peripheral resitance; NE = norepinephrine; E = epinephrine.

* $P < 0.05$ for change produced by CPT.

† $P < 0.05$ *versus* change produced by cold pressor test 1 (stage II–stage I).

Table 3. Kendall τ b Correlation Coefficient and Probability for Correlation of Analgesia Level with Changes in Hemodynamic Variables and Catecholamine Concentrations during CPT 2

Variable	Epidural Anesthesia		Spinal Anesthesia	
	Coefficient	P Value	Coefficient	P Value
Mean arterial pressure	−0.14	0.62	−0.34	0.19
Heart rate	−0.16	0.55	−0.05	0.85
Cardiac index	0.03	0.92	−0.44	0.09
Total peripheral resistance	0.08	0.77	0.10	0.71
Norepinephrine	0.03	0.92	0.05	0.85
Epinephrine	−0.08	0.77	0.42	0.11

The level of analgesia was not related to change in any hemodynamic variable during the second cold pressor test.

form of anesthesia resulted in complete sympathetic blockade. This was surprising because the motor block of the lower extremities was complete (Bromage score = 3) during spinal anesthesia.

For many years, anesthesiologists have assumed that, when local anesthetic is given to produce a sensory or motor block, blockade of preganglionic sympathetic fibers would be present.[10] *In vivo* investigations of spinal[11,12] and epidural anesthesia[13,14] have concluded that sympathetic denervation is present during sensory and motor centroneuraxis block and that the level of sympathetic block exceeds the level of sensory block by at least two dermatome segments. However, these conclusions are based on a loss of cold sensation,[9,11] an increase in skin temperature,[12] or thermography.[10] None of these methods are sufficiently quantitative to establish a complete sympathetic denervation. Studies evaluating sympathetic blockade by monitoring skin conductance responses[15,16] have reported that spinal anesthesia (upper level of sensory analgesia T4–T6) produced an incomplete sympathectomy of the lower extremity. To assess integrity of the sympathetic nervous system to reflex stimulus, Lundin, *et al.*[17] used percutaneous peripheral neurography to quantitatively measure sympathetic nerve traffic. Using apnea for 30–60 s as a sympathetic stimulus, they demonstrated complete attenuation of sympathetic nerve impulses in the peroneal nerve during mepivacaine lumbar epidural anesthesia. However, they noted sympathetic activity returned to normal when sensory anesthesia had regressed to the T10 dermatome. Other studies using indirect methods of measuring sympathetic response to stress, *e.g.,* intubation of the trachea,[18] physical ex-

ercise,[19] or hypercapnia,[20,21] have shown that cervical and thoracic epidural anesthesia, although producing sensory anesthesia of the upper thoracic dermatomes, do not attenuate the HR response to stress. Therefore, evidence is lacking for complete sympathetic blockade by direct and indirect assessment in the dermatome segments where analgesia is present during either spinal or epidural anesthesia.

The data reported here also support the incompleteness of sympathetic blockade by spinal and epidural anesthesia sufficient to produce almost complete thoracolumbar anesthesia. The increase in HR observed in the current study could be explained by failure to block the upper four thoracic segments in all subjects. However, Greene and Brull maintain that a sympathetic block should be present at least two or three segments above the level of analgesia to pin-prick.[10] By this criterion, most of our subjects should have had at least a partial sympathetic blockade of the cardio-accelerator fibers. HR during spinal anesthesia was lower than control (table 1). Nevertheless, sympathetic function during CPT measured by changes in HR or plasma catecholamine concentrations was not attenuated with either form of anesthesia. This means that, even if spinal anesthesia decreased sympathetic cardio-accelerator function in the resting individual, when subjected to the stress of a CPT, the sympathetic response (increases in HR and catecholamines) was not impaired.

The blood pressure response to the CPT was attenuated by both spinal and epidural anesthesia. In rats, the pressor response appears to be wholly mediated by norepinephrine released at peripheral nerve terminals.[22] Epinephrine and norepinephrine released into the blood from the adrenal medulla play only a small, insignificant role in the pressor response. If this situation holds for humans, then in the current study, attenuation of the blood pressure response to the cold pressure test is an indication of attenuation by spinal and epidural anesthesia of vasoconstriction. This interpretation is supported by the decrease in TPR during epidural anesthesia (table 2). The main effect of epidural block appears to be in the periphery, whereas the adrenal medulla appears to be little affected (see below).

Levels of analgesia ranged from T6 to C8 (spinal anesthesia) and T5 to T3 (epidural anesthesia). Importantly, the adrenal medulla, which is the only known source of plasma epinephrine, receives its sympathetic innervation from preganglionic fibers having their cell bodies in spinal segments T6 through L2.[23] Therefore,

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lock (Stage III)

	E (ng/L)
4	35 ± 7
7	40 ± 8
5	41 ± 9
5	55 ± 11

catecholamine variables were een level of an- he second CPT were found (ta-

more profound e than did epi- sponse to a CPT ural anesthesia, CPT by spinal study, despite dence of mod- spinal nor epi- n plasma cate- sponse to CPT. ween these two heir ability or ic response to e body. Neither

CPT before and

	E (ng/L)
	71 ± 16*
	62 ± 19*
	72 ± 20*
	38 ± 13*

NE = norepinephrine;

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all of our volunteers should have had a sympathetic block of the adrenal medulla. Despite sensory analgesia of those dermatomes in all volunteers, the CPT consistently produced an increase in plasma epinephrine.

How can the failure of centroneuraxis block to produce complete block of preganglionic sympathetic fibers be explained? It may be that a block sufficient to provide surgical anesthesia is not sufficiently "dense" to completely eliminate all neural transmission. Lund *et al.* measured somatosensory evoked potentials during epidural anesthesia. During cutaneous electrical stimulation, they found that the L1 dermatome, close to the site of lumbar epidural local anesthetic injection, demonstrated a blockade of fast-conducting sensory fibers, whereas evoked potentials at a distant dermatome (S1) were normal, despite surgical anesthesia of both regions.[24] Injection of a small dose of local anesthetic (45 mg bupivacaine) *via* a thoracic epidural catheter did not change somatosensory evoked potentials during electrical stimulation of the skin at either the T10 or L1 dermatomes, despite surgical anesthesia extending from T3 to L2.[25] A larger dose of drug,[26] closer to the injection site,[27] or a different local anesthetic, *e.g.,* 0.75% bupivacaine, 3% 2-chloroprocaine,[3] or spinal tetracaine,[4] may produce a more profound block. It would appear that, *in vivo,* it is difficult to achieve a complete sympathetic block during epidural or spinal anesthesia using usual clinical doses of local anesthetics. It may be that preganglionic sympathetic fibers are more resistant to local anesthetic block than previously thought. An analogous situation is the poorly understood phenomenon of tourniquet pain, which is incompletely blocked during spinal or epidural anesthesia, despite otherwise adequate sensory and motor block.

Limitations of this study include the normal variability of human plasma catecholamine concentrations. However, single samples of plasma catecholamines drawn at the time used here have been used previously as a reproducible measure of sympathetic response to CPT.[7,28] Absolute accuracy of trans-thoracic impedance determination of cardiac output has not been demonstrated. However, to assess the response to the CPT, the current study relied only on changes in measured variables, not absolute values. Changes measured with this technique are well correlated with changes measured using thermodilution methods.[5] There was some variability in level of analgesia in our volunteers, but all volunteers had sensory levels of analgesia to the T6 dermatome or above, which should have resulted in a

sympathetic blockade of the adrenal medulla. Level of analgesia in the range we studied was not correlated with changes in plasma catecholamine concentrations during the cold pressure test during either spinal or epidural anesthesia.

Anesthesiologists often assume that, when a motor block is present during spinal or epidural anesthesia, sympathetic nerve transmission is blocked. Thus, epidural and spinal anesthesia have been used diagnostically and therapeutically in patients with presumed sympathetically mediated pain syndromes (*e.g.,* reflex sympathetic dystrophy). The results of the current study call into question usefulness of information gained from epidural or spinal anesthesia for the purpose of differentiating among somatically, sympathetically, and centrally mediated pain.

In summary, we found that neither spinal nor epidural anesthesia using plain lidocaine attenuated the HR and catecholamine response to a CPT despite midthoracic levels of analgesia. In response to a CPT, spinal anesthesia blocked the increase in CI, and epidural anesthesia blocked the increase in TPR compared to the pre-anesthesia state. However, there were no statistical differences between techniques; these differences are of uncertain clinical importance. Despite a more complete motor block during spinal anesthesia, spinal anesthesia did not produce a more complete sympathectomy than epidural anesthesia. These results suggest that sensory and motor block during centroneuraxis blockade using lidocaine by either technique are not reliable indicators of complete sympathetic blockade.

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