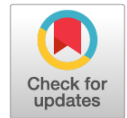


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# Neuropathic pain syndrome during surgical interventions on the lumbar spine

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## ABSTRACT

**BACKGROUND:** The presence of neuropathic pain syndrome (NPS) in patients with degenerative spinal diseases can make determining the tactics of surgical treatment challenging and increases the risk of residual or recurrent pain syndrome after surgery.

**AIM:** To investigate the perioperative course in patients with degenerative diseases of the lumbar spine depending on NPS.

**MATERIALS AND METHODS:** This prospective observational study included patients with planned surgical treatment for degenerative lumbar spinal stenosis. The study design included two visits: preoperative and 3 months after surgery follow-up. NPS assessment (DN4), back and leg pain intensity (NPRS back, NPRS leg), and disability index (ODI) were collected in both visits.

**RESULTS:** Overall, 169 patients were included; 48.5% of patients had NPS initially and 26% had NPS after surgery. NPS remained in 7.3% of patients and developed in 13% without initial signs before surgery. Patients with NPS upon admission had a higher intensity of pain in the back ( $6.82 \pm 2.41$  vs.  $5.42 \pm 2.66$ ;  $p=0.041$ ) and legs ( $7.43 \pm 2.34$  vs.  $6.32 \pm 2.16$ ;  $p=0.017$ ) than non-NPS patients. Patients with NPS at 3-month follow-up had higher intensity of pain in the back ( $4.31 \pm 2.52$  vs.  $2.31 \pm 2.38$ ;  $p=0.012$ ) and legs ( $4.71 \pm 2.91$  vs.  $1.55 \pm 2.27$ ;  $p=0.003$ ) than non-NPS patients.

**CONCLUSION:** Thus, 48.5% of patients with degenerative lumbar spinal stenosis had NPS before surgical treatment, and in 13% of patients, neuropathy developed after surgery. Patients with NPS, identified before surgical treatment or after surgery, have a higher pain intensity (1.2–1.3 times higher before surgery, 1.9–3 times higher after surgery) and report less pain regression after surgery. The presence of neuropathic pain syndrome at all periods of observation (or its appearance) complicates patient recovery and postoperative observation.

**Keywords:** neuropathy; neuropathic pain syndrome; pain intensity; degenerative spinal disease; degenerative stenosis; surgical treatment.

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# Нейропатический болевой синдром при хирургических вмешательствах на поясничном отделе позвоночника

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## АННОТАЦИЯ

**Обоснование.** Нейропатический болевой синдром НБС у пациентов с дегенеративными заболеваниями позвоночника может вносить диссонанс в определение тактики хирургического лечения и повышает риск остаточного или рецидивирующего болевого синдрома после хирургических вмешательств.

**Цель.** Определить особенности периоперационного течения у пациентов с дегенеративными заболеваниями поясничного отдела позвоночника в зависимости от нейропатического болевого синдрома.

**Материалы и методы.** Дизайн исследования — проспективное наблюдательное. В исследование вошли пациенты с запланированным хирургическим лечением по поводу дегенеративного поясничного стеноза. Дизайн исследования включал два визита: предоперационный и контрольный осмотр через 3 месяца после операции. На обоих визитах оценивались интенсивность боли в спине и ноге (NPRS спина, NPRS нога), нейропатический болевой синдром (DN4), индекс дееспособности (ODI).

**Результаты.** В исследование были включены 169 пациентов. Исходно у 48,5% пациентов были выявлены признаки НБС, после операции доля лиц с НБС составила 26%. При этом НБС сохранился у 7,3% пациентов, а у 13% появился при изначальном его отсутствии. Пациенты с НБС при поступлении имели более высокую интенсивность болевого синдрома в спине ( $6,82 \pm 2,41$  vs.  $5,42 \pm 2,66$ ,  $p=0,041$ ) и в ноге ( $7,43 \pm 2,34$  vs.  $6,32 \pm 2,16$ ,  $p=0,017$ ) по сравнению с группой лиц без НБС. Пациенты с НБС через 3 месяца после операции имели большую интенсивность болевого синдрома в спине ( $4,31 \pm 2,52$  vs.  $2,31 \pm 2,38$ ,  $p=0,012$ ) и в ноге ( $4,71 \pm 2,91$  vs.  $1,55 \pm 2,27$ ,  $p=0,003$ ).

**Заключение.** Нейропатический болевой синдром ещё до хирургического лечения имеют 48,5% пациентов с дегенеративным поясничным стенозом, у 13% больных нейропатия развивается после хирургического вмешательства. Пациенты с выявленным до хирургического лечения НБС или подтверждённым после имеют более высокую интенсивность боли (в 1,2–1,3 раза до операции, в 1,9–3 раза после операции) и отмечают меньший её регресс после операции. Наличие НБС на всех сроках наблюдения осложняет выздоровление пациента и его послеоперационное наблюдение ввиду меньшего регресса болевого синдрома.

**Ключевые слова:** нейропатия; нейропатический болевой синдром; интенсивность боли; дегенеративные заболевания позвоночника; дегенеративный стеноз; хирургическое лечение.

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## BACKGROUND

Somatosensory nervous system lesions or diseases can paradoxically lead not only to loss of function but also to increased pain sensitivity, distorted pain variants, and spontaneous pain [1]. Such a neuropathic component is present in radicular pain syndrome caused by nerve root compression, and increasing evidence shows that a neuropathic component is also part of localized back pain or reflected (pseudoradicular) leg pain [2–4]. The identification of nociceptive and neuropathic components of pain is clinically important because they require different treatments. Between 12% and 55% of patients with chronic back pain syndrome also experience neuropathic pain. In the general population, neuropathic pain affects 7%–10% of adults [8–10]. Compared with nociceptive pain syndrome, neuropathic pain is expressed in severe pain, disability, anxiety, depression, and a greater reduction in the quality of life than [11–13]. When compared with other types of pain, neuropathic pain syndrome (NPS) has greater effects on the quality of life related to physical, psychological, and social aspects and increases health-related costs by 28%–52% [14].

Moreover, 3%–34% of patients report pain 6–24 months after spinal surgery and 5%–36% at follow-up >2 years after the intervention [15, 16]. The reasons for the persistence of pain syndrome or its recurrence in the back or leg after spinal surgery remain unclear [17] and lack any clear prognostic factors and predictors [18]. NPS may also be one of the possible causes of residual or recurrent pain syndrome in the postoperative period [19, 20]. Postoperative residual or recurrent pain syndrome can complicate the postoperative course and introduce doubts into the treatment process. The type of pain syndrome determines the most appropriate treatment; thus, the identification of patients with NPS requires greater care. Furthermore, identifying individuals with degenerative spine disease who are at risk for residual or recurrent pain after surgery is challenging. Thus, how to predict which patients are more or less likely to benefit from surgery remains unanswered. Similarly, the association between specific pain characteristics, such as the presence of a neuropathic component in back pain or radicular pain syndrome, and outcomes remains unclear. Such information would help surgeons and patients make informed decisions when choosing an appropriate management strategy.

**This study aimed** to determine the peculiarities of the perioperative course in patients with degenerative lumbar spine diseases depending on NPS.

## MATERIALS AND METHODS

### Study design

A prospective observational study was conducted.

### Eligibility criteria

#### *Inclusion criteria:*

- Age 40–75 years
- A planned decompressive or decompressive-stabilizing intervention on the lumbar spine for degenerative lumbar spinal canal stenosis at one or more levels.
- Completed clinical questionnaires.
- Written informed consent to participate in the study.

#### *Exclusion criteria:*

- Sagittal imbalance in decompensation (Barrey index >1).
- Previous surgical intervention at the lumbar spine.
- Nondegenerative nature of the pain syndrome, such as osteoporotic vertebral fractures, spinal trauma fractures, or spinal tumors.

### Settings

The study included patients with degenerative lumbar spine diseases who were scheduled for surgery. The surgical indications were pain syndrome in the lumbar spine in conjunction with nerve root compression syndrome and/or neurologic deficit and/or neurogenic intermittent claudication syndrome that had not responded to prolonged (>3 months) conservative therapy. The morphologic substrate of the clinical manifestations was degenerative lumbar spinal canal stenosis, which was either present alone or in conjunction with degenerative spondylolisthesis.

### Study duration

The study design included two visits: visit 1 was a preoperative examination, and visit 2 was a control examination 3 months after surgery. Clinical data were collected at both visits. All data were collected in an electronic database designed for clinical research. Postoperatively, patients were activated early according to the volume of surgical intervention and condition.

### Description of the medical intervention

The surgical intervention was either decompressive (group D) or decompressive-stabilizing (group DS) surgery on the lumbar spine, depending on the morphological substrate of the clinical syndrome. Decompression of neural structures in the spinal canal is an obligatory stage of any surgical intervention.

A prospective study of the neuropathic component of pain syndrome demonstrated that the detection of this syndrome did not influence surgical techniques. The assessment of NPS in patients with planned lumbar interventions is not a routine procedure. Consequently, the collection and analysis of these data constituted a separate study. Compression or compression-ischemic syndrome resistant to conservative treatment is indicated for surgery. The presence of NPS alone is not an indication for surgical treatment.

### Main outcome of the study

Clinical data included data from questionnaires and scales, including the assessment of NPS (Douleur Neuropathique en

4 questions, DN4), intensity of back and leg pain according to the numeric pain rating scale (NPRS back, NPRS leg), and disability index (Oswestry disability index [ODI]). The NPS was assessed using the DN4 questionnaire. Specifying the features of the pain syndrome can help researchers suspect and determine the neuropathic origin of pain with sufficient sensitivity and specificity. A sum of scores >4 points registers the presence of a neuropathic component. However, the severity of NPS was also assessed by summarizing the questionnaire scores. The presence of NPS (DN4 >4) was used to identify those with and without NPS. These two subgroups were then compared.

## Ethical review

The study was approved by the local Ethics Committee of the N.N. Priorov National Medical Research Center for Traumatology and Orthopedics (Meeting No. 1/23 dated May 5, 2023).

## Statistical analysis

### Methods of statistical processing

Quantitative variables are provided as descriptive statistics: mean, standard deviation, medians, quartiles, minimum and maximum values, and number of valid observations. Categorical variables are presented as the frequency of values and percentages relative to the number of valid observations. The paired *t*-test was used to compare pre- and postoperative measures, with the nonparametric Wilcoxon criterion for

related samples serving as a supporting analysis. The results were consistent. Groups formed according to predetermined attributes were compared using analysis of variance (with a Mann–Whitney test as a supporting analysis) for quantitative attributes and Pearson's chi-square test for categorical attributes. The level of significance (*p*-value) was set at less than or equal to 0.05 ( $p \leq 0.05$ ). Statistical analysis was performed using the SPSS Statistics version 15.0.

## RESULTS

### Study participants

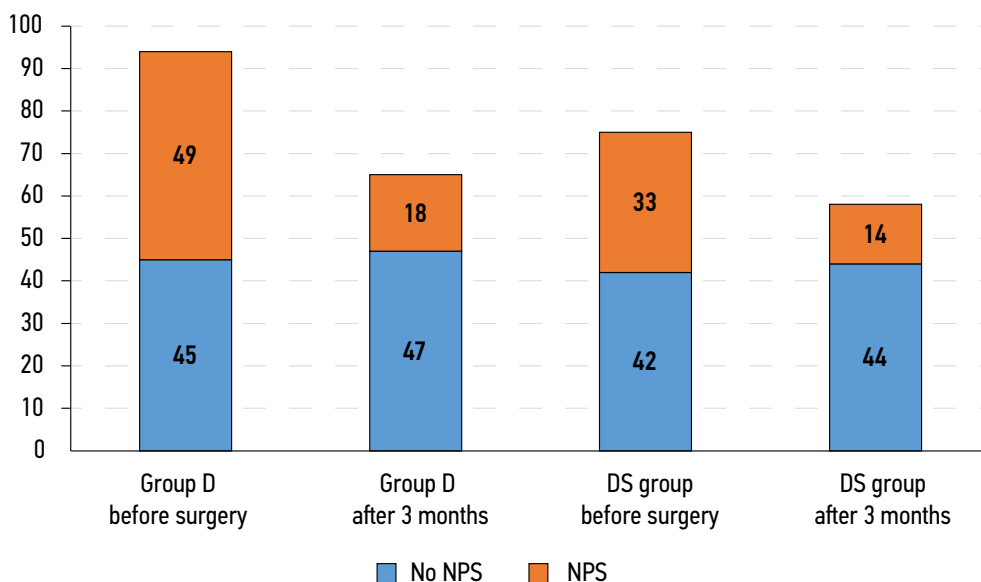
A total of 169 patients were included in the study, comprising 94 who had undergone a planned decompressive surgery and 75 who had undergone a planned decompressive-stabilizing surgery. At visit 2 (3 months postoperatively), 123 patients (72.8% of the total cohort) were available for evaluation: 65 (69.1%) after decompressive surgery and 58 (77.3%) after decompressive-stabilizing surgery.

At the initial visit (on admission), patients in group D group were older and had a greater proportion of females than group DS ( $p = 0.003$  and  $0.012$ , respectively) (Table 1). Group DS underwent predominantly monosegmental interventions, whereas group D underwent monosegmental and multilevel interventions ( $p = 0.035$ ). The morphologic substrate in both groups was comparable, with degenerative stenosis combined with degenerative spondylolisthesis representing the majority of cases ( $p > 0.05$ ).

**Table 1.** Clinical characteristics of the patients upon admission\*

Parameters	Group D	Group DS	All patients	Group I vs. group II, <i>p</i>
Quantity	94	75	169	
Age, years	67 [61; 71]	52 [47; 64]	63 [55; 71]	0.003
Sex	Women: 70.2% (66/94)	Women: 41.3% (31/75)	Women: 57.4% (97/169)	0.012
Body mass index, kg/m <sup>2</sup>	29.7 [25.6; 33.1]	28.5 [25.9; 33.8]	29.1 [25.2; 33.7]	0.633
Number of intervention levels	One level: 57.4% (54/94); Two levels: 35.1% (33/94); Three or more levels: 7.5% (7/94)	One level: 89.3% (67/75); Two levels: 10.7% (8/75)	One level: 71.6% (121/169); Two levels: 24.3% (41/169); Three or more levels: 4.1% (7/169)	0.035
Degenerative spondylolisthesis	Detected: 41.5% (39/94)	Detected: 56.0% (42/75)	Detected: 47.9% (81/169)	0.77
<i>Data from clinical questionnaires</i>				
Presence of NPS (>4 DN4)	52.1% (49/94)	44% (33/75)	48.5% (82/169)	0.522
Intensity of pain in the leg (VAS leg)	8 [5; 10]	5 [3; 7]	7 [5; 9]	<0.001
Back pain intensity (VAS back)	4 [3; 8]	5 [4; 8]	5 [4; 8]	0.075
Functional capacity (ODI)	55.00 [42.22; 62.22]	62.00 [40.11; 68.22]	57.22 [42.00; 65.22]	0.351

Note. \* Quantitative parameters are presented as MED [IQR], and categorical parameters are presented as % of frequencies. NPS, neuropathic pain syndrome.



**Fig. 1.** The changes of NBS between the decompressive (group D) and decompressive-stabilizing (group DS) groups before surgery and 3 months after surgery.

Group D was more concerned about radicular pain syndrome in the leg and had greater intensity of leg pain on admission than group DS ( $p < 0.001$ ). Back pain intensity and functional disability were comparable in both groups ( $p = 0.075$  and  $0.351$ , respectively). Notably, the proportion of patients with NPS according to DN4 in groups D and DS was comparable before and after surgery ( $p = 0.522$ ) (Fig. 1).

**Main results of the study**

Initially, 48.5% (82/169) of the patients showed signs of NPS (DN4>4) (Fig. 1). Postoperatively, the proportion of patients with NPS significantly decreased to 26% (32/123) in the total cohort. The proportions of patients with NPS at 3 months postoperatively were comparable in groups D and DS (27.7% (18/65) and 24.1% (14/58), respectively,  $p = 0.669$ ). In addition, NPS persisted in 7.3% (6/82) of the patients and reappeared in 13% (16/123) of the patients. Thus, depending on the dynamics of NPS, the number of patients changes between groups.

**Additional findings**

Patients with NPS had higher pain intensity at admission: 1.3 times higher back ( $6.82 \pm 2.41$  vs.  $5.42 \pm 2.66$  points,  $p = 0.041$ ) and 1.2 times higher leg ( $7.43 \pm 2.34$  vs.  $6.32 \pm 2.16$  points,  $p = 0.017$ ) pain intensity than those without NPS. In addition, patients with NPS had less regression of pain syndrome (in both back and leg pain) 3 months after surgery ( $p < 0.05$ ) (Table 2).

Although all patients reported a decrease in pain intensity after treatment, patients with initial NPS had significantly greater back ( $4.31 \pm 2.52$  vs.  $2.31 \pm 2.38$  points,  $p = 0.012$ ) and leg ( $4.71 \pm 2.91$  vs.  $1.55 \pm 2.27$  points,  $p = 0.003$ ) pain intensity at 3 months postoperative follow-up than patients without NPS (Table 3). Patients with initial NPS had 1.9 times higher back pain intensity and 3 times higher leg pain intensity after surgery than patients without NPS. In general, patients with preserved or acquired NPS reported less regression in pain intensity ( $p = 0.004$ ).

Patients with or without NPS at all postoperative follow-ups reported a significant reduction in pain

**Table 2.** Presence of neuropathic pain syndrome and intensity of pain syndrome at admission and 3 months after surgery

Indices	Subgroup I: NPS on admission (n=78)		Subgroup II: no NPS on admission (n=79)		Subgroup I vs. subgroup II on admission, p	Subgroup I vs. subgroup II 3 months after surgery, p
	On admission	Three months after surgery	On admission	Three months after surgery		
DN4 leg	6.43±1.77	1.67±1.59	1.73±1.54	1.31±1.14	<0.001	0.059
NPRS leg	7.43±2.34	3.07±2.48	6.32±2.16	1.78±1.91	0.017	0.012
NPRS back	6.82±2.41	4.12±2.49	5.42±2.66	2.84±2.63	0.041	0.005

Note. NPS, neuropathic pain syndrome.

**Table 3.** Intensity of pain and neuropathic pain according to clinical scales in accordance with the presence or absence of NPS

Indices	Subgroup I: NPS on admission (n=82)			
	NPS after 3 months (n=6)		No NPS after 3 months (n=76)	
	On admission	Three months after surgery	On admission	Three months after surgery
DN4 leg	5.39±1.91	4.09±2.19	5.48±1.63	0.79±1.08
NPRS leg	6.59±2.51	4.71±2.91*	6.69±2.11	1.55±2.27*.#
NPRS back	7.61±2.11	4.31±2.52*	6.43±2.27	2.31±2.38*.#
	Subgroup II: no NPS on admission (n=87)			
	No NPS after 3 months (n=71)		NPS after 3 months (n=16)	
	On admission	Three months after surgery	On admission	Three months after surgery
DN4 leg	1.47±1.21	0.63±0.88	1.84±1.41	4.13±2.28
NPRS leg	5.61±2.79	1.12±1.63*	5.71±3.22	2.63±1.62*.#
NPRS back	5.37±2.66	2.67±2.33*	5.61±2.38	3.67±2.47

Note. \* significant differences at follow-up periods (preoperative and 3 months after surgery),  $p < 0.05$ ; # significant differences between groups,  $p < 0.05$ . NPS, neuropathic pain syndrome.

intensity compared with preoperative values in both back ( $2.67 \pm 2.33$  vs.  $5.37 \pm 2.66$  points,  $p = 0.007$ ) and leg ( $1.12 \pm 1.63$  vs.  $5.61 \pm 2.79$  points,  $p = 0.002$ ) pains. Patients who did not have NPS at all follow-ups still reported nonsignificant levels of neuropathy, up to  $0.63 \pm 0.88$  points in the leg. Paresthesias could accompany any pain syndrome in any of its manifestations.

## DISCUSSION

The treatment of NPS is a complex multidisciplinary problem involving many specialists. Although NPS is not an indication of surgical intervention, doctors of surgical specialties (neurosurgeons, orthopedic traumatologists, and vertebrologists) regularly encounter this condition in their practice. NPS can complicate the clinical diagnosis and subsequent determination of treatment techniques. Timely detection and dynamic monitoring of neuropathy are difficult.

Some authors consider the influence of concomitant diseases (diabetes mellitus, pathology of peripheral arteries of the extremities, etc.) on the occurrence of NPS [1, 10]; however, whatever the cause of NPS, its presence is reflected in the severity of the pain syndrome in degenerative spine diseases.

According to our data, nearly half of the patients with degenerative lumbar spine diseases (48.5%) had signs of NPS before surgery. Many authors also noted the presence of NPS in their patients before surgery: 19.8% in patients with spinal stenosis [22] and 20.4% in patients with degenerative lumbar spine diseases [23]. The wide variation in the proportion of patients with NPS is attributed to the use of different clinical questionnaires, cohorts of patients of different ages, and

different durations of pain and neuropathic syndromes [23]. The present study included patients with a conservative treatment duration of at least 3 months; such a prolonged presence of pain syndromes, including initially non-neuropathic ones, may increase the proportion of patients with NPS. Compared with nociceptive pain, NPS is not well tolerated by patients and has a greater effect on their quality of life [8]. Because NPS has central sensitization, it is less amenable to treatment [24].

Moreover, 13% of patients develop NPS after surgery, although it was initially absent. However, these data differ only slightly from the data obtained from a cohort of patients who did not undergo surgery in which up to 10% of the adult population also exhibited signs of NPS [9]. Although all patients in the present study underwent decompression of neural structures, delicate intracanalicular workup may account for only a small increase in the proportion of NPS. However, after aggressive surgery (laminectomy), up to 77% of patients with degenerative lumbar spine diseases had nonspecific neuropathy in the postoperative period [25].

In this study, patients with NPS have greater back and leg pain intensity preoperatively, and these patients report less pain relief after surgical treatment. This is also supported by data from a cohort of patients who underwent lateral lumbar interbody spondylosis with indirect decompression at the lumbar level [23]. The neuropathic component of the pain syndrome is hereditary in 37% of cases [26], i.e., in every third patient with NPS, its presence is not related to the pathology, intervention, or rehabilitation measures. Nevertheless, the probability of NPS in patients with planned and/or performed decompressive and decompressive-stabilizing interventions for degenerative spinal diseases must be considered.

Thus, the presence of NPS at all follow-up periods (or its appearance after surgery) complicates the patient's recovery and postoperative follow-up because of a generally lower regression of the pain syndrome intensity. The perioperative evaluation of patients with degenerative lumbar spine diseases for NPS will allow timely identification of vulnerable individuals, preoperative preparation if possible, and avoidance of inflated patient expectations and caution against reoperations. Prospective studies, including basic research, will shed light on the cause of NPS and its treatment options.

## CONCLUSIONS

NPS is present before surgery in 48.5% of patients with degenerative lumbar spine diseases, and neuropathy develops after surgery in 13%. Patients with NPS diagnosed preoperatively or postoperatively generally have higher pain intensity (1.2–1.3 times higher before surgery and 1.9–3 times higher after surgery) and report less pain relief after surgery. The presence of NPS at all follow-up periods (or its appearance) complicates the patient's recovery and postoperative follow-up because of the generally lower regression of pain intensity.

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## ADDITIONAL INFO

**Author contribution.** All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

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**Competing interests.** The authors declare that they have no competing interests.

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**Вклад авторов.** Все авторы подтверждают соответствие своего авторства международным критериям ICMJE (все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией).

**Источник финансирования.** Авторы заявляют об отсутствии внешнего финансирования при проведении исследования и подготовке публикации.

**Конфликт интересов.** Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с проведённым исследованием и публикацией настоящей статьи.

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