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Original Research

Neuropathic Pain and Positive Sensory Symptoms in Brachial Plexus Neuropathy: An Exploratory Study of Outcomes after Surgical Decompression and Proposal of a New Sensory Frequency of Symptoms Scale

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Abstract

Background: There are no articles that aim to evaluate the specific role of surgical decompression on the recovery of pain and positive sensory symptoms (PSS) in patients with brachial plexus neuropathy (BPN), as well as the relationship between pain and frequency of sensory manifestations. **Methods**: A prospective before and after study was performed, considering the pain intensity through the visual analogue scale (VAS), and the frequency of PSS through a proposed new scale: Sensory Frequency of Symptoms Scale (SFSS). To compare the patients before and after the intervention, a paired *T*-test, a Wilcoxon signed-rank test, and Cohen's D test were made, coupled with a Spearman analysis in order to establish the relationship between pain and PSS. **Results**: Sixteen patients were included in the study, the clinical evaluation showed changes in pain according with VAS, going from a mean preoperative state of 8.19 to 1.31 after surgery, showing significant changes (84%, $p < 0.00006$, $\Delta = 2.776$). Within the PSS, a significant decrease was observed in paresthesias (74%, $p < 0.0001$, $\Delta = 1.645$), dysesthesias (80%, $p < 0.002$, $\Delta = 1.453$), and allodynia (70%, $p = 0.031$, $\Delta = 0.635$). Conversely, the preoperative correlation analysis between pain and dysesthesias/allodynia showed a low and non-significant relationship ($R < 0.4$, $p > 0.05$). **Conclusions**: Surgical decompression is an effective technique for the relief of pain and sensory manifestations in adult patients with BPN of compressive origin. No relationship was observed between pain and dysesthesias/allodynia. Therefore, during clinical evaluation, they should be considered as independent manifestations, highlighting the need to validate new scales.

Keywords: brachial plexus neuropathy; surgery; outcomes; pain; sensory

1. Introduction

Brachial plexus neuropathy (BPN) occurs from different etiologies that affect the upper extremity, causing severe functional impairment mainly manifested as motor, pain, and sensory disturbances [1–4]. BPN is commonly caused by a compressive disorder, related to ischemic and mechanical origin. Regarding the pathophysiology of nerve compression, studies suggest a positive correlation between pressure and neural dysfunction [5]. These patients also present electrophysiological findings of demyelination. In some cases, demyelination is minimal, these patients present normal electrodiagnostic studies without neurogenic pattern. In these cases, it is possible to complement the diagnosis with imaging studies that allow identifying the presence of a compressive pathology [6]. Moreover, the clinical repercussion is related to thickening of the external epi/peri-neurium. These histopathological changes contribute to blood flow deprivation and produce dynamic ischemia to the nerve fibers. The compressive syndromes can be caused by different mechanisms, such as bone/muscle structures (Outlet Thoracic Syndrome [OTS]), neoplasm (tumors), or the development of fibrosis secondary to an injury/intervention (trauma or radiation) [7]. The severity of the injury depends on the location and extension of nerve damage. Surgical decompression allows these nervous structures to be released by separating the surrounding tissues, solving the compression phenomenon that causes neuropathic pain and other concomitant alterations [8].

Neuropathic pain is caused by a lesion or disease of the somatosensory nervous system. Patients with neuropathic pain have several sensory manifestations; this sensory impairment involves two types of symptoms: "negative" and "positive". A negative sensory phenomenon is a deficit in sensory function (loss of sensation). The positive sensory symptoms (PSS) are an abnormally increased function of the sensory system, manifested as paresthesias, dysesthesias, and/or allodynia; these sensorial abnormalities could

be presented alone or accompanied by neuropathic pain [9]. A study reported by Dy CJ *et al*. [10] in which they evaluated the frequency of how clinical outcomes in BPN are reported, shows that the attention of the surgeons is mainly focused on the restoration of the motor component (94%), and of these, only 5.68% of the studies reported outcomes in terms of pain. Another systematic review about the clinical outcomes shows that only 14.63% of the articles include symptoms related to the sensory component [11]. However, these articles were focused only on the evaluation of negative sensory symptoms, none of them talked about the changes that surgery has on PSS. These observations contrast considerably with the prevalence of neuropathic pain in BPN, symptoms manifested by 69% of the patients [12]. On the other hand, relative to pain clinical assessment, there are several scoring systems for neuropathic pain assessment [13]. These wide alternatives of scores have been validated in different types of pain etiologies and clinic settings, but they still need to be studied in BPN. There are no articles that quantitatively measure the PSS frequency in BPN. For this reason, the aim of this study was to evaluate whether surgical decompression is effective in reducing the intensity of neuropathic pain, as well as reflecting changes in the frequency of PSS in adult patients with BPN of compressive origin. In addition, the study seeks to establish the relationship between the intensity of neuropathic pain and the frequency of PSS, through a proposed new scale: Sensory Frequency of Symptoms Scale (SFSS).

2. Materials and Methods

A prospective, longitudinal, self-controlled, before and after study was performed according to Consolidated Standards of Reporting Trials (CONSORT) 2010 statement for reporting the non-randomized studies [14], to evaluate neuropathic pain and PSS in a group of patients with BPN after surgical management with surgical decompression. The first measurement was done before the surgical intervention and the second, at the last time of follow-up after surgical management. The study was carried out in a tertiary referral hospital. Written informed consent for surgery was obtained from each subject. During the selection process, the inclusion criteria were the following: patients of both genders and adulthood between 18 and 70 years old, patients with neuropathic pain or PSS (paresthesias, dysesthesias, allodynia) as main clinical manifestations refractory to pharmacological treatment, BPN of compressive origin were determined through the use of preoperative electrodiagnostic studies (neurogenic pattern with positive fibrillations, polyphasic units, and an increase of firing rate). The diagnostic approach to determine a compressive origin was complemented with an imaging study (magnetic resonance imaging [MRI]). We also include patients with compromise at high level of injury (proximal third of upper extremity) and presence of nerve continuity, determined by MRI, electrophysiological pre-operative studies, and intra-operative nerve visualization. Patients with pre-ganglionic injuries, nerve transections (in traumatic etiology), avulsions, and pre-cervical injuries were excluded. The elimination criteria also correspond to those individuals with high surgical risk, and patients who rejected the surgical treatment. During the selection, a total of 21 patients that could meet the inclusion criteria were identified, only 16 patients presented inclusion criteria for this study. The selection process is mentioned in Fig. 1.

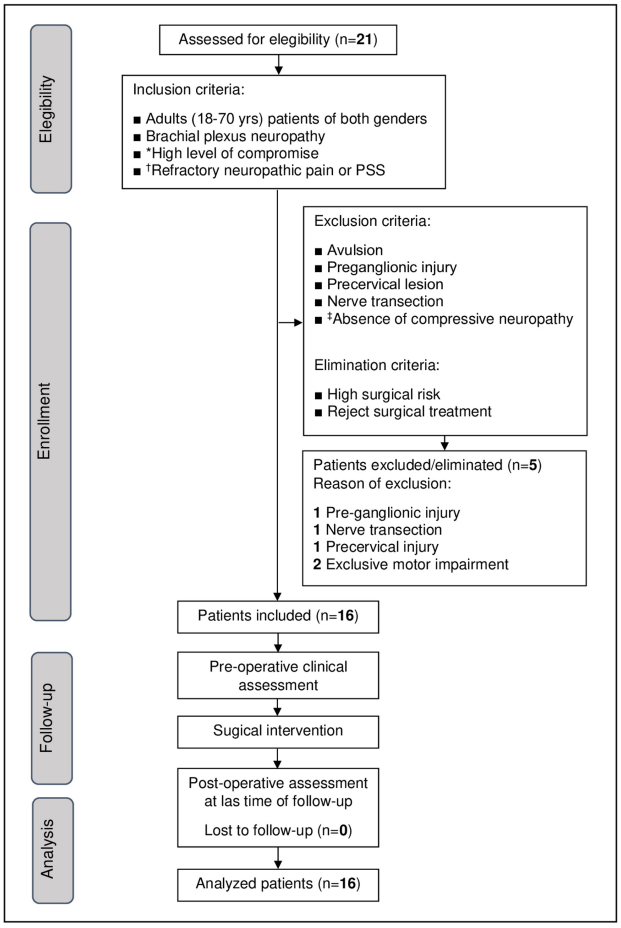

Fig. 1. CONSORT trial flow diagram. *Compromise located in the proximal third of the upper extremity (before reaching the proximal third of the humerus). †Pain or Positive sensory symptoms (PSS) refractory to medical treatment with at least 2 different analgesic drugs during three months of management. ‡Compressive origin was determined through a preoperative electromyography study determined by a neurogenic pattern with positive fibrillations, polyphasic units, and an increase of firing rate, complemented with magnetic resonance imaging, in order to identify the presence of an anatomopathological structure (bone, muscle), neoplasm (tumor) that was causing a compressive phenomenon, or the presence of inflammation/fibrosis surrounding the nerve structures.

Table 1. Sensory Frequency of Symptoms Scale (SFSS).

Items in questionnaire		Positive sensory symptom*
1.- Do you feel pins-and-needles sensation over the affected arm?		Paresthesias
2.- Do you feel abnormal sensations like skin-stiff or other indescribable sensations?		Dysesthesias
3.- Do you feel superficial pain with the air or by the clothes touching your skin?		Allodynia
If the answer for any of the previous questions was "yes", the next question was: How much time do you feel these sensations during the day?		
Frequency of symptoms (Patient answer)	Percentage (%)	Score
Never	0	0
Infrequent	<10%	1
Very frequent	11–49%	2
Most of time	50–89%	3
All the time	>90%	4

*Each symptom (paresthesias, dysesthesias, or allodynia) was defined as the presence of at least two events after BPN. Operational definition of an event: patient description of a typical symptom with at least 5 seconds long.

2.1 Data Collection

Data collection was focused on record the information of demographics, etiology, location, affected side, injury-surgery interval, follow-up, and clinical status (neuropathic pain and PSS). The clinical evaluation of the patients was focused on the collection of data corresponding to the pre-operative and postoperative status of two clinical components. It was decided to assess pain according to the visual analogue scale (VAS) [15]. Conversely, since there is no standardized scale to evaluate the frequency of how PSS manifest, such as paresthesias, dysesthesias, and allodynia, it was decided to create a new scale that allows quantifying the repercussion that these manifestations have on the patients; the Sensory Symptom Frequency Scale (SFSS). SFSS was used to determine the frequency of each PSS rating from 0 to 4, Table 1 described in detail the scale. The clinical results were evaluated at 2 moments, before surgery and at the last follow-up time of the patient (average: 41.19 $\pm$ 42.35 months).

2.2 Surgical Maneuver

Surgical approaches were performed in the supraclavicular fossa through a "L-shaped" incision on the posterior border of the sternocleidomastoid muscle and the inferior border of the clavicle. The platysma aponeurosis was lifted, subsequently, the omohyoid muscle (fundamental anatomical reference of the approach) was delimited, displacing it (without section it). Under the adipose tissue, the transverse cervical artery was identified and sectioned. Thereafter, a dissection of the anterior interscalene triangle aponeurosis was performed (preserving the phrenic nerve) without scalenectomy. Subsequently, the exposure of the upper trunk was carried out, which was displaced (superior displacement) for the exposure of the middle and lower trunks. The macroscopic appearance of the brachial plexus was dependent on the etiology. In many cases, tissue (connective, fibrous or tumor) was seen around the nerve structures. All the trunks of the brachial plexus were explored, no muscles were sectioned, and all anatomical corridors between nerves, muscles, and aponeurosis were used to perform the procedure. Not internal neurolysis were performed, only external surgical decompression was realized. This consisted in releasing the fascia, muscle, and tendon that were compressing the nerve and cutting out the scar tissue (to avoid the compressive phenomena). It was not possible to use an intraoperative electrophysiological study due to the lack of availability of equipment. The extent was determined by the compression sites observed at the time of surgery.

2.3 Statistical Analysis

Descriptive statistics were used to analyze the patients characteristics by calculating the mean and standard deviation of the demographic information and procedural factors, as well as frequencies to describe complementary characteristics (gender, mechanism of injury, location of injury, and side affected). To establish significant changes after surgery in pain and PSS, a paired Student's *t*-test and a Wilcoxon signed-rank test were performed (the choice between test's was decided based on the results of a Shapiro-Wilk test of normality) to establish the relationship between the preoperative and postoperative changes. In order to determine the magnitude of these changes, an effect of post-operative outcomes in pain and sensory components was measured, the effect was calculated using the Cohen's D test and recalculated considering the correction coefficient for small sample sizes to avoid overestimating measures. In order to establish the relationship between neuropathic pain and PSS, considering the interrelation among the different PSS (paresthesias, dysesthesias and allodynia), Spearman correlation tests were performed. Statistical comparisons of the outcomes involved were carried out using SPSS 25.0 for Windows software (SPSS, Inc., Chicago, IL, USA). A p-value < 0.05 was considered significant.

Table 2. Demographic, procedural characteristics of the included patients with brachial plexus neuropathy.

No. of patient (Gender)	Age (year)	Etiology	Location of injury	Side affected	Interval Injury-surgery (mos)	Follow-up (mos)
1 (F)	29	PT	C5-C6	L	12	24
2 (F)	62	RT	C5-T1	R	5	48
3 (M)	43	PT	C5-C6-C7	L	19	108
4 (F)	21	OTS	C7-C8-T1	L	14	12
5 (M)	20	PT	C5-T1	R	6	60
6 (M)	41	TCS	C5-T1	L	4	60
7 (M)	29	OTS	C7-C8-T1	R	10	12
8 (M)	46	OTS	C7-C8-T1	R	16	12
9 (F)	28	OTS	C7-C8-T1	R	11	36
10 (M)	35	PT	C5-T1	R	7	156
11 (F)	22	PT	C5-T1	R	9	18
12 (M)	22	PT	C5-C6	R	8	3
13 (M)	21	PT	C5-C6-C7	R	20	12
14 (M)	32	PT	C5-C6	L	6	72
15 (M)	26	PT	C5-C6-C7	R	14	24
16 (M)	28	PT	C5-C6	R	8	2
Mean $\pm$ SD	31.56 $\pm$ 11.48				10.56 $\pm$ 4.9	41.19 $\pm$ 42.35

PT, Post-traumatic; RT, Radiotherapy; OTS, Outlet thoracic syndrome; TCS, Tumor compressive syndrome.

3. Results

Sixteen patients were eligible for the study. Table 2 shows the demographic and procedural characteristics. The gender distribution was five females (31.25%) and eleven males (68.75%). The patient's age was reported from 20 to 62 years-old, with a mean of 31.56 $\pm$ 11.48 years. All of them had BPN from different etiology, where trauma was the main mechanism of neuropathy (62.5%). The main mechanism of injury was vehicular trauma (motorcycle accident) in 7 cases, followed by stab injury, industrial trauma, and hit by a vehicle (1 case each); followed by OTS (25%), tumor (6.25%), and radiotherapy injury after breast cancer management (6.25%). The most frequent location of injury was in the upper trunk C5-C6 (43.75%). The lesions predominated at the right side (68.75%), the mean interval injury-surgery was 10.56 $\pm$ 4.9 months, and the mean follow-up was 41.19 $\pm$ 42.35 months.

Clinical Outcomes

Sixteen patients were included, where 15 presented pain as the main symptom (93.75%). The clinical outcomes described by the number of patients are shown in Fig. 2. The pain was described by the patients as "electric-type", irradiated over the injured arm. One patient was managed surgically without pain but has other sensorial symptoms. Relative to pain intensity according to VAS after surgery, nine patients (56.25%) reported a decrease to grade 0, the rest of them had a decrease presented between grade 2 and 5, highlighting that all patients modified their baseline status. The mean preoperative pain intensity according to VAS goes from 8.19 $\pm$ 2.37 to 1.31 $\pm$ 1.99 after surgery, showing statistically significant clinical changes ($p < 0.00006$, Δ = 2.776) (Fig. 3A). Relative to the sensory symptoms, the patients with paresthesias decreased their symptomatology as followed: fifteen patients (93.75%) had paresthesias before surgery, and after surgery, only 1 patient presented persistence of the symptom (6.25%). The paresthesias were described predominantly in the anterior face over the injured arm, where 3 patients exhibited before surgery a score of 3; 7 patients, score 2; 5 patients, score 1; and 1 patient, score 0, according to SFSS, the surgery change the preoperative mean state of 1.75 $\pm$ 0.86, to a postoperative mean value of 0.44 $\pm$ 0.51, showing statistically significant changes ($p < 0.0001$, Δ = 1.645) (Fig. 3B). Regarding dysesthesias frequency of symptoms measure, 15 patients (93.75%) mentioned manifestations before surgery, and after surgery only 5 patients presented the symptom (31.25%). Most of the patients described this symptom as located at the anterior surface over the injured arm. Before surgery, 3 patients evidenced a score of 3; 5 patients a score of 2; 7 patients, score 1; and 1 patient, score 0 according with SFSS, that comprised a preoperative mean value of 1.56 $\pm$ 0.96. After surgery 5 patients showed a score of 1, and 11 patients presents a score of 0 according with SFSS, corresponding to a postoperative mean value of 0.31 $\pm$ 0.48, and demonstrating statistically significant changes ($p < 0.002$, Δ = 1.453) (Fig. 3C). In relation to allodynia, this symptom was presented in 7 patients before surgery (43.75%), and only 2 patients after surgery remain with symptomatology (23.57%). The mean values according with SFSS goes from 0.44 $\pm$ 0.51 preoperative to 0.13 $\pm$ 0.34 postoperative, with statistically significant changes ($p = 0.031$, $\Delta = 0.635$) (Fig. 3D).

The correlation analysis between the intensity of neuropathic pain according to VAS and the frequency of PSS according to SFSS, shows that the most considerable significant preoperative relationship was observed with pares-

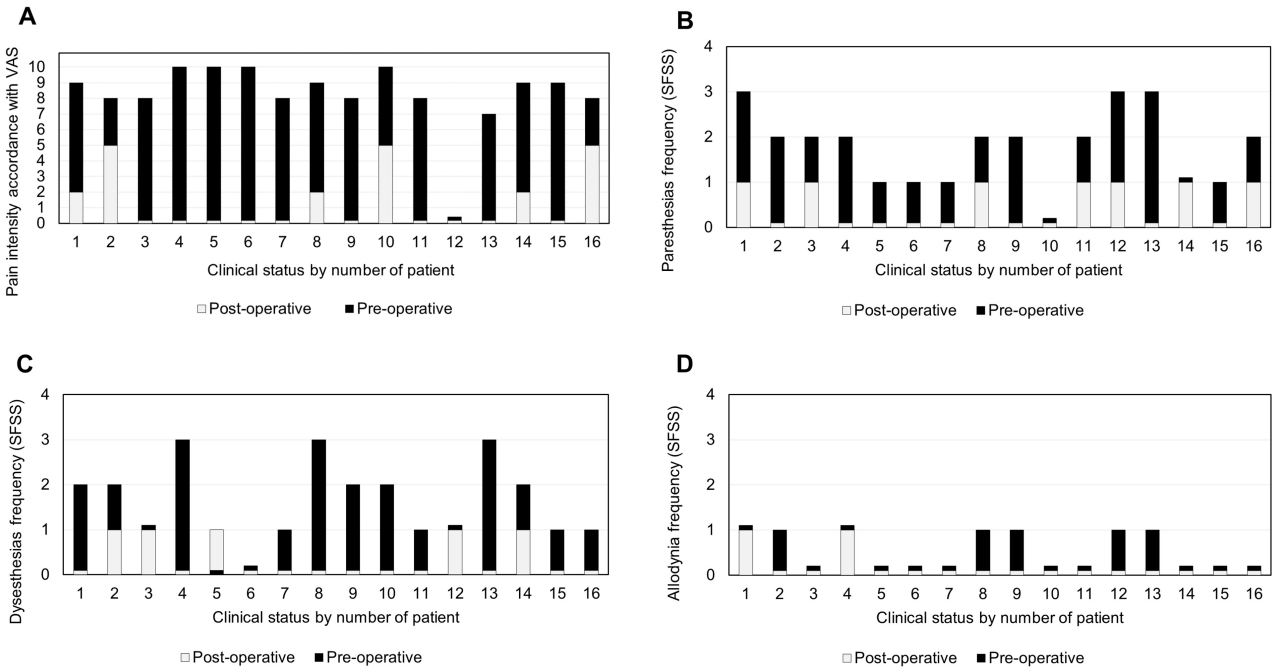

Fig. 2. Clinical outcomes per patient. (A) Pain: Shows a complete postoperative decrease in 9 patients, as well as 1 patient who did not present pain in the preoperative period, who was surgically managed because he manifested another sensory perturbation. (B) Paresthesias: Demonstrating a decrease in 93.3% of the patients who presented an alteration. (C) Dysesthesias: Highlighting that one patient with preoperative absence of manifestations showed a worsening after surgery (patient number 5). However, there was a decrease in the manifestations in 80% of the patients who presented the symptom. (D) Allodynia: Only 43.75% presented this alteration, being the more infrequent symptom, showing an improvement in only 5 of 7 patients.

thesias (R = 0.736, p = 0.001). However, there was no relationship with dysesthesias (R = 0.073, p = 0.794), and allodynia (R = 0.346, p = 0.206) (Fig. 4A–C). Regarding the postoperative analysis, the most important association was observed with paresthesias (R = 0.207) without a significant association (p = 0.457). On the other hand, the relationship between postoperative pain and interval injury-surgery showed that the decrease in pain is related to shorter intervals injury-surgery with a slight relation (R = 0.370), without statistically significant results (p = 0.174) (Fig. 4D). Regarding the analysis of the interrelation between PPS in the preoperative evaluation, shows that all PSS demonstrate a slight relationship at the preoperative evaluation (R > 0.3), where paresthesias and allodynia were the most related (R = 0.712, p = 0.002). However, the analysis of the postoperative status did not show a significant result (p > 0.05) (Fig. 5). After surgery three main surgical complications were presented by the patients; temporal paresthesia in regions of the arm (12.5%), local injury dehiscence (12.5%), and pain in the surgical site (6.25%). They were temporal and disappeared after two weeks.

4. Discussion

Surgical decompression has shown to be effective in relieving neuropathic pain and improving PSS in adult patients with BPN, neuropathic pain improved in 100% of patients who presented it, where 9 showed complete recovery (56.3%), the group that showed complete recovery from pain had a mean age of 27.89 ± 8.63 years compared with patients who did not show a complete recovery 36.29 ± 13.55, a factor that may possibly be associated. On the other hand, regarding paresthesias, 93.3% of the patients showed an improvement, whereas 56.2% of the patients showed complete recovery, similar to what was observed with the intensity of pain, highlighting one patient (number 14) who persisted with symptoms. Of those patients with paresthesias who showed complete recovery, they presented a lower mean of injury-surgery compared to the group of patients who persisted with some deficit. However, this factor may not be the one that is the most associated, because the patients did not show improvement underwent surgery 6 months after the injury. The factor possibly most associated with the decrease in paresthesias is the etiology of the injury, since the group of patients that did not show complete improvement were predominantly patients with BPN of traumatic etiology (80%). Conversely, in relation to dysesthesias, 80% of the patients showed an improvement, where 67% of the affected patients showed complete recovery, results similar to those observed with allodynia, where despite being an infrequent symptom presenting only in 43.8% of the population, there was a complete resolution

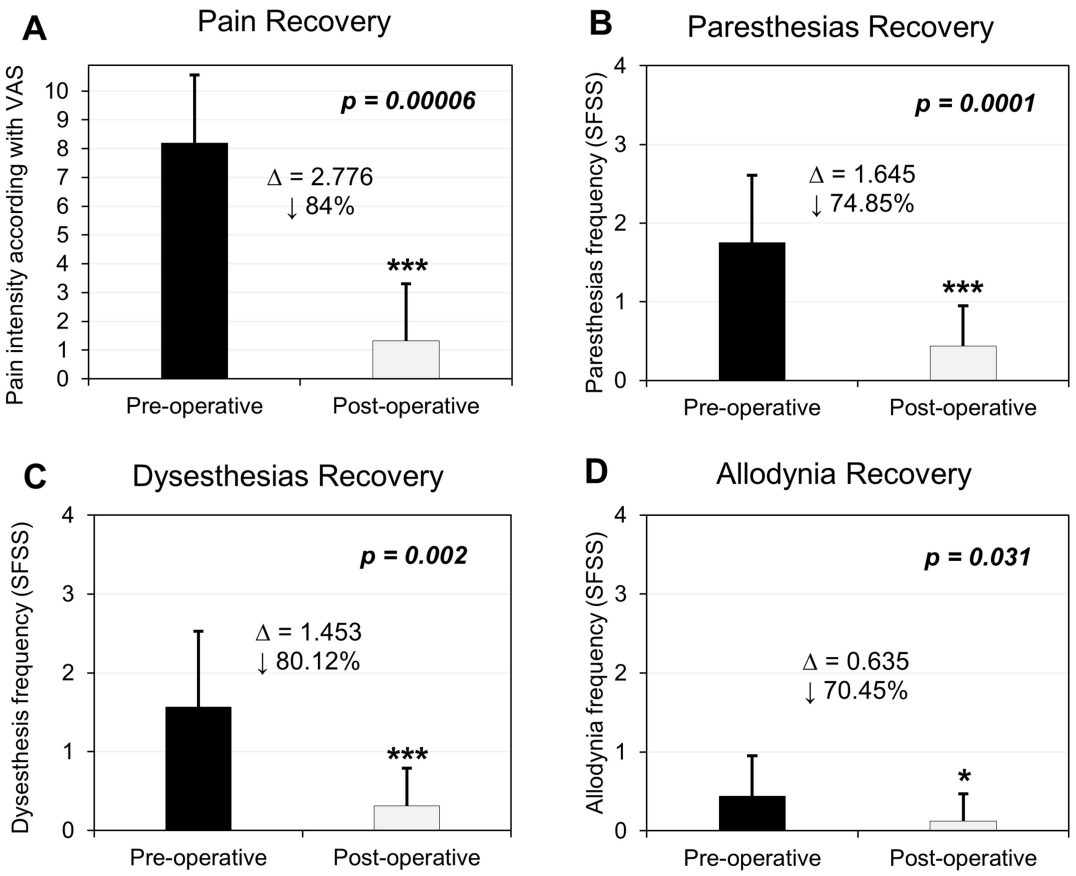

Fig. 3. Clinical outcomes. (A) Pain. (B) Paresthesias. (C) Dysesthesias. (D) Allodynia. A significant decrease was shown after surgical intervention in all components.

of 71.4% of the cases. The results show that the intervention is really useful to completely disappear the sensory alterations and the pain, allowing to decrease the alterations in more than 50% of the affected patients. On the other hand, the report published by Azmi F *et al.* [16], shows that long-term evaluation ($\geq$6 months) on pain reduction according to VAS has a greater effect compared to early evaluation, where early assessment underestimate final recovery by 18%. Results that could correlate with those of our study, since patient number 16, who is one of those whose last follow-up date is very early (3 months), shows a lower proportion of pain reduction compared to the other patients included in the analysis (Fig. 2A). Although it is true that there may be a placebo effect conditioned by surgery, this depends on the context and the type of intervention [17], so it would be worth studying the optimal time to examine patients who undergo pain surgery in BPN.

One of the most important findings of this study was the lack of relationship between PSS and pain, since these components are usually evaluated together. However, the only component that is related to pain intensity was paresthesias (R = 0.736, p = 0.001), in contrast to the other PSS that did not show a significant relationship (R $<$ 0.2, $p >$ 0.05). The observation highlights the need of analyzing these components independently. On the other hand, the interrelation between the PSS showed that most of these represented a considerable and significant relationship (Fig. 5). Nevertheless, it is clear that PSS and neuropathic pain have a relationship with a neurophysiological foundation [1]. The peripheral disorders that cause neuropathic pain involve small unmyelinated C fibers and myelinated A-fibers (Aβ and Aδ). Microneurography studies have shown that a spontaneous activity in C fibers is most closely related to pain [18]. However, Schmid AB *et al.* [19] studied animal models with nerve compression, they showed that this condition predominantly causes degeneration of small-diameter axons, where large-diameter myelinated axons show demyelination at the site of compression but remain structurally intact in variable proportions. Injury leads to imbalances between central excitatory and inhibitory signaling, associated with ectopic activity in primary afferent fibers that have a key role in the pathophysiology of pain, paresthesias, dysesthesias, and allodynia following peripheral nerve injury [9]. Therefore, the association between neuropathic pain intensity and PSS most likely depends on multiple factors, such as the type of fibers being mainly affected and the extent of the damage. For this reason, it is necessary to assess whether the extension of the damage in a

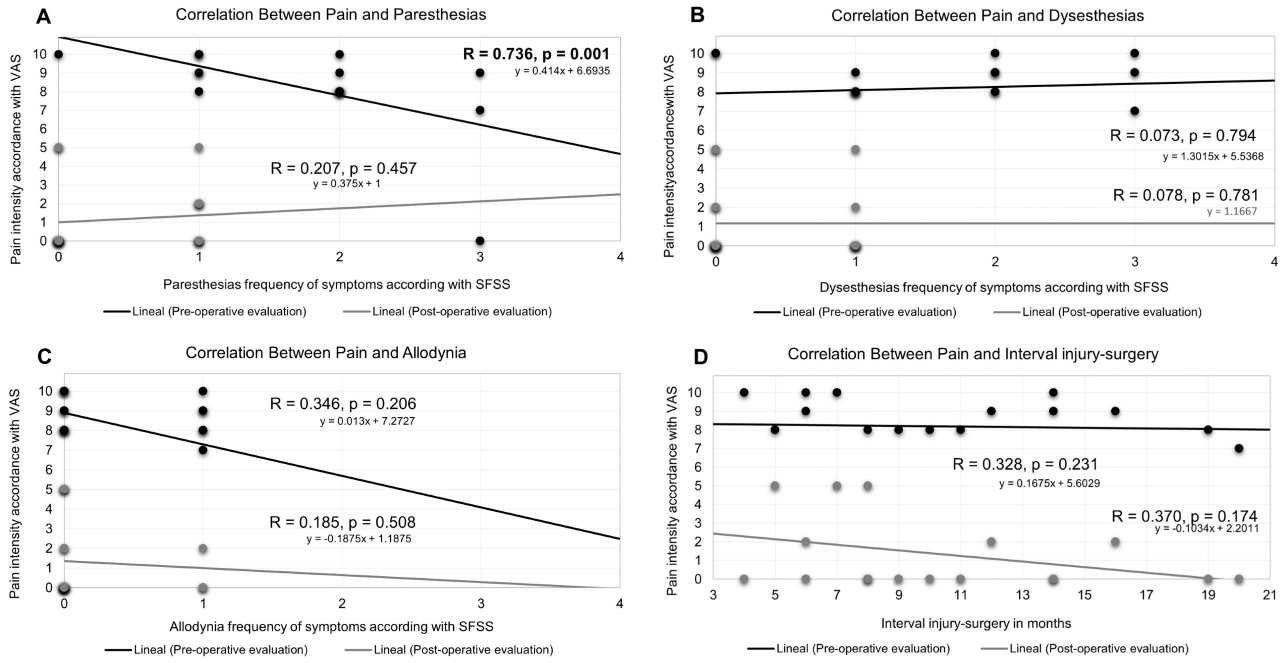

Fig. 4. Correlation between neuropathic pain components. (A–C) shows the correlation analysis between the intensity of neuropathic pain and positive sensory manifestations (paresthesias, dysesthesias, allodynia), where it is demonstrated that there is a low correlation without statistically significant changes between pain and dysesthesias and allodynia ($R < 2$, $p > 0.05$). (D) shows the relationship between pain intensity and the interval injury-surgery that represents the time of intervention, exhibits an inverse relationship between postoperative pain intensity and intervention time.

compressive neuropathy is related in some way to the type of manifestations that the patient will present and, consequently, the prognosis that the surgical intervention would have in these patients according to the severity of the injury. The absence of a relationship between neuropathic pain and PSS highlights the need to evaluate the components individually and independently of pain.

Relative to PSS, paresthesias are the clinical outcome that has been the most frequently reported in the literature related to BPN surgery, displacing and omitting the results of other outcomes such as allodynia and dysesthesias. However, despite being reported on some reports [20–22], these are not commonly reported through the use of clinimetric scales and independently of neuropathic pain, for that reason, it is not possible to clearly observe the degree of improvement that surgery offers in sensory outcomes. Axelrod DA *et al.* [20] carried out a retrospective observational study where they evaluated multiple clinical outcomes in 170 patients with OTS after surgical decompression, where they considered paresthesias, showing that there was an improvement of 81%. Unfortunately, this evaluation was done considering only the presence or absence of these manifestations, so, the assessment of the degree of improvement is not clear [20]. Another study reported by Balci AE *et al.* [21], evaluated different treatment options for BPN and their outcomes in 47 patients through the use of a scale that evaluated the impact that these manifestations had on the patient's quality of life, showing that the most frequent symptom was paresthesia (72.3%), and the presence of asymptomatic patients changed from 0% to 74.5%. However, an individualized evaluation of paresthesias was not performed, carried out in conjunction with other manifestations [21]. Guo J *et al.* [22], reported a study comparing the clinical characteristics of neuropathic pain in 30 patients with BPN before and after surgery. The evaluation of the PSS was made by breaking down these components from the Neuropathic Pain Symptom Inventory (NPSI) questionnaire, showing that the joint clinical assessment of paresthesias and dysesthesias represented a change from the preoperative mean score of 5.10 to a postoperative one of 3.65 with statistically significant changes ($p = 0.003$). Guo J *et al.*'s [22] study highlights an in-depth and clinimetric evaluation of neuropathic pain and its commonly associated symptoms (paresthesias, dysesthesias). Nevertheless, the evaluation of PSS was directly related to the presence of neuropathic pain, as an individual evaluation of each of these components was not performed [22]. The published results are related to those observed in our study, since the most frequent sensory manifestations were paresthesias and dysesthesias, manifesting in 93.75% of the patients included.

There are different scales and questionnaires that allow evaluating neuropathic pain, among the most used are The Leeds Assessment of Neuropathic Symptoms

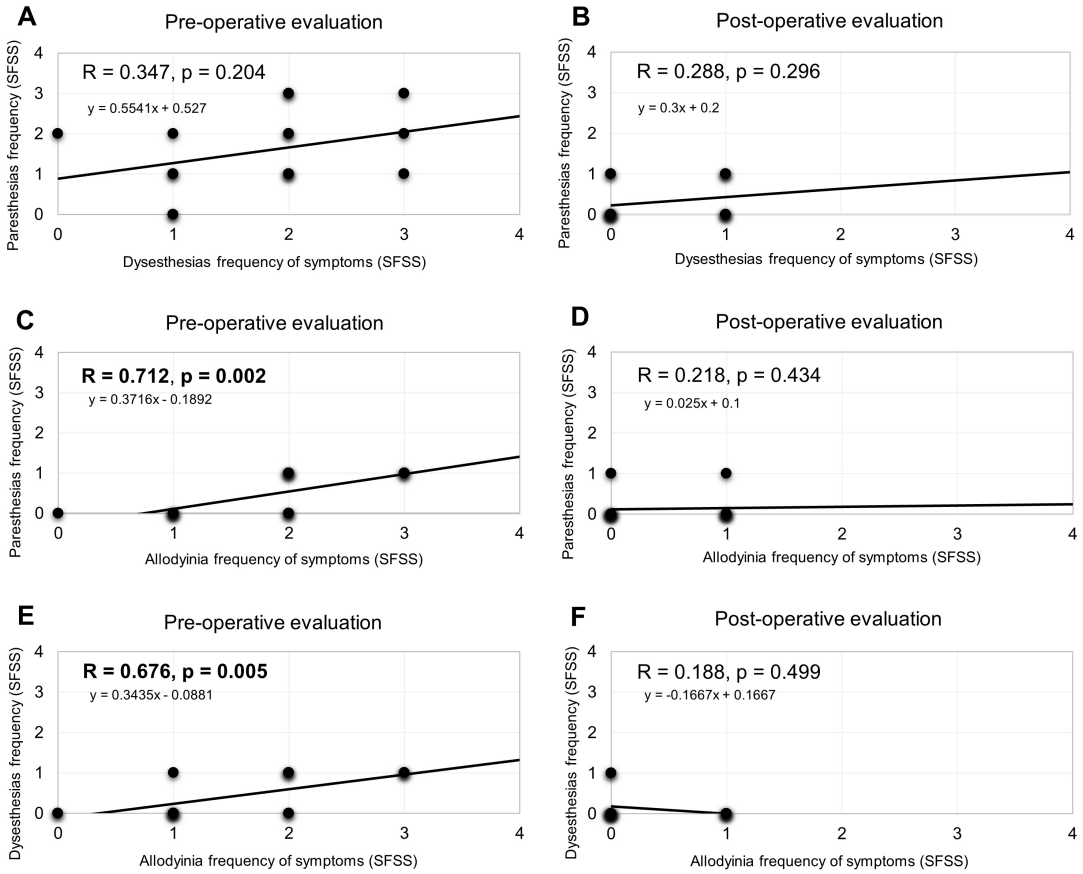

Fig. 5. Analysis of the interrelation between positive sensory manifestations. (A,C,E) preoperative assessment. (B,D,F) postoperative assessment. Highlighting the presence of a considerable preoperative relationship ($R > 5$, $p < 0.05$) in most of the sensory components, in contrast with the loss of this relationship at the postoperative moment ($R < 4$, $p > 0.05$), a result probably justified by the lack of complete resolution of the sensory components after the intervention, showing different effectiveness for each sensory symptom.

and Signs (LANSS), Douleur Neuropathique en 4 Questions (DN4), The Neuropathic Pain Questionnaire (NPQ), painDETECT, ID Pain, The Neuropathic Pain Scale (NPS), Brief Pain Inventory (BPI), NPSI, among others. According to the PSS components associated with neuropathic pain, all the questionnaires evaluate the presence of paresthesias, 4 of them evaluate the presence of allodynia (LANNS, NPQ, Pain DETECT, and ID Pain), and none of them evaluate the presence of dysesthesias [23]. PainDETECT is a self-report questionnaire really useful because it considers graded answers compared with the yes/no criteria in other questionnaires, added to the evaluation of temporal patterns. However, the questionnaire is designed to identify neuropathic components in patients with back pain and does not consider the frequency of symptoms [24]. These questionnaires are very useful and have been validated for use in multiple conditions [23,24]. Regrettably, they do not allow for an individual assessment of the impact of surgery on the frequency of sensory manifestations in BPN, so we decided to use a simple scale, which consisted of a questionnaire performed by the surgeon to assess the frequency of paresthesias, dysesthesias, and allodynia, stratifying patients on a scale from 0 to 4 (0 = no symptoms, 4 = all-time manifestations) (Table 1).

Regarding to the apparent variability of the etiologies (radiation induced BPN, post-traumatic BPN, OTS, and tumors), it is important to mention that they all converge on a similar pathophysiological mechanism [5,7]. Radiation induced BPN is a neuropathy following radiation treatment for carcinomas, involving changes in electrophysiology and histochemistry, characterized by the development of fibrosis surrounding the nerve and vessels, caused by the thickening of the endoneurium, with extensive loss of myelin, disappearance of axis cylinders, hyalinization, and obliteration of the blood vessels [25,26]. Furthermore, the origin of injury in radiotherapy has a mixed compound: axonal damage and nerve strangulation, so the surgical technique was focused on the nerve release. A process very similar to that which occurs after a traumatic event, where a compressive syndrome develops secondary to the fibrosis surrounding the neural structures, because the trauma conditions a local inflammatory process that leads to the development of fibrosis through the activation of fibroblasts, resulting in an increased collagen synthesis and accumulation of thin and

disorganized collagen fibers [27]. This fibrotic process produces a scar tissue that surrounds the affected nerve structures, generating a compressive phenomenon that results in strangulation of the nerves depriving it of blood flow; phenomenon not seen in the acute stages of radiation and trauma [4]. On the other hand, the compressive syndrome secondary to tumors or OTS is clearer, where neoplastic tissue or bone/muscle tissue trigger a compressive syndrome [7].

In relation to the operational definition of compression (defined as compressive neuropathy in the selection criteria), in terms of the upper extremity, terms related to compression in the literature are commonly referred to distal entrapments of the ulnar, radial, or median nerve [28], there is no well standardized operational definition for brachial plexus compressive neuropathy, displacing compressive syndromes that are in that region [7]. However, we consider any phenomenon of compressive neuropathy manifested electrophysiologically as a neurogenic pattern with demyelination [29,30], added to an MRI with a nerve strangulation secondary to any type of etiology (e.g., supernumerary rib, muscle inflammation, fibrosis secondary to radiation or trauma, or some type of neoplastic growth, among others), could benefit from surgical decompression. Therefore, we understand this technique as the release of the nerve from the surrounding structures.

Surgical decompression is an effective technique for pain relief in patients with post-traumatic brachial plexus injury (BPI). The management of BPI through the use of surgical decompression has been controversial, some authors affirm that it is a technique comparable to spontaneous recovery [31], because the conventional management of traumatic injuries focuses on the use of techniques such as end-to-end side suture, nerve graft, nerve transfer, and muscle/tendon transfer [11]. However, the usefulness of surgical decompression to reduce pain in patients with a chronic BPI associated with compressive neuropathy has recently been suggested, a phenomenon previously explained (development of fibrosis secondary to trauma that conditions ischemia and upregulation of inflammatory cytokines) [4,27]. The results of the studies are encouraging, showing a decrease between 59% and 78% according to the VAS scale [8,16,32], these being very similar to those observed in the present study (84%). Based on the results recently published in our last article on the use of decompression for pain relief, we decided to exclude those patients who showed signs of nerve transection in the preoperative electrophysiological analysis or during the surgical procedure [32]. Conversely, Morgan R *et al.* [8] reported motor recovery after the use of surgical decompression in trauma patients [8], these results are relevant, so we decided exclusevely to disccuss the clinical outcomes of these patients in motor terms in another article with a systematic review of the literature (on published). To sum up, we can understand that traumatic injuries with preservation of nerve continuity in a chronic period can behave like a compressive neuropathy that benefits from the use of surgical decompression.

This study presents some limitations, the main one was related to the study design, where randomization, blinding, and comparison with another standard therapeutic have not been performed. Having used a self-controlled design is very convenient because the surgical intervention totally changes the history of the disease [33], so that taking pre and postoperative evaluations allows to reliably observe the magnitude of these changes, without naturally conferring negative ethical implications that will limit the development of the study, such as using a control group to which therapeutic is not offered. It is desirable to perform a complete clinical trial with a well-randomized, and well-controlled design in order to evaluate the impact of this technique on other neuropathic pain components such as negative sensory symptoms. Furthermore, some patients presented different mechanism of injury (Postraumatic, OTS, compressive phenomena associated with tumor growth, and radiotherapy lesion). However, despite being different etiologies, they coincide in the same pathophysiological mechanism of neuropathic pain production, where there is a local inflammatory process [5], that affected nerve structures, generating a compressive phenomenon that originates strangulation of the nerves, and induces hypernociception. Regarding the compressive neuropathy diagnosis, electrodiagnosis remains the cornerstone, nerve conduction studies provide quantitative functional data that allow assessment of localization, severity, and type of nerve injury. Electromyography provides further information related to the detection of other superimposed conditions. It would have been appropriate to consider the use of ultrasound to localizing anatomic and nerve structural information [34]. However, in these patients an MRI was carried out, so the added of an ultrasound was not necessary. Moreover, early clinical assessments to establish a short-term relationship between surgery and symptom improvement has the limitation of being able to describe the results, this is because patients over/under-estimate their symptom relief while they are healing during the first few weeks after surgery [35]. Accordingly, an early evaluation was not considered in the analysis. In order to avoid this bias caused by the early recognition of the results, it was decided to consider the last time of follow-up for each of the included patients, obtaining a mean follow-up time of 41.19 months (from 2 to 156 months). In addition, regarding sensory evaluation, negative sensory symptoms were not considered from the beginning as part of the clinical analysis. However, we understand the relevance of these manifestations due to their close relationship with motor function and protection mechanism against nociceptive stimuli, so we suggest that they be considered for future studies. Finally, the sample size is relativelly small; however, a previous study perfomed a sample size calculation to evaluate the effectivenes of surgical decompression for pain relief [32], these measures were

based on the observations described by Morgan R *et al*. [8]. The analysis showed that due to the large effect of surgery (1.6), 7 patients are enough to have a statistical power of 80% (minimun required for external validity). Regardless of, we decided to define the study as an exploratory one, because the conclusions would be stronger if a larger population were available.

5. Conclusions

Surgical decompression is an effective technique for the relief of neuropathic pain and PSS in adult patients with BPN of compressive origin. Paresthesias are the sensory symptom that showed the greatest improvement, being also the most prevalent symptom and most strongly associated with pain. Conversely, no relationship was observed between the intensity of neuropathic pain and dysesthesias/allodynia. Therefore, during the clinical evaluation, they should be considered as independent manifestations, highlighting the need to validate new scales that allow assessing the repercussion that PSS independently of neuropathic pain have in the patient's outcomes.

Author Contributions

AIG and AA wrote the manuscript with support from LG and JDC. AIG and JDC conceived and presented the idea. AA performed the analysis and measurements. JLN and MAE verified the analytical methods and contributed to the interpretation of the results. JDC supervised the project. All authors discussed the results and contributed to the final manuscript.

Ethics Approval and Consent to Participate

The study protocol was approved by the Ethics Committee (Institutional Number: DI/16/403/03/152) and was conducted in accordance with the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

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