ORIGINAL PAPERS

Predictive Factors in Compressive Neuropathies Treatment Outcome

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Abstract

Nerve entrapment syndromes in the upper extremity represent a common occurrence, but in many cases these are not correctly diagnosed, leading to severe complications. Carpal tunnel syndrome is the most frequent compressive syndrome. The promptitude in establishing a correct diagnosis and initiating an adequate treatment is essential in reducing the morbidity associated with nerve compression in upper limb, improving the quality of life of the patient and also ensuring a faster socio-professional reinsertion. Nerve lesions demonstrate a variable evolution, with different recovery and prognosis. We developed a prospective clinical study with the aim to evaluate a series of patient characteristics that influence the disease evolution and may serve as predictive factors for treatment outcome in compressive neuropathies. Further manipulation of those parameters may direct our therapeutic strategies for obtain a maximal functional recovery, the supreme desiderate in peripheral nerves pathology.

Keywords: compressive neuropathies/ nerve entrapment syndromes; risk factors; quality of life; socio-professional reinsertion

Rezumat

Neuropatiile compresive la nivelul membrului superior apar frecvent în rândul populației, însă în multe cazuri acestea nu sunt corect diagnosticate, ajungându-se la complicații severe. Cea mai frecvent întâlnită neuropatie compresivă este sindromul de canal carpian. În sindroamele de compresie nervoasă la nivelul membrului superior, promptitudinea în diagnosticarea corectă a afecțiunii și inițierea tratamentului adecvat sunt esențiale în reducerea morbidității, îmbunătățirea calității vieții pacientului și reinserția socio-profesională rapidă a acestuia. Leziunile nervoase pot prezenta evoluție diferită la fiecare pacient, cu rată de recuperare si prognostic variabile. Am desfășurat un studiu clinic prospectiv cu scopul de a evalua diferite caracteristici ale pacienților ce pot să influențeze evoluția afecțiunii și pot constitui factori predictivi ai rezultatului terapeutic în neuropatiile compresive. Controlul acestor parametri poate ghida strategia terapeutică în vederea obținerii unei recuperări funcționale maximale, dezideratul suprem în patologia nervilor periferici.

Cuvinte cheie: neuropatii compresive/sindroame de compresie nervoasă, factori de risc, calitatea vieții, reinserție socio-profesională.

OVERVIEW OF NERVE ENTRAPMENT SYNDROMES IN UPPER LIMB

Peripheral nerve damage may lead to substantial morbidity, and the costs associated with these conditions can be elevated for both the individual and society.

Nerve entrapment syndromes represent a common occurrence, but sometimes are not correctly diagnosed. They appear more frequently and are better known in upper limb. Carpal tunnel syndrome has the higher prevalence, of 3.72% in USA[1].

Compression of median, ulnar or radial nerve in the upper limb may appear in some specific anatomic areas, determining a series of nerve entrapment syndromes with particular manifestations. The anatomic compression sites are presented in Table 1[2, 3]:

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Table 1.

Nerve	Sites of Compression
Median	The ligament of Struthers The bicipital bursa Abnormal arteries and muscles (Gantzer's muscle, accessory FPL muscle) Pronator syndrome Anterior interosseous nerve syndrome Carpal tunnel
Ulnar	The arcade of Struthers The medial inter-muscular septum The medial epicondyle The cubital tunnel The deep flexor aponeurosis Guyon's Canal
Radial	Spiral Groove of Humerus Radial tunnel syndrome Posterior interosseous nerve compression Compression of the superficial radial nerve: Wartenberg syndrome

The clinical manifestations encountered in patients with chronic compression of a nerve are variable, denoting a large spectrum of histopathological modifications affecting nerve structure[3]. In compressive syndromes, pressure increase in the anatomic compartment that includes the nerve, altering the neural microvasculature with subsequent ischemia. Persistent nerve compression leads to inflammatory process, fibrosis, and severe alteration like demyelization and axonal loss[1,2].

Compressive neuropathy represents a chronic problem that goes progressive trough various stages, correlating symptoms, clinical and histopathology findings as we can see in Figure 1[3]:

The main entrapment syndromes encountered in upper limb, with their clinical findings and paraclinical relevant tests are synthesized in Table 2[3-5]:

Functional recovery following a nerve injury is variable and is considered to be primarily dependent on the severity of the lesion, the ability of nerve regeneration and preservation of motor end-plates[6,7].

Sometimes, lesions that appear to have similar severity demonstrate a variable evolution, with different recovery and prognosis.

Currently, there is no unanimous accepted evaluation method for accurate determine the prognosis after compression neuropathies. Physical evaluation alone is inappropriate, resulting in incomplete overview of nervous lesion.

Always we need to keep in mind the possibility of double-crush injury, relating cervical spine dysfunction and distal compression like carpal tunnel syndrome; all compression sites must be carefully examined and treatment should be addressed to all affected areas[3,8].

It is mandatory to reveal all the parameters that influence the impact of the disease on quality of life, psychosocial and professional environment, routine activities, as it is well known the severe morbidity associated with neglected nervous pathology.

The promptitude in establishing a correct diagnosis and initiating an adequate treatment is essential for reduce the morbidity associated with nerve compression,

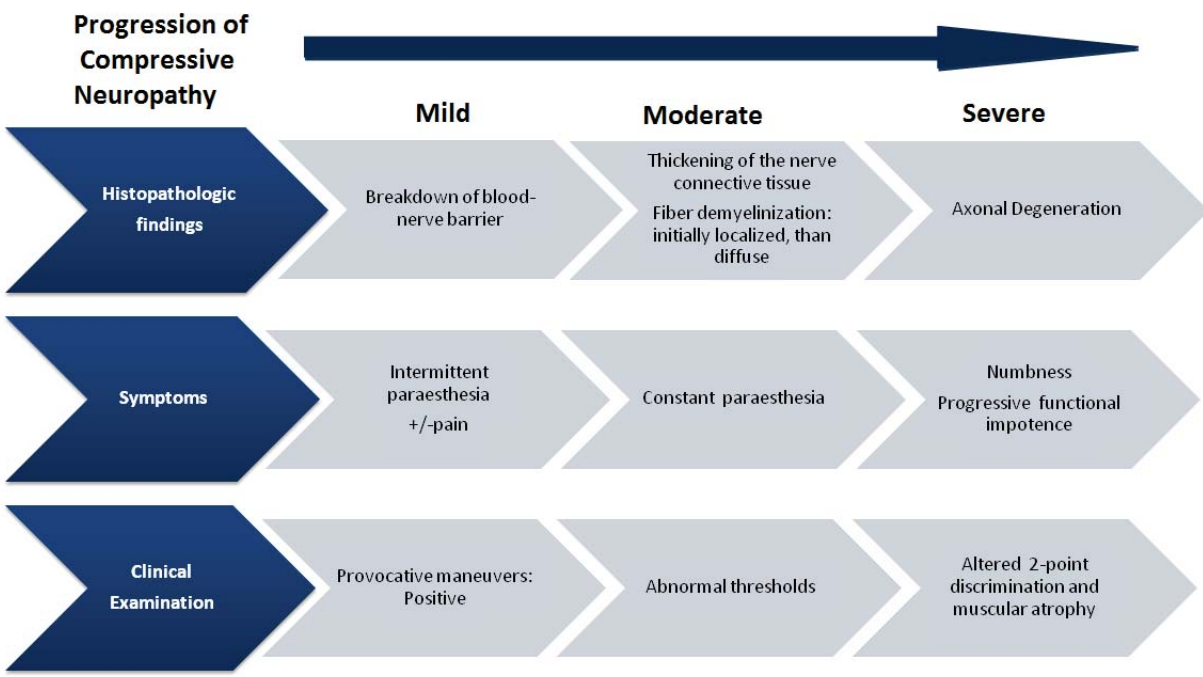


Figure 1.

Table 2.

Nerve	Median			Ulnar		Radial	
Syndromes	**Pronator**	**Anterior interoseous nerve**	**Carpal tunnel**	**Cubital Tunnel**	**Guyon's Canal**	**Posterior iterosseous nerve**	**Wartenberg's**
Sensitive	proximal forearm pain; paresthesia; hypoesthesia over pronator teres and hand median nerve distribution	unaffected	pain (worse at night), paresthesia over hand median nerve distribution triggered by sustained wrist flexion and extension	pain and paresthesia over forearm and hand ulnar nerve distribution, atrophy (late sign)	wrist, hand ulnar nerve distribution pain and paresthesia - zone I & III conpresion	pain and paresthesia during movement at the elbow radiating distally to the dorsal hand	pain and numbness at dorsal radial aspect of distal forearm and hand
Motor	weakness FPL and FDP	weak/loss of function of the FPL, index/middle FDP and pronator quadratus	weakness of thumb opposition, thenar eminence atrophy (late sign)	loss of hand dexterity	decreased grip strenght - zone I & II compression	decreased grip strenght; loss of thumb and finger extension, hand radial deviation during wrist extension	
Clinical signs	Tinel + over the pronator teres	Pinch deformity (inability to make "OK" sign)	Phalen's test and Tinel sign +; Durkan's compression test	Tinel and compression testing ovet the cubital tunnel; elbow flexion and scratch collapse tests; Duchenne's, Masse's, Watenberg's, Froment¦s and Jeanne's signs	Allen test for potential ulnar artery thrombosis	Middle finger test: pain over ECRB during extension of the middle finger, with the elbow fully extende	+Tinel's sign over radial styloid process
Electrodiagnostic	not very helpful for pronator syndrome	useful in diagnosis	increased sensitive and motor nerve conduction velocities (>3.5; >4.5 ms)	helpful – motor conduction velocity less than 50 m/s	can help to determine zone of injury	EMG testing is helpful both to confirm the diagnosis and monitor motor recovery	testing is of limited value
Other diagnosic tools				radiography (elbow arthritis, instability, posttraumatic deformity), ultrasound	CT and MRI for boney (hook of hamate fracture) and soft-tissue pathology	Ultrasound and MRI evaluation of soft-tissue masses and operative planning	

improving the quality of life of the patient and also a faster socio-professional reinsertion.

Therapeutic approach includes both surgical and non-surgical methods, with the final aim of regaining limb function, with minimum morbidity and costs and ensuring a rapid socio-professional reinsertion.

OUR CLINICAL EXPERIENCE

Aim

The primary aim of this study was to evaluate a series of factors encountered in our patients with compressive neuropathy diagnosis and establish their potential role in predict the treatment outcome. Based on relevant results, further treatment strategies may be approached, in order to reduce the morbidity associated with nerve compression, increase the quality of life for an optimal functional recovery and socio-professional reinsertion.

Material and methods

We analyzed patient admissions in Plastic Surgery Clinic of Bucharest Emergency Clinical Hospital between June 2014 – March 2016: from 6987 admissions 113 (1.62%) were compressive neuropathies diagnostics. The patients were invited to participate in a more elaborate study (including specific questionnaires, detailed physical and paraclinical examination) in order to establish the potential prognostic factors in compressive neuropathy outcome. From all 113 patients with compressive neuropathies, 76 were enrolled in the study, after their inform consent (the rest refused the participation or they were not available to fulfill all steps included in the study).

In our patients, positive diagnostic was based on clinical examination and confirmed by electro-diagnostic studies. All 76 patients included in the study benefited of surgical treatment, with open surgical techniques. Postoperatively, patients were referred to rehabilitation medicine department and they were included in a follow-up program.

The data were exported from hospital's eHealth program (Hipocrate), centralized in Excel and analyzed using SPSS statistic software.

The socio-demographic data of the patients were analyzed using descriptive statistics and analysis of the correlations between their characteristics. Differences were studied using the chi-square test, with a series of variables: residence area, gender, level of education, professional activity.

The homogeneity of our study group was evaluated regarding the presence of smoking, the practice of sporting activities, the repetitive activities, the dominance of the damage, also using the chi-square test.

Average values, standard deviations as well as the maximum and minimum of the value series were determined for all continuous-type quantitative variables. Outliers were removed. We studied the distributions of continuous quantitative variables like age, height, conduction velocity, motor speeds, sensory latencies and further we tested the data distribution using the Kolmogorov-Smirnov test.

The Gaussian normal distribution of data recommended the use of parametric tests for comparison (student *t* test), and non-Gaussian distribution recommended the use of non-parametric tests (Kruskal-Wallis test, Welch's *t* test). The comparison was made regarding multiple parameters: gender, residence environment, severity of the disease, existence of repetitive activities, affected side and compressed nerve.

We analyzed also the correlations between the indicators of the quality of life and the other variables collected, using the Spearman coefficient.

The quality of life determinants were: number of days/week when analgesics are administered, the degree of self-perceived discomfort, the number of nights when the patient wakes up from sleep due to pain.

The importance of predictors for "days of analgesic use" and the "degree of discomfort" was studied, using the multivariate linear regression for the variables correlated with the dependent variables that were studied.

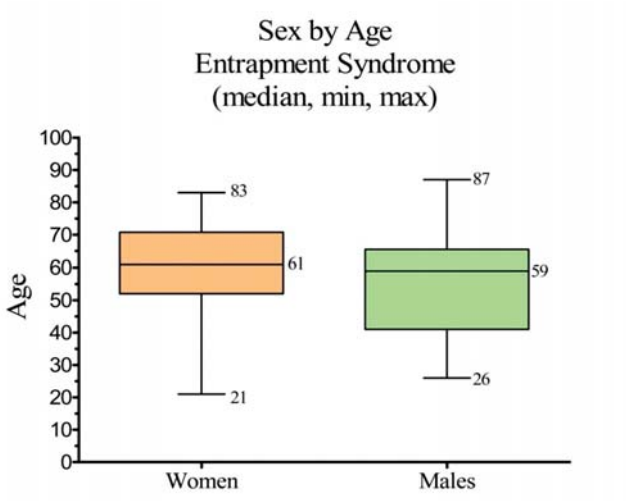
The method of selection of the predictor analysis model was Forward Stepwise, an accuracy of 57.9% adjusted R square = 0.579 for the number of "days of analgesic use" and an accuracy of 44.8% adjusted R square = 0.448 for the "degree of discomfort" felt.

The threshold of statistical significance was 0.05.

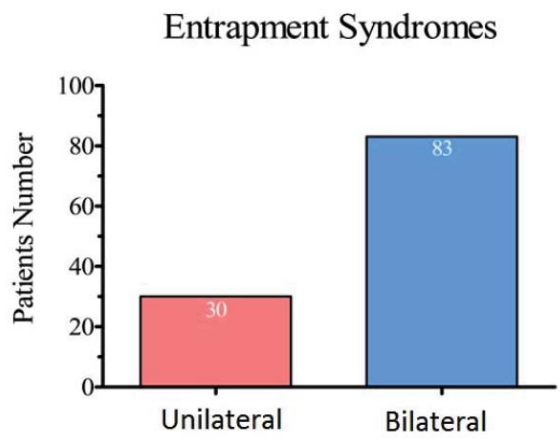
RESULTS

For all 113 patients admitted with compressive neuropathy diagnosis, only general data, available in eHealth program were processed, with following results:

- From 113 patients, 80 were females (median age = 61, min = 21, max = 83) and 33 males (median = 59, min = 26, max = 87) as we can observe in Graphic 1:
- Distribution of compressive neuropathies identified in the studied group shows a predominance of carpal tunnel syndrome in this pathology, followed by cubital tunel syndrome (Graphic 2):



Graphic 1.

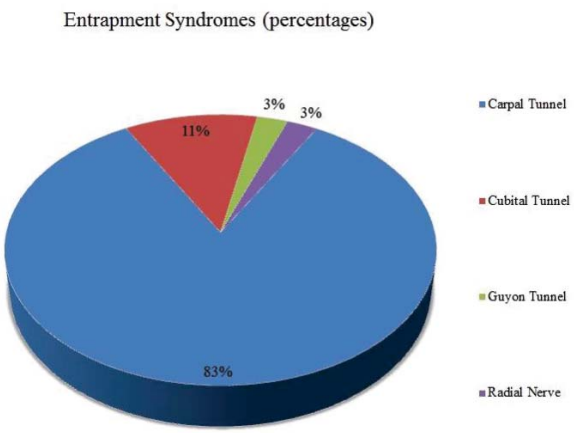


Graphic 3.

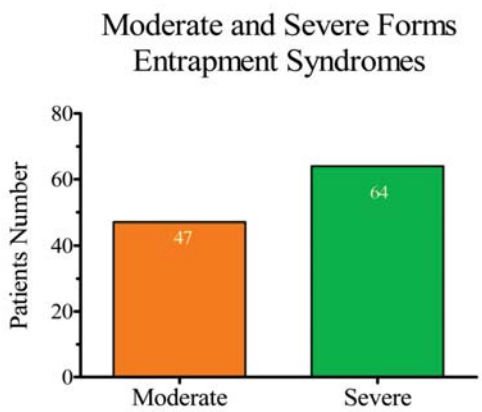
- The bilateral presentations (83) were more frequent than unilateral one's (30) as we can see in Graphic 3:
- The severe presentations (64 patients) were more frequent than moderate one's, encountered in 47 patients (Graphic 4):

As we mentioned, in 76 patients, included in our study, a more elaborate evaluation protocol was applied, with the following results:

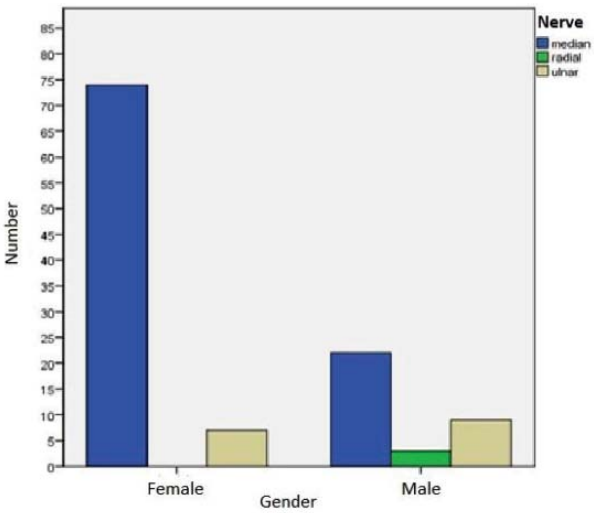
- The studied population has a significantly different gender distribution, 69.7% being female and 30.3% male patients (p = 0.001).
- The median nerve (81.6%) is predominantly affected than the ulnar (14.5%) and radial (3.9%) nerves (statistically significant finding, p <0.001).
- The studied population is significantly differently affected, depending on patient gender (p = 0.0003) as we can see in Graphic 5:
- People with residence in rural areas (25%) were significantly less than urban residents (75%) (p <0.001).
- The frequency of retired persons (31 persons) is significantly higher than those who have another situation: 25 employees, 15 without occupation or unemployed, 5 others (p <0.001).
- The distribution of our patients by the educational level(illustrated in Graphic 6) is significantly different (p = 0.001).
- Right-side impairment (55.3%) is statistically significant more frequent in the study population (p <0.001)



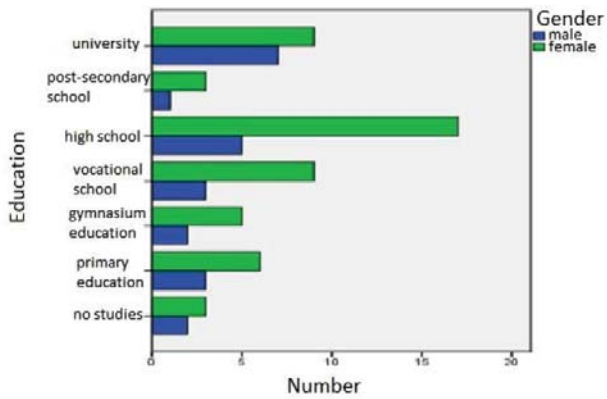
Graphic 3.



Graphic 4.

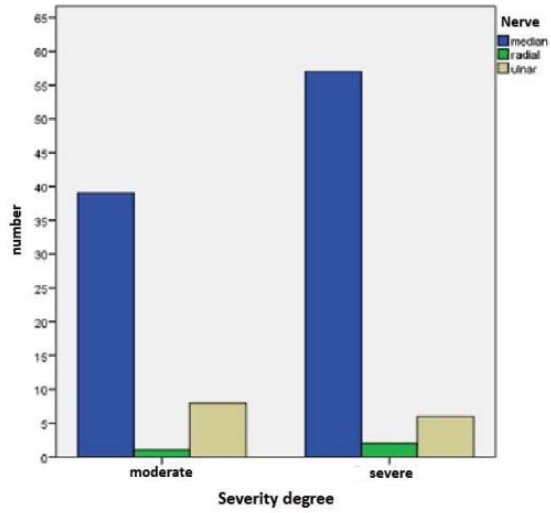


Graphic 5.



Graphic 6.

- The frequency of smokers (48.7%) is insignificantly lower than that of non-smokers (51.3%) (p = 0.909)
- Only 6 of the 76 participants in the study are engaged in sports activity, therefore sport practice occurs with very low frequency in our group (p <0.001)



Graphic 7.

- Patients that perform repetitive activities (47.4%) are found to have similar probability as those who do not perform such movements (52.6%) (p = 0.731)
- There is no statistically significant difference between each nerve involvement and the severity degree of the entrapment syndrome (p = 0.616) - Graphic 7:

In our study, from 76 patients, 63 were diagnosed with carpal tunnel syndrome. In these patients we identified a series of potential risk factors as follows (Table 3):

From all the 27 patients with arterial hypertension, 25 followed an anti-hypertensive treatment, 15 of them taking beta blockers agents; 4 patients stopped the beta blockers administration and they noticed a benefic effect in reducing of symptoms in upper limb.

Nerve conduction velocities and motor latencies were compared with those of the healthy upper limb or, in the case of patients with bilateral entrapment syndromes, with the less affected side. For the statistical analysis of the difference between the nervous con-

Table 3.

Number of risk factors	Risk factors encountered	Number of patients
No risk factors	–	13
One risk factors	Arterial hypertension	7
	Menopause	11
	Hypothyroidism	2
	Cervical spondylosis	5
	Rheumatoid arthritis	3
	Obesity	2
Multiple risk factors	Associating pathologies as: arterial hypertension, diabetes mellitus, obesity, menopause, hysterectomy, thyroid pathology, rheumatoid arthritis, cervical spondylosis	20

duction velocities between the healthy upper limb and the affected one, we used the Mann-Whitney test, which revealed delayed conduction speeds on the affected side. We considered abnormal a distal latency greater than 4.4 ms.

In our group we had a significant presence of people without professional activity (43 patients), followed by profession with light physical activities in 20 patients and 13 heavy workers. In order to evaluate postoperatively the prehensile force, we analyzed only the patients with professional activity (33 patients), performing any work, simple or complex. We observed that heavy workers (13 patients) regained more difficult the prehensile force. Also those patients returned slower (around 8 weeks) to light daily activity in comparison with the 20 patients that usually performed this kind of easier work level (they return to work in around 3 weeks). The whole working group had an average period of postoperative inactivity of about 3 weeks (range between 1-10 weeks).

The full-time return to the work performed preoperatively was also slower in heavy workers(around 6 weeks, range between 1-15 weeks) than in patients performing lighter activities.

There is no statistic significance in terms of surgical treatment performed and the recovery of prehensile force, but we observed that patients undergoing additional surgical procedures returned later to their work.

Regarding quality of life alteration, we analyzed the correlation between the predictive factors and parameters like discomfort described by patient, number of days/week of analgesic used and night awakening from sleep by pain.

- We didn't find any significant correlation between the predictive factors and discomfort felt by the patient.
- Regarding analgesic use and different predictive factors correlation we conclude:
  - Gender (Spearman coefficient=0.417, p <0.001): female gender is associated with higher consumption of analgesics.
  - Residence (-0.375, p = 0.001): urban residence is associated with higher consumption of analgesics.
  - Education (0.298, p = 0.009): higher education level is associated with higher consumption of analgesics.
  - Nerve (0.356, p = 0.002): median nerve compression is associated with a higher number of analgesic consumption days.
  - Diagnosis (-0,315, p = 0,006): Carpal tunnel syndrome is correlated with higher analgesic consumption.
  - Uni- or bilateral involvement (0.278, p = 0.015): bilateral impairment is associated with a higher analgesic consumption.
  - Smoking (0.327, p = 0.004): Tobacco consumption is associated with fewer days consuming analgesics.
  - Discomfort (0,354, p = 0,002): higher analgesic consumption in patients with higher discomfort.
  - Antihypertensive therapy (-0,306, p = 0,007): antihypertensive use increases the number of days with analgesics.
  - Waking up in the night due to pain (-0,462, p <0,001): awakening from sleep due to pain increases the consumption of analgesics.
- We analyzed the correlation between patient's night awakening from sleep by pain and the predictive factors, with following results:
  - Gender (-0.334, p = 0.003): higher rate of awakening do to pain in female patients.
  - Nerve (-0.365, p = 0.001): median nerve entrapment is associated with higher awakening episodes.
  - Diagnosis (0.311, p = 0.007): awakening is more frequent in carpal tunnel syndrome.
  - Severity (-0.234, p = 0.044): awakening by pain correlates with severe impairment.
  - Uni-or bilateral involvement (-0.260, p = 0.024): awakening is more frequently encountered in bilateral cases.
  - Dominant versus non-dominant hand(0.315, p = 0.006): awakening occurs especially in those with predominant affection in the right hand.
  - Smoking (-0.360, p = 0.002): awakening appears especially in non-smokers.
  - Sport practice (-0.242, p = 0.037): patients who do not practice a sport activity are more exposed to awakening by pain.
  - Discomfort (-0,359, p = 0,002): patients awake episode are worse as the degree of discomfort increases.
  - Driving (-0,290, p = 0,012): patients who do not drive wake up more due to pain.
  - The Phalen test (0.431, p <0.001): a positive Phalen test is associated with awakening by pain.

DISCUSSIONS

Within the presented study, we carefully analyzed a series of factors incriminated in influence of the patient recovery prognostic in compressive neuropathies.

In our selected study group, women patients were more predisposed to compressive neuropathies.

Average age of patients at the time of initial diagnosis was 56 years (an interval between 21 and 87 years), with 62 patients having right hand as dominant, the rest of 14 been left-handed.

The most frequent compressive neuropathy encountered in our group was carpal tunnel syndrome followed by ulnar nerve compression at elbow level.

A Mayo Clinic study reported in the literature shown carpal tunnel syndrome a gender ratio of 3:1, female patients being third time more affected than men, a higher incidence in elderly male patients and a peak of these pathology at age 45–54 in women[9].

Only a quarter of patients have residence in rural areas, but we noticed that rural provenience along with lower education level and less addressability to specialized medical assistance determine a delayed and defective diagnosis and poor quality socio-professional rehabilitation and reintegration.

The diagnosis of certitude for most nerve compressions consists of clinical presentation orientation, confirmed by electrophysiological studies. Nerve conduction studies have high specificity but are not diagnoses in 10-25% of cases of clinically obvious carpal tunnel syndromes. New diagnostic techniques approaching a 98% sensitivity are reported but are not yet widespread-peripheral nerve ultrasonography is a promising method of diagnosis for compressive neuropathies, and in particular for carpal tunnel syndrome[10-12].

In the large majority of the cases, the etiology is not known. One patient with carpal tunnel syndrome presented a palmar tumor mass, with the resolution of symptoms after tumor excision; a 21 years old woman patient was admitted for a post-traumatic compressive neuropathy of ulnar nerve at elbow level and she had a poor prognosis; in 2 patients with radial nerve compression etiology was specific - a forearm tumor determining compression of sensitive branch of radial nerve, with complete recovery after tumor excision in one patient and a post-traumatic radial nerve compression with incomplete postoperative recovery in the other patient.

Besides these situations, other compression mechanisms were noticed intra-operatively: narrow anatomical structures like fibro-osseous tunnels, presence of aberrant muscles, distal musculo-tendinous junction in carpal tunnel, synovial thickness, amyloidal deposit, osteophytes.

In literature, a large series of situations are described to predispose patients to compression neuropathies in the upper extremity: inflammatory pathology of soft tissues, synovitis, autoimmune diseases, hypothyroidism, diabetes, alcoholism, pregnancy[13].

There is no uniform conclusion between association of smoking and compressive neuropathies and also the same situation is encountered when analyzing sedentarism as potential risk factor in this pathology.

Beta-blockers are incriminated for having an unfavorable effect in nerve entrapment syndromes, increasing symptoms level in carpal tunnel syndrome, with amelioration when beta-blocker therapy was ceased[14,15]. We noticed this association also in our group of patients.

Repetitive daily activities aggravate the symptoms in 36 of our patients. Only six patients practiced a sport activity, in consequence aerobic effort cannot be considered aggravating factor in our study.

It is difficult to establish an accurate correlation between physical activity while working and symptom occurrence in entrapment syndromes, due to limitation of a good analysis in terms of type and frequency of repetitive or specific movements[16].

We didn't find a statistic correlation between the onset of the symptoms and the duration of work activity. Some patients experienced severe symptoms in less than one year after onset of work, while others had symptoms for more than ten years.

Improvement of clinical status, trough decreasing of symptoms occurred after approximately 2 weeks postoperatively. Follow-up period varied between 3 and 35 weeks, with an average of 11 weeks. We noticed a difficult adherence in follow-up program in patients from rural areas and with low educational level.

Amelioration of quality of life was objected by a the degree of postoperative discomfort which decreased significantly in all patients, by decreasing the number of hours when patients had difficulty working, through the use of analgesics that was reduced to the minimum, by the fact that all operative patients did not wake up in the night because of pain.

Young patients with bilateral upper limb impairment and describing pain as central symptom had poor recovery prognostic, without full recovery of nervous function and consequent delayed return to work and difficult socio-professional reinsertion. These patients

also often associate myofascial painful syndromes multi-level compressive neuropathies and obesity.

We also experienced poor prognosis in patients with compressive neuropathies and other soft tissue lesions (tendinitis, myofascial inflammatory syndromes, trauma, etc.) in which pain persisted, they continued analgesics administration and socio-professional reintegration was delayed and incomplete.

The postoperative prognosis was generally satisfactory and we advised all patients to return to their daily activities and also professional attributions as quickly as possible, especially where there is a good collaboration between the employee and the employer. Theoretically, analgesic consumption is no longer needed after around 3 days postoperatively, driving the car is also allowed, except for patients wearing gypsum immobilization or splints for a longer period.

Interdisciplinary collaboration represents an important aspect in compressive neuropathies therapeutic management, knowing that various medical conditions and personal factors, including diabetes, hypothyroidism, alcoholism, obesity, and smoking are associated with nervous affection. The interdisciplinary collaboration between plastic surgeon-neurologist/neurosurgeon - diabetologist - rheumatologist is mandatory for an accurate differential diagnosis with other neurological pathologies, with similar symptoms that do not benefit from surgical treatment.

CONCLUSIONS

The incidence of the nerve compression syndromes increased recently, driving the clinicians to a close interdisciplinary collaboration for correct management of each case.

Without an adequate treatment, started early in evolution of the disease, the long-term prognosis is poor, associated with nerve damage and significant morbidity. The remission of symptoms and functional recovery in nerve pathology are mandatory to ensure a rapid socio-professional reintegration and restoration of adequate quality of life in our patients.

Therefore, we consider extremely important to highlight this complex pathology characterized by multiple etiological factors, with numerous clinical syndromes and a variable response to treatment and subsequent different long-term outcomes.

Key points for obtain better results in patients suffering from compressive neuropathies are: early diagnosis, accurate determination of the operative moment and the therapeutic procedures, the sustained medical rehabilitation program, identification of prognostic predictors with focus on reducing risk factors and a well-established program of long-term follow-up.

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