Balneo and PRM Research Journal
English Edition
e ISSN 2734 - 8458 p ISSN 2734 - 844X ROMANIAN ASSOCIATION OF BALNEOLOGY

Research article

Study on evaluation of the sensitivity and specificity of the electrophysiological parameters LD and AR in carpal tunnel syndrome

Lenuța Bîrsanu [1], Roxana Covali [2], Andrei Ionuț Cucu [3,4], Amelian Mădălin Bobu [5], Ioana Păvăleanu [6], Robert-Constantin Anicăi [7], Alin Ciubotaru [8,9,*] and Mihaela-Dana Turliuc [3,10]

1 Doctoral School of Medicine and Pharmacy, University "Grigore T. Popa" University of Medicine and Pharmacy, 700115 Iași, Romania;
2 Department of Radiology, Biomedical Engineering Faculty, "Grigore T. Popa" University of Medicine and Pharmacy, 700115 Iași, Romania;
3 Department of Neurosurgery I, "Prof. Dr. N. Oblu" Clinical Emergency Hospital, Ateneului 2, 700309 Iași, Romania
4 Faculty of Medicine and Biological Sciences, University Stefan cel Mare of Suceava, 720229 Suceava, Romania
5 Department of Cardiology, Sf. Spiridon Hospital, 700111, Iași, Romania;
6 Mother and Child Department, "Grigore T. Popa" University of Medicine and Pharmacy, 700115 Iași, Romania;
7 University of Medicine and Pharmacy "Grigore.T.Popa" Iasi, Romania;
8 Department of Neurology, "Grigore T. Popa" University of Medicine and Pharmacy, 700115 Iași, Romania;
9 Department of Neurology, Rehabilitation Hospital, 700661 Iași, Romania
10 Department of Surgery II, "Grigore T. Popa" University of Medicine and Pharmacy, Universității 16, 700115 Iași, Romania;
* Correspondence: Alin Ciubotaru, alinciubotaru94@yahoo.com

Citation: Bîrsanu L., Covali R., Cucu A.I., Bobu A.M., Păvăleanu I., Anicăi R.C., Ciubotaru A., Turliuc M.D. - Study on evaluation of the sensitivity and specificity of the parameters electrophysiological parameters ID and AR in carpal tunel syndome
Balneo and PRM Research Journal **2025**, *16(1): 768*

Academic Editor(s):
Constantin Munteanu

Reviewer Officer:
Viorela Bembea

Production Officer:
Camil Filimon

Received: 23.12.2024
Published: 31.03.2025

Reviewers:
Mihai Hoteteu
Andrei Iordan

Publisher's Note: Balneo and PRM Research Journal stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Abstract: The study introduces the 2LIO test as a novel diagnostic tool for assessing carpal tunnel syndrome (CTS) severity by combining distal motor latency (DML) differences and the amplitude ratio (AR) of interosseous and lumbrical muscles. This retrospective cohort study included 264 patients grouped by CTS severity, highlighting the demographic and clinical features of each group. The mean age varied slightly across groups, with a notable female predominance. The 2LIO test demonstrated high diagnostic accuracy, with sensitivity and specificity of 93.3% and 97.7%, respectively, surpassing traditional methods like distal latency (AUC 0.600). Notably, the AR parameter achieved an exceptional area under the curve (AUC) of 0.971, signifying its robust sensitivity and specificity as a marker for CTS progression. AR showed the strongest predictive value for severe CTS progression (Exp(B) = 189.586), while occupational stress and age were significant risk factors for disease worsening. Negative correlations between moderate and severe CTS groups suggest timely intervention during moderate impairment can delay progression. Logistic regression validated the 2LIO test as a sensitive and cost-effective alternative to nerve conduction studies and imaging. While limitations, such as a modest sample size, are acknowledged, the 2LIO test offers promise in guiding earlier interventions and optimizing care. Further studies with larger cohorts and consideration of comorbidities are recommended to generalize findings and enhance clinical applications.

Keywords: Carpal Tunnel Syndrome; Distal Motor Latency; Amplitude Ratio; Diagnostic Accuracy; 2LIO Test; Disease Severity

1. Introduction

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy, affecting approximately 0.1-1% of the general population []. CTS is a compressive neuropathy of the median nerve at the carpal tunnel leading to sensory and motor disturbances in the median nerve distribution. Symptoms that can be commonly seen in the clinical presentation of patients with CTS are numbness, tingling, pain, and paresthesias within the median nerve distribution, especially at night.

Other presenting complaints that patients may present with are dropping objects or difficulty performing fine motor skills [2]. In more advanced stages, patients present with thumb weakness and thenar muscle atrophy [3]. Diagnosis and management of CTS are necessary due to its clinical and economic burden [4].

According to previous studies, clinical examination tests for diagnosing CTS can be divided into four major categories: 1) provocative maneuvers (e.g., Phalen test, Tinel sign), 2) sensory and motor tests (e.g., two-point discrimination, Thenar weakness test), 3) diagnostic scales (e.g., CTS-6) and questionnaires (e.g., Kamath and Stothard questionnaire), and 4) hand symptom charts/maps (Katz and Stirrat HSD) [5].

Several diagnostic methods are used to assess median nerve damage in CTS, each with its own set of advantages and disadvantages. Nerve conduction studies (NCS) have been considered the gold standard for diagnosing CTS, providing objective measures of median nerve function. However, NCSs have limitations, including invasiveness, patient discomfort, and the potential for false-negative results [6].

In addition, NCSs have been reported to have the highest sensitivity (94%) but the lowest specificity (50%) of all diagnostic tests. Ultrasonography (US) has emerged as a valuable tool for the assessment of median nerve injury in CTS. US offers several advantages over NCS, including that it is non-invasive, allows dynamic assessment, and provides visualization of anatomical structures in the carpal tunnel [6]. Various US parameters have been investigated for their diagnostic accuracy in CTS, including median nerve cross-sectional area (CSA) [7].

The use of US for diagnosing CTS has been shown to be a more cost-effective strategy than electrophysiologic studies alone [8]. Magnetic resonance imaging (MRI) has also been explored for its potential to assess median nerve damage in CTS. MRI provides detailed images of the median nerve and surrounding structures, helping to identify anatomic abnormalities and space-occupying lesions. However, MRI has limitations, including cost, availability, and contraindications for patients with certain medical implants [9].

Clinical examination findings, such as the Phalen's test, Tinel's sign, and Durkan's test, have traditionally been used to evaluate CTS [10]. While these tests can provide valuable information, their diagnostic accuracy varies and may not be sufficient on their own to establish a definitive diagnosis of CTS [11]. In addition to the methods mentioned above, several clinical diagnostic tools have been developed to aid in the diagnosis of CTS.   The study did not analyze data from MRI or ultrasonographic imaging studies on the extent of CTS damage.

Aim of the study

The 2LIO test presents a promising new diagnostic tool for assessing median nerve injury in CTS by combining electrophysiologic parameters from routine nerve conduction studies. It evaluates the difference in distal motor latencies (DML) between the median and ulnar nerves and incorporates the ratio of 2 interosseous to 2 lumbrical amplitudes, enhancing sensitivity and specificity.

Compared to imaging techniques like US and MRI, the 2LIO test offers advantages in affordability, accessibility, and objectivity. By providing a comprehensive assessment of motor nerve function, it represents a valuable alternative to clinical examination and patient-reported outcomes, contributing to improved diagnosis and severity assessment in CTS.

Objectives

The main objective of this new test is to improve diagnostic accuracy and sensitivity in identifying CTS severity, particularly in cases where conventional nerve conduction studies may be inconclusive. By incorporating both DML and the ratio of interosseous to lumbrical amplitudes, the 2LIO test attempts to capture a broader spectrum of motor nerve dysfunction, which could lead to an earlier and more accurate diagnosis of CTS.

The present study explores the diagnostic accuracy of the 2LIO test in a group of patients with CTS and compares its performance with that of other diagnostic tests already available. The outcome of this study could be quite significant, with possible clinical implications by providing a new tool for clinicians in assessing the severity of median nerve damage during CTS and thereby guiding subsequent treatment approaches.

2. Results

This Demographic characteristics of the "normal" study group

The mean age of the study group is 47.03 years and the median is 47 years, the two variables are almost identical, which shows a relatively symmetric distribution of the age variable. The standard deviation is 10.82, this value suggests a moderate variability of the ages. The minimum and maximum values ranged from 26 to 69 indicating a wide age range. The study group is dominantly female which could influence the statistical analysis of the results and hypotheses tested, Table 1.

Table 1. General characteristics of the variables age, sex and occupation in the study group of normal group

		Age	Sex
Mean		47.03	1.20
Median		47.00	1.00
Std. Deviation		10.820	.406
Kurtosis		-.451	.297
Std. Error of Kurtosis		.613	.613
Minimum		26	1
Maximum		69	2
Percentile	25	38.00	1.00
	50	47.00	1.00
	75	54.00	1.00

Gender frequency regarding the distribution of women-men for all the studied groups, a number of 47 women 62.7% and 12 men 16% was identified, respectively, the distribution in this case is not a normal one, but without having a statistically significant impact, Table 2.

Table.2 Male-female ratio in the study group

		Frequency	Percentage
Valid cases	Females	47	62.7
	Male	12	16.0
	Total	59	78.7

Demographic characteristics of the "mild, moderate and severe" study group

Mild impairment group: the mean age is 52.81 years, the median of the group is 52, the two statistical indicators are clinically correlated, thus the data presented confirm a symmetrical distribution of the data. The standard deviation is 8.91 which suggests a moderate degree of variability for the age criterion.

Regarding the variable gender: the mean is 1.05, and the minimum variability (standard deviation = 0.228) suggests that the majority of individuals in this study group is predominantly female.

Variable on type of occupation: a mean of 1.11 was noted for those performing manual labor or mechanical stress, suggesting that the majority of individuals who fall into a particular occupational category, are predicted to correlate with their falling into a particular risk category.

The set of variables analyzing the general characteristics of the group studying the moderate impairment, it was observed that the mean age is 54.49 years and the standard deviation is 8.01 which suggests a slightly lower variability of age compared to the mild impairment group.

Demographic analysis of sex variable: shows a mean of 1.09 with female predominance but with a slightly higher variability compared to mild group. For the type of occupation: a mean of 1.19 was shown, and for the non-manual labor group the data are not statistically significant, but an almost normal distribution of occupational categories is present.

The last category represented by the severe type of impairment showed a mean age of 56.14, representing the group of individuals with the oldest age group, in this case the standard deviation was 9.07, suggesting a higher variability for the age criterion compared to the moderate group.

The gender variable, also within this group the female gender also predominates, this being constant for all study groups. In terms of occupation type, the occupation type is similar to the moderate group, figure 1.

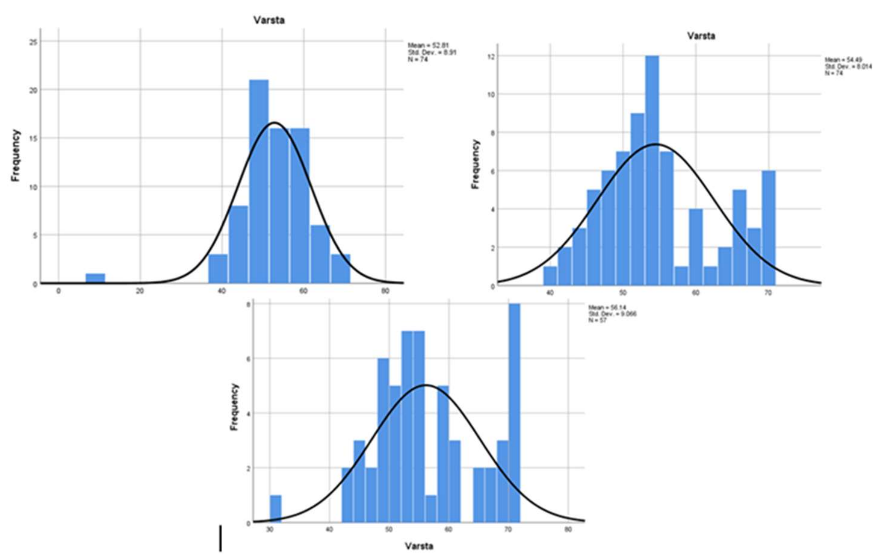

Fig.1 Histogram of age distribution in the study group in the following order: mild, moderate, severe

Spearman correlation coefficient analysis

The results of the correlations between the "normal" type of impairment and the other variables analyzed in the Spearman correlation model showed $r= -0.345$, $p=0.007$, which indicates a moderate but negative correlation between the "normal" and "easy" type of impairment. And as the 'normal' affection type increases, the 'easy' type tends to decrease.

The set of correlations involving the 'moderate' type of impairment in relation to the 'severe' type: r=-0.274, p<0.05, a weak but negative type correlation with the 'severe' type was revealed. As the 'moderate' type increases, the 'severe' type tends to decrease slightly. Most variables show weak correlations between each other, suggesting little or no monotonic relationship.

Interpretation of significant correlations:

-The negative relationship between normal and mild impairment type suggests that higher scores in the "normal" type are associated with lower scores in the "mild" type, which could indicate a possible bias between these variables, a possible explanation of the heterogeneity of the study groups;

-low but negative correlation between moderate and severe type of impairment is due to the fact that these 2 variables are inversely related in terms of type of impairment in the CTS,.

The model summary on the binary logistic regression revealed the following: the "Log-likelihood -2" is 39.768, which indicates a good fit of the variables tested, and with respect to the indicators "Cox & Snell model" $R2$=0.556 and "Nagelkerke" R2 =0.751, these suggest a strong model fit, which confirms the clinical validity of the variables tested, Table 8.

Table 8. Static analysis on the degree of validity of the developed model

Model summary			
Pas	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	39.768[a]	.556	.751

Contingency rank analysis for Hosmer and Lemeshow test, this indicator compares the observed and expected frequencies for each decile, more precisely each variable can be any of the 9 values that divide the analyzed data in 10 equal ways, whereas each part will represent 1/10 of the data sample studied in relation to the type of probabilities expected and categorized according to the levels of a dependent variable "Severity Score = 1", namely the group that had a value of less than 3 on the AR ratio in the electrophysiological test and respectively "Severity Score = 2" for the group that had a value of this score greater than 3. The observed and predicted numbers appear to be close for some groups, but differ substantially relative to others, but these contribute significantly to the validation of the Hosmer and Lemeshow test,.

In Table 10, the classification of the severity of the RA ratio according to the following values <3 low risk ("severity score 1"), > high risk ("severity score 2") in relation to the need for surgical intervention as an early treatment method is represented. The results of this analysis demonstrated that this model is able to correctly classify about 95.9% of the cases analyzed on the basis of a value that represents in statistical terms the "cut-of" calculated at a level of evidence of <0.5.

The degree of sensitivity (rate of true/concrete positive results) is 93.3% of the cases that were classified as severe "Severity score = 1", so in this situation the degree on the prediction mode can be considered valid. With regard to the analysis of the degree of specificity (true negative/false positive rate), the results of this analysis revealed that 97.7% of the cases in which "Severity score = 2" were correctly predicted, considerably reducing the risk of a systematic type of confounding bias error. In conclusion, the interpretation of these results highlights a very high classification accuracy of the data.

Table 10. Sensitivity and specificity analysis of the predictive logistic regression model

Observed		Preconized		
		Severity score		Percentage corrected
		1	2	
Severity score	1	28	2	93.3
	2	1	43	97.7
General procent				95.9

Correlation Matrix analysis for the following set of variables: age, gender, moderate type of impairment

Table 11 shows the analysis of the correlation matrix coefficients for the type of variables included in the logistic regression model. Thus, for the variables age and occupation a negative correlation was obtained, but of strong type (R-0.717), while for the variables age and moderate type of impairment a negative correlation was observed (-0.244), and for the variables sex and moderate type a positive correlation was obtained (0. 312). In this case, for the variable "age" and "occupation" a negative but high type of correlation is present (R-0.717), which is why the 2 markers may become prognostic factors in the clinical course of CTS for the moderate type of affectation. For the parameters classifying the moderate type LD and AR, they show positive but moderate type correlations with all other variables tested.

Table 11. Correlation Matrix coefficient analysis

		Constant	Age	Sex	Ocupation	LD	AR
	Constant	1.000	-.397	.003	.017	-.271	-.735
	Age	-.397	1.000	-.246	-.717	-.244	-.049
	Sex	.003	-.246	1.000	.198	.012	-.309
	Ocupation	.017	-.717	.198	1.000	.273	.117
	LD	-.271	-.244	.012	.273	1.000	.154
	AR	-.735	-.049	-.309	.117	.154	1.000

Analysis of the coefficient "Exp(B)", or the "ods ratio", which represents the expected change in this indicator in relation to the unit and uniform type increase of the predictor, in this case being "severity type 1/2".

The results of the statistical analysis in the present case emphasize that for the AR variable it is statistically significant with $p = 0.001$, suggesting a predictive influence of strong type. However, for all the other predictors (age, sex, occupation, LD) remain statistically insignificant at $p > 0.05$, for this type of indicator.

Interpretation of the ods ratio (Exp(B)) revealed the following for the AR parameter: Exp(B) = 189.586, which demonstrates that a unit increase in the AR indicator will lead to a significant increase in the odds of CTS progression, indirectly the need for surgery will be early. Regarding the variable "age": Exp(B) = 1.022, which emphasizes that it exerts a negligible effect on the odds, but is insignificant from a statistical point of view.

Type of occupation is considered to be an aggravating marker of the clinical evolution of CTS, the following results were obtained: Exp(B) = 1.437, which determines a slight increase in the odds of clinical worsening of CTS, more precisely in the category with moderate type of impairment. For the variable LD: Exp(B) = 1.829 showed an increase in the odds regarding the prediction of the exposed event within the objectives of this study, Table 12.

Table 12. Exp(B) coefficient analysis in relation to age, sex, occupation, LD and AR

		B	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
						Superior	Inferior
	Age	.021	1	.771	1.022	.884	1.181
	Sex	-2.041	1	.249	.130	.004	4.168
	Ocupation	.362	1	.791	1.437	.098	20.995
	LD	.604	1	.258	1.829	.643	5.201
	AR	5.245	1	.000	189.586	13.979	2571.257
	Constant	-16.649	1	.001	.000		

Multinomial logistic regression model of variables analyzing age, sex, occupation, LD, RA, Bland Scale in relation to "severity score 1/2"

The multinomial logistic regression multinomial logistic regression model analysis had as reference variable analyzing "severity score 1/2", it represents the dependent variable and the other variables included in the model are reported in relation to it. The statistical analysis uses a binomial probability distribution model, which illustrates that this model refers to binary outcomes (e.g. "severity score 1/2").

Corrected Akaike Adjusted Akaike Statistic Indicator (AIC): 6.782, this value suggests that a lower AIC indicates a better fitting and generalizable model. With respect to the Bayesian indicator (BIC): 9.030, in this case a lower BIC was obtained which indicates that the model is a sensitive model and consists of a good model fit, Table 13.

Table 13. Summary of the multinomial linear regression model

" severity score 1/2"		Variables tested
Measuring level		Biominal
Probability distribution		Log
Criterion	Akaike Corrected	6.782
	Bayesian	9.030

Analysis regarding the classification for the whole study group of the "severity score 1/2" obtained an overall percentage of 59.5% for all observed cases in the moed (predicted/observed), in conclusion this model predicts for 59.5% of cases the possibility that this study group may require earlier treatment for CTS, Table 14.

Table 14. Classification of cases on the estimation of risk of CTS progression

" severity score 1/2"		Preconized	
		1	2
1	severity score 1	0	30
	% Observed	0.0%	100.0%
2	severity score 2	0	44
	% Observed	0.0%	100.0%

Figure 3 illustrates the Fixed Coefficients statistical analysis, which is intended to demonstrate the causal relationship of a cut-of type variable with other variables in a model. In this case being the "severity score 1/2" type in correlation with a series of dependent variables such as: age, sex, occupation, LD and AR indicators. The "Intercept" indicator from a statistical point of view represents the reference point of this model in this situation regarding the "severity score 1/2".

In this case the "Intercept" has a negative value, which suggests that in the absence of other predictor variables, the log odds of the outcome (target variable), more precisely of the "severity score 1/2" are negative, and the corroboration of the results of these variables shows that they are dependent on each other. The analysis of the "Predictor" indicator, which in this case is also the "severity score 1/2", in the histogram of the superimposed type a distribution curve is shown in which the data are normal.

In conclusion, the predictor also holds a negative type estimate of the analyzed coefficient, as illustrated by the blue color. A negative coefficient highlights the fact that as the "severity score 1/2" decreases, the probability of the event tends to decrease, which shows that a value of less than 3 of this score is a protective factor.

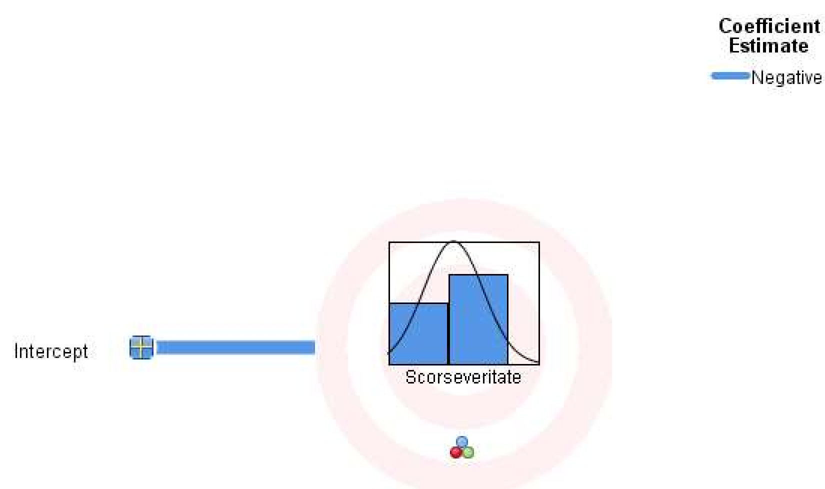

Fig 3. Graphical representation of the model called "Fixed Coefficients"

Sensitivity analysis of the variables age, sex, occupation, LD and AR in order to identify the appropriate timing of the type of treatment for the group with moderate type of impairment by means of ROC analysis. The analysis of the degree of sensitivity and specificity of the variables age, sex, occupation of the LD and AR indicators, reported according to the following cut-of: "severity score 1/2", this ROC curve demonstrates that the variables mentioned above are associated with AR, thus this electrophysiologic parameter can be considered a sensitive and specific marker in monitoring the severity of the disease evolution in this group of patients, or the negative influence that it may have on the therapeutic conduct, Figure 4.

On the other hand, a low to moderate level of sesnibility of the LD parameter was observed, and no statistically significant values were found for the other variables in the ROC function, Figure 4.

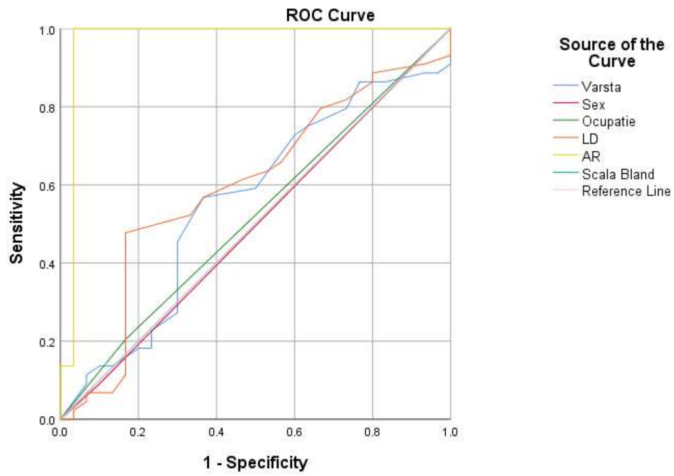

Fig.4 ROC curve in relation to age, sex, occupation, LD and AR indicator as a function of "severity score 1/2"

The analysis of the area under the curve (AUC) revealed that among the series of variables tested, a high degree of specificity and statistically significant sensitivity was identified only for the parameter AR AUC:0.971 and for the LD test AUC: 0.600. Thus a high degree of sensitivity and very high specificity was detected only for the AR parameter, its application in clinical practice in the process of monitoring the clinical evolution for this category of patients represents an effective method, Table 15.

Table 15. Values obtained from the ROC analysis on the evaluation of the sensitivity of the "severity score 1/2"

Aria under the curve					
Tested variable	Aria	Std. Error[a]	Asymptomatic Sig.[b]	Confidence interval 95% asymptomatic	
				Lower limit	Upper limit
Age	.556	.069	.412	.421	.692
Sex	.495	.069	.947	.360	.630
Ocupation	.519	.068	.783	.385	.653
LD	.600	.069	.162	.462	.731
AR	.971	.028	.000	.916	1.000
Scala Bland	.500	.069	1.000	.365	.635

Univariate Cox regression analysis on the prediction of CTS progression between age criteria in relation to "severity score 1/2" of RA

This graph represents a Kaplan-Meier survival curve, the aim of applying this statistical method was to emphasize the degree of cumulative survival over time, thus on the Y-axis is represented the probability of cumulative survival, the range is from 1 which represents 100% survival.

The X-axis depicts time, in this case age, illustrated by a stepped curve starting at 1.0, this as it decreases over time, demonstrates that the probability of survival decreases as age tends to increase. From a statistical point of view, each 'downward step' describes an event, such as death or the risk of an event, while the 'flat portions' indicate periods when no event occurred. With respect to the results of the present curve it can be observed that initially, survival remains stable, exemplified by the flat line, approximately until around age 45. But after the age of 45, this phenomenon of decreasing survival appears, but it is slightly progressive.

Whereas by around the age of 70, the cumulative survival decreases to about 20%, indicating significant morbidity or the occurrence of a major disabling event with a major impact on survival. In conclusion, this graph emphasizes that this survival pattern shows that the probability of death remains low at the onset of the disease, but decreases slightly to moderately with age, Figure 5.

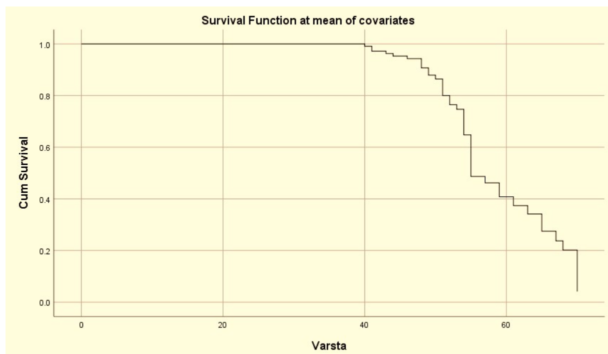

Fig.5 Impact on survival of age in relation to "severity score 1/2" of RA

Figure 6 plots the hazard ratio function of the variable "age" on the x-axis and the cumulative hazard function is depicted on the y-axis. The graphical interpretation of the Cumulative Hazard function shows that as the patient advances in age the risk of occurrence or occurrence of the event indicates an increasing risk with increasing age, thus the age criterion can be considered as a risk factor for the group of patients with moderate CTS. The graphical analysis shows a noticeable increase in the cumulative hazard ratio after the age of 65-70 years, suggesting a higher risk, which suggests this age group being the most at risk. This graph is useful as it helps to identify trends in the risk of the event by age. Recommended medical intervention should focus on individuals over 65 years of age, where the cumulative risk increases sharply.

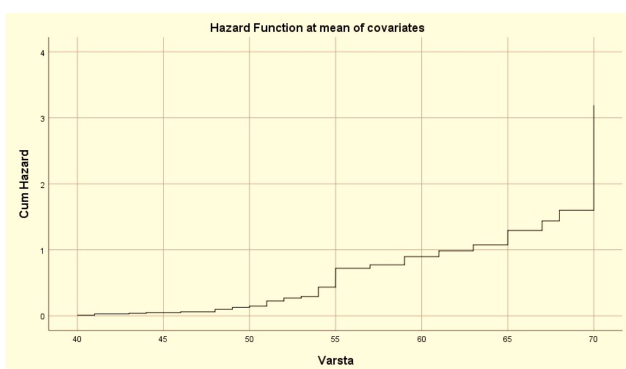

Fig 6. Estimation of the risk of occurrence of the event using the Hazard function

Results of statistical processing of the "Kaiser-Meyer-Olkin - Measure of Sampling Adequacy", "Bartlett's Test of Sphericity" on the statistical validation of the prognostic model for moderate type of STC. The result of the analysis in the present study showed for the "Kaiser-Meyer-Olkin" indicator a value of 0.500, this result illustrates that the validity of the factors introduced in the study: age, gender, electrophysiological parameters LD and AR, as well as the "severity score 1/2" show statistically adequate values regarding the clinical validity of the proposed algorithm for the diagnosis of the moderate form.

The results of the "Bartlett's Test of Sphericity" analysis obtained a statistical significance level p=0.0001, this value emphasizes that the above listed parameters show a high degree of sensitivity in establishing the therapeutic and diagnostic behavior of the moderate type of CTS, in conclusion, this proposed algorithm is clinically and paraclinically valid.

Discussion

The design of utility and performance studies for diagnostic tests follows key steps, including identifying relevant pathological factors, analyzing clinical and paraclinical signs, selecting an appropriate study type, and applying statistical analysis. This study employed a retrospective cohort approach with 264 individuals, of whom 74 formed the main study group.

To validate a diagnostic tool, it must be sensitive and specific enough to confirm or rule out a condition, as demonstrated in this study's evaluation of electrodiagnostic and clinical tests for moderate CTS. The proposed algorithm helps prevent neuromotor disability, excludes unnecessary therapeutic interventions like surgical decompression, and supports patient monitoring and screening, given CTS's high prevalence.

Recent advancements highlight the role of artificial intelligence in CTS diagnosis. Elseddik et al. tested AI-driven machine learning and deep learning models, achieving superior diagnostic accuracy (0.969%) compared to traditional methods. The most reliable results were obtained at six months, demonstrating AI's potential in clinical practice to improve efficiency, reduce costs, and minimize invasive procedures. [12].

Currently, there is no consensus or precise recommendations for using artificial intelligence in diagnosing specific diseases, requiring larger cohort studies to validate its sensitivity and specificity.

Our study is clinically valuable for managing moderate CTS, but future trials could explore the correlation between clinical and AI-based testing, as both methods may complement each other.

CTS diagnoses are often insufficiently documented, leading to treatment failures. Electrodiagnostic studies remain the gold standard for diagnosis and disease monitoring, as nerve conduction studies provide objective evidence of CTS. Without such measurements, misdiagnosis and inappropriate treatment may occur, potentially causing severe consequences for patients [13].

For a more sensitive and specific CTS diagnosis, consistent data and standardized clinical tests—such as the Semmes-Weinstein monofilament test, vibration threshold assessment, and pain provocation tests—are essential. Using validated diagnostic methods improves the therapeutic process and ensures accuracy [13].

A standardized protocol for diagnosing, monitoring, and predicting CTS progression would help eliminate inconsistencies, misdiagnoses, and unnecessary testing.

In contrast, inaccurate methods like thermography have shown limited reliability. Bargiel et al. found that dynamic thermography did not improve pain control post-surgery, highlighting the need for better standardization due to its low sensitivity and limited clinical value.[14].

Avoiding unnecessary and costly diagnostic methods that may misguide clinical decisions is essential in CTS management.

Spearman correlation analysis revealed an inverse relationship between moderate and severe CTS cases. This suggests that for moderate cases, the need for surgical treatment is uncertain, whereas for severe cases, surgery is a priority. Given the unpredictable progression from moderate to severe CTS, standardizing treatment decisions for moderate cases is crucial to prevent severe functional impairment.

Delays in diagnosis can lead to ineffective treatment, especially for manual laborers. Various studies, including Hernández-Secorún et al., have used the Spearman correlation to assess treatment effects and quality of life. Their study on neuronal mechanosensitivity via the "Upper Limb Neurodynamic Test 1" found a low correlation (Spearman's rho = 0.367) for general health perception but a moderate correlation (rho = 0.553) for functional outcomes. These findings emphasize the need for precise diagnostic and treatment protocols in CTS management.[15].

Statistical parameters, such as correlation type, help characterize factors as either protective or aggravating in CTS progression.

Logistic regression analysis in this study confirmed statistical validity for variables like age, sex, occupation type, and key electrophysiological parameters (LD and AR). The model was statistically sensitive only when the severity score and AR were included, with an Exp(B) value of 1.467. However, the study's moderate sample size limits its generalizability, necessitating larger cohort studies to account for confounding factors like diabetes mellitus.

The predictive model demonstrated statistical significance for moderate CTS cases, emphasizing the need for prediction studies due to the high variability in disease progression. Similarly, Graham et al. validated CTS diagnostic criteria using Delphi analysis, with logistic regression showing a strong predictive correlation (0.71), confirming the model's statistical sensitivity in forecasting clinical deterioration [17].

The relationship between type of occupation and CTS severity was studied in the analysis by Curti et al. They assumed that the relationship between the two is not sufficiently sensitive to characterize the adverse course of the disease. A total of 183 subjects with clinically confirmed CTS and 445 subjects who constituted the control group were included in the analysis, thus the results showed that in the multinomial logistic regression analysis those who performed higher biomechanical stress were included in the moderate/severe type of impairment group [16].

This study included 59 individuals in the normal group, with demographic differences that could introduce confounding bias. Logistic regression analysis confirmed that occupation significantly contributed to the model's predictive power ($p < 0.001$), though individual significance was lower, indicating variable interdependence. The severity score (1/2) was validated as a diagnostic marker for moderate CTS.

Moderate and severe CTS management remains a priority due to uncertainty about surgical intervention timing. Ng et al. used MRI for diagnosis and severity prediction, achieving 100% sensitivity and 94% specificity. For severe CTS, a median nerve circumferential area >19 mm^2 showed moderate predictive value (75% sensitivity, 65.9% specificity). The study concluded that MRI is highly accurate for CTS diagnosis and recommends using a median nerve area >15 mm^2 as a diagnostic criterion and >19 mm^2 as a severe CTS marker [18].

Reliable and reproducible diagnostic methods are essential for understanding disease progression and treatment needs. The present study focused on predicting the evolution from moderate to severe CTS, while previous research highlighted MRI's usefulness in severe cases.

The Hosmer-Lemeshow test validated the severity marker based on RA impairment, confirming its accuracy in the binary regression model. Sasaki et al. investigated CTS severity using electrophysiology, analyzing sensory nerve conduction velocity and distal motor latency. Their findings showed a strong negative correlation

(-0.786) between these parameters, suggesting that severity classifications may not always align with clinical presentation [19].

The present study differs from previous research by incorporating various demographic parameters that could influence disease progression, including RA, which was further subclassified for sensitivity analysis. A correlation matrix analysis revealed a strong negative correlation between age and occupation, suggesting that older individuals in specific occupations are at greater risk for moderate CTS progression. Additionally, the correlation between LD and RA parameters was moderate, likely due to the study's small sample size.

Comparing this with literature findings, Almigdad et al. conducted a cross-sectional study on 139 CTS patients, using nerve conduction studies and the Boston Carpal Tunnel Questionnaire. Their results showed that electrophysiological studies, particularly nerve conduction velocities, are highly effective in determining CTS severity. Furthermore, nocturnal pain and paresthesias strongly correlated with the questionnaire's functional scale [20].

The analysis of the "Exp(B)" coefficient (odds ratio) indicates that the AR parameter has high statistical significance in predicting CTS severity, making it a valuable diagnostic marker for disease progression from moderate to severe stages. Similarly, LD is a strong predictor for classifying moderate and severe cases. Occupation type also appears to contribute to CTS worsening, particularly in moderate cases.

A key limitation of this study is the lack of data on comorbidities, such as diabetes, which has been identified as a significant risk factor for CTS progression. Sanjari et al. conducted a meta-analysis of 42 studies, demonstrating a strong association between diabetes and CTS (OR: 1.64–2.21; $p < 0.001$). This aligns with the present study's findings, where occupation type was identified as an aggravating factor for CTS severity [21]

The multinomial logistic regression model validated the "severity score 1/2," demonstrating its generalizability for individuals with moderate CTS. Subclassification of the AR parameter revealed that patients with a score below 3 had no risk of severe progression (100% sensitivity), while those with a score above 3 showed a more accelerated progression, also with 100% sensitivity. The overall accuracy of the severity score in predicting CTS progression was 59.5%, highlighting its potential as an electrodiagnostic marker for determining the need for intensive treatment or early surgical intervention.

Timely treatment is crucial, as delayed therapy can negatively impact motor and sensory functions. However, the optimal timing for surgery remains unstandardized, sometimes leading to adverse outcomes. Zimmerman et al. analyzed sociodemographic factors influencing CTS outcomes using data from the Swedish hand surgery registry. Their study found that patients with lower socioeconomic status had worse functional outcomes (higher QuickDASH scores). Additionally, postoperative results after 12 months showed no significant overall improvement across all patient groups [22].

This study highlights the lack of standardization in determining the optimal timing for surgical intervention in CTS, which may contribute to therapy failure. The statistical analysis of the "Fixed Coefficients" indicator confirms that the "severity score 1/2" has a specific causal relationship with the tested variables, supported by a normal data distribution. The graphical representation of the "intercept" indicator underscores the predictive power of the severity score, showing that patients classified under score 1 are less likely to progress to severe CTS.

In the literature, studies on the prediction of bilateral CTS progression emphasize the importance of identifying risk factors and monitoring markers. Singjam et al. found that among patients with paresthesia-like symptoms, males over 45 years old with thenar atrophy had an 80.7% prevalence of developing bilateral CTS [23].

The analysis of sensitivity and specificity for age, sex, occupation, LD, and AR parameters identified AR as the best predictor, with an AUC of 0.971, indicating nearperfect accuracy. LD followed with an AUC of 0.600, suggesting a moderate predictive level.

Similar studies in the literature have used ROC curves to assess diagnostic test performance. Moschovos et al. analyzed echogenicity in relation to CTS progression and found that for individuals under 39, the AUC was 0.97, while for those over 65, it was 0.88. Their findings suggest that echogenicity measurements provide a similar level of sensitivity and specificity compared to median nerve area assessments [24].

The performance of electrodiagnostic tests has been widely discussed, which is why the classification of patients into groups of impairment is a necessity, studies on the analysis of "F" waves in the electrodiagnostic examination has been of interest to Ege et al. This group wanted to measure the latency of F waves and their classification as mild, moderate, severe in order to analyze the degree of sensitivity for each category. Thus the results of the study revealed that for the moderate and severe group the measurement of F-wave latency is statistically significant $p<0.001$. In conclusion, the post-hoc analysis on the severe group, the measurement of F-wave latency seems to be more sensitive for this group [25].

Univariate Cox regression analysis showed that for CTS patients around 70 years old with moderate disease, the survival rate decreases by 20%, correlating with increased morbidity due to nerve fiber loss and motor deficits, which negatively impact quality of life. However, despite significant hand motor disability, overall survival is not drastically affected, emphasizing the importance of early clinical monitoring to prevent irreversible nerve demyelination.

Similar studies have examined the impact of CTS severity and age on survival. Zhang et al. analyzed individuals over 80 years old with prolonged symptoms and found that their Boston questionnaire scores for symptom severity (1.6) and functional status (1.8) indicated a minimal effect on mortality, which remained close to that of the general population [26].

The study is limited as it does not provide information on the conservator treatment modality, categorization of patients according to the severity of symptomatology or electrophysiologic parameters. Compared to our study which is specific to a category of patients, the results in this case are more sensitive and specific.

The interpretation of the hazard ratio in this study indicates that patients aged 65–70 have a higher risk of CTS progression from moderate to severe stages. This risk increases cumulatively with age, making age an additional risk factor, particularly for those with an RA severity score >3. Consequently, electrophysiological monitoring is essential for this group.

Identifying factors that contribute to CTS progression requires further investigation. Carvajal et al. studied the link between bisphosphonate use and CTS, analyzing 59,475 female patients. They found that 1.2% of those treated with bisphosphonates developed CTS compared to 0.8% in the untreated group. The hazard ratio for bisphosphonate users was 1.38 (95% CI: 1.15–1.64), suggesting that bisphosphonates may be a risk factor for CTS development [27].

Given the chronic nature of CTS, diagnosing, monitoring progression, and estimating risk are crucial. This study's hazard ratio model analyzed variables such as age, the Bland Scale, and electrophysiological parameters LD and AR, as key markers of disease evolution.

Statistical validation using the Kaiser-Meyer-Olkin measure and Bartlett's Test of Sphericity confirmed the model's robustness. Although electrophysiological assessments were conducted only once, dynamic evaluation was found unnecessary for predicting progression. The data effectively characterize the transition from moderate to severe CTS, with the statistical marker providing a strong correlation for defining this phase.

4. Materials and Methods

The present research represents a retrospective cohort study that included a number of 59 individuals who constituted the control group, 74 individuals who represented the study group with mild type, 74 patients diagnosed with moderate and severe type a number of 57 patients.

The research was carried out between January and December 2022, patients hospitalized in the Neurology Clinic of "Prof. Dr. N. Oblu" Hospital "Prof. Dr. N. Oblu" Iași, Romania, in the "day hospitalization" type or patients who were evaluated through outpatient clinic consultation in the same hospital were included in the study.

Study inclusion criteria:

- Written agreement of the patient to participate in this study by signing the informed consent;

- age over 18 years;

- age over 70 years (to minimize the impact of age-induced changes on the study group)

- Patients diagnosed with CTS for the mild, moderate and severe study groups;

- the presence of clinical elements suggestive and specific for a median nerve damage, but also the presence of subjective signs (e.g. paresthesias in the form of numbness, burning, tingling, etc.), with regard to objective signs, we took into account the presence of sensibility tubulation such as hypoesthesia in the median nerve invervation territory, the presence of motor deficit, trophic changes such as atrophy of the tendon eminence;

- presence of electrodiagnostic elements suggestive of median nerve neuropathy and analysis of LD-distal latency and AR-amplitude ratio parameters.

Exclusion criteria:

- age less than 18 years;

- pregnant women

- Patient refusal to participate in this study;

Patients over 70 years of age (to minimize the influence of age-induced changes on the study group)

--Presence of psychiatric conditions that severely influence judgment;

-rheumatologic diseases such as psoriatic arthritis, rheumatoid arthritis and gout.

The present research was carried out in accordance with the approval of the Ethics Committee of the Clinical Emergency Hospital "Prof. Dr. Nicolae Oblu" Iasi and the University of Medicine and Pharmacy "Grigore T. Popa" Iasi, the study also complied with the international recommendations and regulations in force mentioned in the Declaration of Helsinki, 2013.

The study did not aim to collect personal data, all parameters assessed were stored under the principle of anonymity, and the investigator was committed to use these data exclusively for scientific purposes.

Data collection. Data collected were recorded in an Excel 2010 database as follows: age, sex, clinical assessment by the Bland Scale, and electrophysiologic parameters: LD and AR.

Parameters assessed

-Age criterion was of interest for the present study because this parameter can be a sensitive marker in highlighting especially patients in the moderate impairment group in relation to the therapeutic decision of these patients;

-sex, also this parameter is also of interest in highlighting a possible difference in the severity of the disease groups studied;

- type of occupation, individuals who perform repetitive manual activities (e.g. confectioner, tailor, butcher, carpenter e.t.c) were coded with the digit "1" and those who do not perform repetitive manual activities were coded with the digit "2", the aim being to analyze the impact of mechanical stress on the occurrence of CTS;

-electrodiagnostic examination was performed on the whole group of patients with the following tests: motor parameters LDM, CMAP amplitude median nerve with recording on the abductor pollicis brevis muscle, comparative test median - ulnar motor 2LIO difference LDM, AR, sensory parameters median nerve with recording on the 2nd and 3rd finger, ulnar nerve - 5th finger.

-The development of the AR parameter severity scale for the moderate CTS group aimed to subclassify CTS into a low and high risk category, respectively, and to evaluate the contribution of this parameter in terms of optimal treatment choice for CTS.

The severity score 1/2 refers to the subclassification of the lot "moderate impairment" according to the AR parameter a value below 3 was coded as 1 and above 3 coded as 2.

Statistical analysis

In the present research, data analysis was performed using the SPSS (Statistical Package for the Social Sciences, Chicago, Illinois version 23.0) program. The following indicators on mean, median and standard deviation, interquartile range and Kurstosis for the following set of variables: age, sex and occupation were analyzed from the demographic point of view. The following statistical indicators were applied to analyze the relationship of LD and AR parameters with the other variables:

- Spearman coefficient;
- binary linear regression;
- univariate and multinomial logistic regression model;
- analysis of the degree of sensitivity and specificity by applying the Receiver operating characteristic (ROC)
- survival rate estimation and calculation

5. Conclusions

This study aimed to evaluate the efficacy of the 2LIO test for the diagnosis and severity classification of carpal tunnel syndrome (CTS) in a cohort of 264 patients divided into a control group of 59 healthy individuals and three groups of patients: 74 with mild CTS, 74 with moderate CTS and 57 with severe CTS. The mean age of the subjects was 47.03 years for the control group, 52.81 years for the mild CTS group, 54.49 years for the moderate CTS group and 56.14 years for the severe CTS group. Regarding gender distribution, a female predominance was observed, with 62.7% female in the control group and a similar proportion in the affected groups.

The performance of the 2LIO test was remarkable, with a sensitivity of 93.3%, specificity of 97.7% and an overall accuracy of 95.9%. Of all parameters, the amplitude ratio (AR) provided the highest predictive value, with an Exp(B) coefficient of 189.586, indicating that this variable is highly influential in terms of the risk of disease progression. The area under the ROC curve (AUC) for RA was 0.971, compared with 0.600 for distal motor latency (DML), highlighting the superior performance of the 2LIO test in diagnosing median nerve dysfunction.

Statistical correlations indicated a negative association between CTS severity and variables such as age and occupation. Thus, patients older than 65 years and those with occupations involving biomechanical stress had a higher risk of progression from moderate to severe form. Logistic regression analysis revealed an inverse correlation, albeit modest, between the 'moderate' and 'severe' groups (r = -0.274, $p <$ 0.05), which may suggest that therapeutic intervention in the moderate stage of this neuropathy may prevent progression.

The study emphasizes that the 2LIO test is a sensitive, specific and cost-effective diagnostic tool, thus offering a valuable alternative to traditional electrodiagnostic studies and other advanced imaging techniques. However, further research in larger cohorts is needed to establish its wider clinical applicability, taking into account additional variables such as comorbidities (e.g. diabetes mellitus) and occupational differences. This test has the potential to guide early therapeutic interventions, reducing the impact of severe complications on the patient's motor function and autonomy.

A novel aspect of this study is its emphasis on early intervention based on logistic regression findings, which suggest that treatment during the moderate stage may help prevent progression to severe CTS. Additionally, the study highlights the impact of occupational and age-related factors, reinforcing the need for targeted monitoring in high-risk groups, such as individuals over 65 or those in biomechanically demanding jobs.

From a broader perspective, this research underscores the importance of refining CTS management strategies by integrating novel diagnostic approaches like the 2LIO test. Future studies could explore its applicability in screening high-risk populations, optimizing treatment timelines, and reducing long-term disability, ultimately enhancing patient quality of life and work productivity. Further research in larger and more diverse cohorts is necessary to validate these findings and expand the clinical utility of the 2LIO test in relation to comorbidities, occupational risks, and long-term functional outcomes.

Author Contributions: For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Con-ceptualization, L.B; A.C, M.DT. and A.I.C.; methodology, AM.B; software, A.C.I; validation, R.C., A.C. and L.B.; formal analysis, A.C.I.; investigation, R.C.; resources, L.B; data curation, M.DT.; writing—original draft preparation, L.B.; writing—review and editing, A.C.; visualization, A.M.B.; supervision, L.B.; project administration, L.B.; funding acquisition, L.B. All authors have read and agreed to the published version of the manuscript." Please turn to the CRediT taxonomy for the term explanation. Authorship must be limited to those who have contributed substantially to the work reported.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and Research Ethics Committee of U.M.F. "Gr. T. Popa" no.481/27.10.2024).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: In this section, please provide details regarding where data supporting reported results can be found, including links to publicly archived datasets analyzed or generated during the study. Please refer to suggested Data Availability Statements in section "MDPI Research Data Policies" at https://www.mdpi.com/ethics. If the study did not report any data, you might add "Not applicable" here.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Aboonq MS. Pathophysiology of carpal tunnel syndrome. Neurosciences (Riyadh). 2015 Jan;20(1):4-9. PMID: 25630774; PMCID: PMC4727604.
2. Hegmann KT, Merryweather A, Thiese MS, Kendall R, Garg A, Kapellusch J, Foster J, Drury D, Wood EM, Melhorn JM. Median Nerve Symptoms, Signs, and Electrodiagnostic Abnormalities Among Working Adults. J Am Acad Orthop Surg. 2018 Aug 15;26(16):576-584. doi: 10.5435/JAAOS-D-17-00034. PMID: 30028751.
3. Park JS, Won HC, Oh JY, Kim DH, Hwang SC, Yoo JI. Value of cross-sectional area of median nerve by MRI in carpal tunnel syndrome. Asian J Surg. 2020;43(6):654-659. doi:10.1016/j.asjsur.2019.08.001
4. Kanagasabai K. Ultrasound of Median Nerve in the Diagnosis of Carpal Tunnel Syndrome-Correlation with Electro-physiological Studies. Indian J Radiol Imaging.
5. Wang WL, Buterbaugh K, Kadow TR, Goitz RJ, Fowler JR. A Prospective Comparison of Diagnostic Tools for the Diagnosis of Carpal Tunnel Syndrome. J Hand Surg Am. 2018;43(9):833-836.e2. doi:10.1016/j.jhsa.2018.05.0222022;32(1):16-29. Published 2022 Apr 6. doi:10.1055/s-0041-1741088

6. Szabo RM, Slater RR Jr, Farver TB, Stanton DB, Sharman WK. The value of diagnostic testing in carpal tunnel syndrome. J Hand Surg Am. 1999;24(4):704-714. doi:10.1053/jhsu.1999.0704
7. Küçükakkaş O, Yurdakul OV. The diagnostic value of clinical examinations when diagnosing carpal tunnel syndrome assisted by nerve conduction studies. J Clin Neurosci. 2019;61:136-141. doi:10.1016/j.jocn.2018.10.106
8. Dabbagh A, MacDermid JC, Yong J, Macedo LG, Packham TL. Diagnosing Carpal Tunnel Syndrome: Diagnostic Test Accuracy of Scales, Questionnaires, and Hand Symptom Diagrams-A Systematic Review. J Orthop Sports Phys Ther. 2020;50(11):622-631. doi:10.2519/jospt.2020.9599
9. Mondelli M, Filippou G, Gallo A, Frediani B. Diagnostic utility of ultrasonography versus nerve conduction studies in mild carpal tunnel syndrome. Arthritis Rheum. 2008;59(3):357-366. doi:10.1002/art.23317
10. Karadağ, Y. S., Karadağ, O., Ciçekli, E., Oztürk, S., Kiraz, S., Ozbakir, S., Filippucci, E., & Grassi, W. (2010). Severity of Carpal tunnel syndrome assessed with high frequency ultrasonography. Rheumatology international, 30(6), 761–765. https://doi.org/10.1007/s00296-009-1061-x
11. Calfee RP, Dale AM, Ryan D, Descatha A, Franzblau A, Evanoff B. Performance of simplified scoring systems for hand diagrams in carpal tunnel syndrome screening. J Hand Surg Am. 2012 Jan;37(1):10-7. doi: 10.1016/j.jhsa.2011.08.016. Epub 2011 Oct 5. PMID: 21975100; PMCID: PMC3438892.
12. Elseddik M, Alnowaiser K, Mostafa RR, Elashry A, El-Rashidy N, Elgamal S, Aboelfetouh A, El-Bakry H. Deep Learning-Based Approaches for Enhanced Diagnosis and Comprehensive Understanding of Carpal Tunnel Syndrome. Diagnos-tics (Basel). 2023 Oct 14;13(20):3211. doi: 10.3390/diagnostics13203211. PMID: 37892032; PMCID: PMC10606231.
13. Georgiew F, Otfinowska E, Adamczyk T. Diagnostic tests used in diagnosis of the carpal tunnel syndrome. January 2008 Rehabilitacja Medyczna 12(3):24-35
14. Bargiel P, Czapla N, Prowans P, Kotrych D, Ziętek P, Lusina D, Łęgosz P, Petriczko J. Thermography in the diagnosis of carpal tunnel syndrome. Open Med (Wars). 2021 Jan 27;16(1):175-182. doi: 10.1515/med-2021-0007. PMID: 33585693; PMCID: PMC7862996.
15. Hernández-Secorún M, Abenia-Benedí H, Lucha-López MO, et al. Understanding the Mechanosensitivity of the Median Nerve in Pre-Surgical Carpal Tunnel Syndrome Patients: A Correlational Study. Brain Sci. 2024 Jun 19;14(6):615. doi: 10.3390/brainsci14060615.
16. Graham B, Regehr G, Naglie G, Wright JG. Development and validation of diagnostic criteria for carpal tunnel syn-drome. J Hand Surg Am. 2006 Jul-Aug;31(6):919-24. PMID: 16886290.
17. Curti S, Ginanneschi F, Salce C, Argentino A, Mattioli S, Mondelli M. Carpal tunnel syndrome severity and work: a case-control study. Occup Med (Lond). 2024 Nov 22:kqae120. doi: 10.1093/occmed/kqae120. Epub ahead of print. PMID: 39
18. Ng AWH, Griffith JF, Tong CSL, Law EKC, Tse WL, Wong CWY, Ho PC. MRI criteria for diagnosis and predicting severity of carpal tunnel syndrome. Skeletal Radiol. 2020 Mar;49(3):397-405. doi: 10.1007/s00256-019-03291-0. Epub 2019 Aug 9. PMID: 31396669.574350.
19. Sasaki T, Koyama T, Kuroiwa T, Nimura A, Okawa A, Wakabayashi Y, Fujita K. Evaluation of the Existing Electrophysiological Severity Classifications in Carpal Tunnel Syndrome. J Clin Med. 2022 Mar 18;11(6):1685. doi: 10.3390/jcm11061685. PMID: 35330012; PMCID: PMC8950957.
20. Almigdad A, Odt M, Almanasir G. Carpal tunnel syndrome: correlation of the severity of the clinical picture and electrophysiological studies. Archives of Hand and Microsurgery. 2022, 28. 10.12790/ahm.22.0043.
21. Sanjari E, Raeisi Shahraki H, G Khachatryan L, Mohammadian-Hafshejani A. Investigating the association between diabetes and carpal tunnel syndrome: A systematic review and meta-analysis approach. PLoS One. 2024 Apr 16;19(4):e0299442. doi: 10.1371/journal.pone.0299442. PMID: 38626071; PMCID: PMC11020394.
22. Zimmerman M, Hall E, Carlsson KS, Nyman E, Dahlin LB. Socioeconomic factors predicting outcome in surgically treated carpal tunnel syndrome: a national registry-based study. Sci Rep. 2021 Jan 28;11(1):2581. doi: 10.1038/s41598-021-82012-x. PMID: 33510278; PMCID: PMC7844239.
23. Singjam A, Charoentanyarak K, Saengsuwan J. Prevalence and predictive factors for bilateral carpal tunnel syndrome by electrodiagnosis: A retrospective study. PLoS One. 2021 Dec 23;16(12):e0260578. doi: 10.1371/journal.pone.0260578
24. Moschovos C, Tsivgoulis G, Ghika A, Bakola E, Papadopoulou M, Zis P, Zouvelou V, Salakou S, Papagiannopoulou G, Kotsali-Peteinelli V, Chroni E, Kyrozis A. Image analysis can reliably quantify median nerve echogenicity and texture changes in patients with carpal tunnel syndrome. Clin Neurophysiol. 2023 May;149:61-69. doi: 10.1016/j.clinph.2023.02.171. Epub 2023 Mar 5. PMID: 36907099.
25. Ege F, Aslanyavrusu M (May 23, 2024) An Evaluation of Minimal F-wave Sensitivity in Carpal Tunnel Syndrome. Cureus 16(5): e60964. doi:10.7759/cureus.60964
26. Zhang D, Earp BE, Benavent KA, Blazar P. Long-Term Outcomes and Mortality Following Carpal Tunnel Release in Patients Older Than 80 Years of Age. World Neurosurg. 2021 Jul;151:e1002-e1006. doi: 10.1016/j.wneu.2021.05.031. Epub 2021 May 21. PMID: 34023463.
27. Carvajal A, Martín Arias LH, Sáinz M, Escudero A, Fierro I, Sauzet O, Cornelius VR, Molokhia M. Carpal Tunnel Syndrome Associated with Oral Bisphosphonates. A Population-Based Cohort Study. PLoS One. 2016 Jan 14;11(1):e0146772. doi: 10.1371/journal.pone.0146772. PMID: 26765346; PMCID: PMC4713232.