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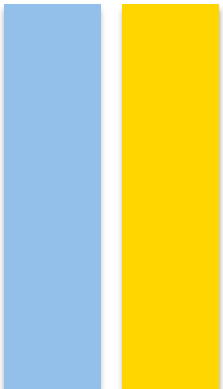
2º CICLO DE ESTUDOS
INFORMÁTICA MÉDICA

Development of Predictive Models for Carpal Tunnel Syndrome Diagnosis and Severity Using Demographic, Anthropometric and Clinical Factors

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M

2026



SEDE ADMINISTRATIVA

FACULDADE DE **MEDICINA**

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Acknowledgments

This dissertation marks the finish line of a demanding journey that would not have been possible without the support, collaboration and encouragement of several people, to whom I would like to express my sincere gratitude.

First and foremost, I would like to thank my supervisor, Daniela Ferreira-Santos, for her availability, rigorous guidance and valuable suggestions, which greatly contributed to the development and improvement of this work. Her support and expertise were invaluable throughout this project.

I am also deeply grateful to my co-supervisors, Dr. José Augusto and Dr. António Campos, for their availability, knowledge and support. To my colleagues Inês, Sara and Catarina, thank you for your help, friendship, daily support and encouragement during the most demanding moments. Your collaboration made it all easier and contributed greatly to the conclusion of this work. Our Neurophysiology Unit is small but filled with amazing people.

I would also like to express my gratitude to all the participants who agreed to take part in this study. Their availability and contribution were crucial.

To my parents and brother, thank you for your unconditional love, support and weekend family lunches. Thank you for being present at every stage of my life and for always believing in me.

To Sérgio, thank you for your love, understanding and patience during these past few months. Thank you for all the meals you cooked and dishes you washed, so that I could dedicate myself to this project. Your unwavering support was both essential and reassuring. Most of all, thank you for just being there, present, every step of the way and for celebrating every small achievement with me.

To Rita, thank you for your long-lasting genuine friendship, constant presence and words of encouragement whenever I needed them most.

Once again, thank you all for accompany me in the development and now finalization of this dissertation.

Abstract

Background: Carpal tunnel syndrome (CTS) is the most common compressive mononeuropathy. Although electrodiagnostic studies are considered the reference standard for diagnostic confirmation and severity classification, access may be limited and clinical–electrophysiological agreement is not always observed. Predictive models based on routinely available information may support clinical assessment and referral prioritisation.

Objective: To develop and compare logistic regression and Bayesian network models for predicting the presence and electrodiagnostic severity of CTS using demographic, anthropometric and clinical factors.

Methods: An observational, analytical and cross-sectional study was conducted among consecutive adults referred for electrodiagnostic evaluation of suspected CTS. The analysis included 247 participants and 451 symptomatic hands. CTS was electrodiagnostically confirmed in 313 hands (69.4%). Binary logistic regression and Bayesian networks were developed for diagnostic prediction. Severity analyses were restricted to confirmed CTS cases, grouped into three ordered categories: mild, moderate and severe. Model performance was assessed using accuracy, sensitivity, specificity, balanced accuracy, Cohen's kappa and area under the receiver operating characteristic curve (AUC).

Results: Age, body mass index (BMI), symptom duration, pain, nocturnal awakenings and square wrist morphology were independently associated with CTS diagnosis in the final logistic regression model. The best diagnostic Bayesian network achieved an accuracy of 80.7%, sensitivity of 91.1%, specificity of 57.3% and an AUC of 88.3%, outperforming the final logistic regression model, which achieved an accuracy of 72.9%, sensitivity of 91.4%, specificity of 31.2% and an AUC of 74.8%. Age, BMI and nocturnal awakenings were independently associated with increasing CTS severity. The final severity Bayesian network achieved an accuracy of 73.5% and a Cohen's kappa of 0.537, with sensitivities of 87.1%, 61.4% and 50.9% for mild, moderate and severe CTS, respectively.

Conclusion: Bayesian networks outperformed logistic regression in predicting both CTS diagnosis and severity, particularly by improving the identification of hands without CTS and the classification of moderate and severe disease. Following internal and external validation, these models may support clinical assessment and prioritisation for electrodiagnostic testing.

Keywords: Carpal Tunnel Syndrome; Bayesian Networks; Logistic Regression; predictive modelling; electrodiagnosis; disease severity.

Resumo

Introdução: A Síndrome do Túnel Cárpico (STC) é a mononeuropatia compressiva mais frequente. Embora os Estudos de Condução Nervosa sejam considerados o método de referência para a confirmação diagnóstica e a classificação da gravidade, o seu acesso pode ser limitado e nem sempre há concordância clínico-eletrofisiológica. Modelos preditivos baseados na informação disponível na prática clínica poderão apoiar a avaliação e a priorização dos pedidos.

Objetivo: Desenvolver e comparar modelos de regressão logística e redes *Bayesianas* para prever a presença e a gravidade eletrofisiológica da STC com base em fatores demográficos, antropométricos e clínicos.

Métodos: Foi realizado um estudo observacional, analítico e transversal em adultos consecutivamente referenciados para avaliação eletrofisiológica por suspeita de STC. Foram incluídos 247 participantes e 451 mãos sintomáticas. A STC foi confirmada em 313 mãos (69.4%). Para a previsão diagnóstica, desenvolveram-se modelos de regressão logística binária, classificadores *Tree-augmented Naïve Bayes* e redes Bayesianas. A análise da gravidade foi limitada aos casos confirmados, agrupados em três categorias ordenadas: ligeira, moderada e grave. O desempenho foi avaliado através da *accuracy*, sensibilidade, especificidade, *balanced accuracy*, *Cohen's kappa* e área sob a curva ROC (AUC).

Resultados: A idade, o índice de massa corporal, a duração dos sintomas, a dor, os despertares noturnos e a morfologia quadrada do punho associaram-se independentemente ao diagnóstico de STC no modelo final de regressão logística. A melhor rede *Bayesiana* para o diagnóstico apresentou *accuracy* de 80.7%, sensibilidade de 91.1%, especificidade de 57.3% e AUC de 88,3%, superando o modelo final de regressão logística, que apresentou *accuracy* de 72.9%, sensibilidade de 91.4%, especificidade de 31.2% e AUC de 74.8%. A idade, o índice de massa corporal e os despertares noturnos associaram-se independentemente ao aumento da gravidade. A rede *Bayesiana* final para a gravidade apresentou exatidão de 73.5% e *Cohen's kappa* de 0,537, com sensibilidades de 87.1%, 61.4% e 50.9% para STC ligeira, moderada e grave, respetivamente.

Conclusão: As redes *Bayesianas* superaram a regressão logística na previsão do diagnóstico e da gravidade da STC, particularmente na identificação de mãos sem STC e na classificação da doença moderada e grave. Após validação interna e externa, estes modelos poderão apoiar a avaliação clínica e a priorização do acesso aos estudos eletrodiagnósticos.

Palavras-chave: Síndrome do Túnel Cárpico; redes *Bayesianas*; regressão logística; modelos preditivos; estudos de Condução Nervosa; gravidade da doença.

Preamble

Carpal Tunnel Syndrome (CTS) is a neuropathy characterised by compression of the median nerve at the level of the wrist and is the most common of all focal compressive mononeuropathies. The primary symptoms consist of pain, numbness, and paraesthesia in the first three digits and the radial half of the fourth digit. Disease progression may lead to decreased hand strength, impaired fine motor function, and atrophy of the Abductor Pollicis Brevis (APB) muscle, among other intrinsic hand muscles. Patients frequently report a sensation of “tingling and pain”, predominantly occurring at night, which they can temporarily relieve by shaking their hands. Diagnosis is confirmed by electrophysiological studies, namely Nerve Conduction Studies (NCS), which constitute the reference standard.

Several demographic, anthropometric, metabolic, and occupational factors are associated with the development of CTS. These include female sex, obesity, advanced age, diabetes mellitus, pregnancy, small and wide hand with a square-shaped wrist (hand anthropometric characteristics), and occupations involving repetitive movements and/or sustained wrist hyperextension.

In the context of the Portuguese National Health Service, particularly at the ULSGE (Gaia Espinho Local Health Unit), most physicians who evaluate patients with clinical symptoms suggestive of CTS request the reference (gold-standard) method to confirm their diagnostic hypothesis. However, within the limited time available during a consultation, it is not always easy to fully describe in the clinical information accompanying the NCS request all the data that would allow for appropriate patient prioritisation.

Furthermore, patients’ complaints may not yet translate into significant abnormalities on nerve conduction assessment, leading to a lack of electroclinical correlation and the need to repeat the exam shortly.

The development of a predictive model based on the factors mentioned above would allow estimation of both the probability of CTS presence and its predicted severity, thereby assisting clinicians in referral decisions and avoiding unnecessary exams. Consequently, this approach may help reduce waiting lists and decrease the number of cases that progress to severe levels due to delayed diagnosis and treatment.

The model's effectiveness will depend on achieving high sensitivity.

Scientific and Financial Results

No scientific results other than this dissertation have yet been developed.

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Acronyms

AAEM American Association of Electrodiagnostic Medicine

ADM Abductor Digiti Minimi

ANN Artificial Neural Network

AP Antero-posterior

APB Abductor Pollicis Brevis

AI Artificial Intelligence

AUC Area Under the Curve

BIC Bayesian Information Criterion

BDe Bayesian Dirichlet Equivalent

BMI Body Mass Index

BN Bayesian Networks

CI Confidence Interval

CMAP Compound Muscle Action Potential

CPTs Conditional Probability Tables

CTS Carpal Tunnel Syndrome

DAG Directed Acyclic Graph

EDX Electrodiagnostic studies

EMG Electromyography

GB Gradient Boosting

GDPR General Data Protection Regulation

IQR Interquartile range

ISS Imaginary Sample Size

KNN k-Nearest Neighbours

LGBM Light Gradient Boosting Machine

ML Machine Learning

ML Medio-Lateral

MLE Maximum Likelihood Estimation

NB Naïve Bayes

NCS Nerve Conduction Studies

NPV Negative Predictive Value

OR Odds Ratio

PPV Positive Predictive Value

RF Random Forests

ROC Receiver Operating Characteristic

SD Standard Deviation

SNAP Sensory Nerve Action Potential

SVM Support Vector Machines

TAN Tree-Augmented Naïve Bayes

XGB Extreme Gradient Boosting

Introduction

1. Introduction

1.1 Carpal Tunnel Syndrome: epidemiology

Median nerve entrapment at the wrist is the most common of all compressive mononeuropathies. In nearly all patients, the usual site of compression is the carpal tunnel, resulting in a set of symptoms and signs known as Carpal Tunnel Syndrome (CTS), which accounts for approximately 90% of all peripheral nerve entrapment syndromes (1–4).

The reported prevalence of CTS varies considerably across studies due to differences in diagnostic criteria, study design and population characteristics, making it difficult to compare epidemiological studies directly. Population-based studies generally estimate a prevalence of 1% to 5% in the general population, whereas substantially higher rates have been reported in specific occupational groups and among individuals with recognised risk factors such as obesity, diabetes mellitus, and pregnancy (5). Recent systematic reviews have highlighted considerable heterogeneity among prevalence estimates, largely reflecting variations in case definitions and diagnostic methods (6,7).

CTS occurs more frequently in women than in men and is most commonly diagnosed between 50 and 60 years, although it may occur at any age. Increasing age, obesity, diabetes mellitus, thyroid disorders and occupational exposure to repetitive or forceful hand activities have consistently been identified as important risk factors of this syndrome (2,8,9).

1.2 Anatomy and pathophysiology

CTS was first described in the 1800s by Paget, who reported a case of median nerve compression after a distal radius fracture (10).

The median nerve enters the wrist through the carpal tunnel: carpal bones are the floor and sides of the tunnel, and the thick transverse carpal ligament forms the roof. Alongside the median nerve, nine flexor tendons transverse the carpal tunnel as well (see figure 1.1). As these anatomical boundaries are rigid and non-distensible, the carpal tunnel has a limited capacity to accommodate increases in its contents, leaving the median nerve particularly susceptible to compression (1,11).

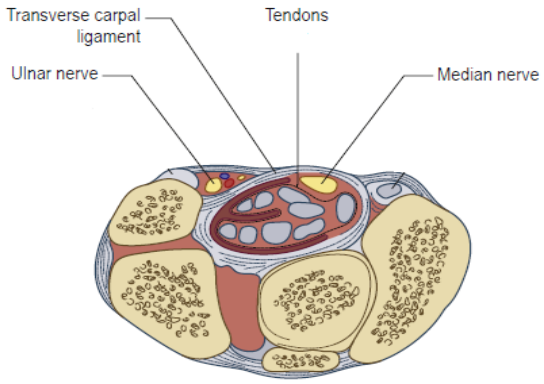


Figure 1.1 - Median nerve at the carpal tunnel. Adapted from: (4).

Such compression can often result from increased compartmental pressure in the carpal tunnel, caused by hypertrophy of the synovial tissue surrounding these tendons. This process occurs in response to extensive use, trauma to the wrist or an underlying inflammatory process such as arthritis. Because the carpal tunnel is confined by rigid anatomical structures, even modest increases in tissue volume can substantially elevate intracarpal pressure, thereby compressing the nerve (11,12).

The earliest pathological changes involve impaired intraneural microcirculation, leading to endoneurial oedema and local ischemia. Persistent compression subsequently disrupts axonal transport and causes focal demyelination, producing slowing of sensory and motor nerve conduction. If compression remains prolonged, axonal degeneration may occur, leading to permanent loss of nerve fibres and functional impairment in advanced stages of the disease. These progressive structural changes constitute the pathophysiological basis of the electrodiagnostic pathological alterations observed during nerve conduction studies (1,4,11).

The severity of neural dysfunction is closely related to both the degree and duration of median nerve compression. Early disease is predominantly characterised by intermittent sensory dysfunction due to reversible demyelination, while prolonged compression may result in persistent sensory deficits, weakness of the thenar muscles and, in severe cases, irreversible motor weakening secondary to axonal loss. This progression explains the spectrum of clinical manifestations observed in patients with CTS and underlies the electrodiagnostic severity classifications currently used in clinical practice (1,4,11).

1.3 Clinical presentation

CTS patients present with a variety of symptoms and signs resulting from compression and conduction compromise of the median nerve at the wrist. Patients commonly report numbness, tingling or paraesthesia affecting the hand, as well as wrist and arm pain. Symptoms are initially intermittent during activities involving sustained wrist flexion or extension, such as driving, reading or holding a telephone and frequently occur at night, often causing sleep disturbance and nocturnal awakenings. The prevalence of symptoms at night is due to fluid redistribution into the distal limbs during the supine rest position, which increases carpal tunnel pressure. Another factor is the lack of interstitial drainage due to reduced muscle pump and movement, adding to the pressure increase (1,4,11).

As median nerve compression progresses, sensory symptoms become more frequent and, in advanced cases, become permanent. Many patients experience temporary symptom relief by shaking or flicking the affected hand, a phenomenon known as the *flick sign*. Although the exact mechanism remains uncertain, changes in wrist position and

transient reductions in intracarpal pressure are thought to contribute to this temporary symptom relief. Patients may also complain of pain radiating from the wrist into the forearm, although the pain distribution is generally more variable than that of sensory symptoms (11,12).

The distribution of sensory symptoms may be difficult for patients to define accurately. Still, paraesthesia and numbness typically involve the thumb, second and third fingers, and the radial half of the fourth finger, corresponding to the sensory territory of the median nerve (see Figure 1.2). Importantly, sensation over the thenar eminence is usually preserved (see the yellow area in Figure 1.2) because the palmar cutaneous branch emerges from the median nerve before it enters the carpal tunnel (1,4,11).

Aggravating disease may eventually involve the motor fibres of the median nerve supplying the thenar muscles (see Figure 1.3). Patients may experience weakness of thumb opposition and abduction, reduced grip and pinch strength, impaired manual dexterity and difficulty performing fine motor tasks such as buttoning clothes. In severe cases, denervation of the thenar muscles may result in visible muscle atrophy, representing an indicator of advanced nerve injury and poorer functional prognosis (1,4,11).

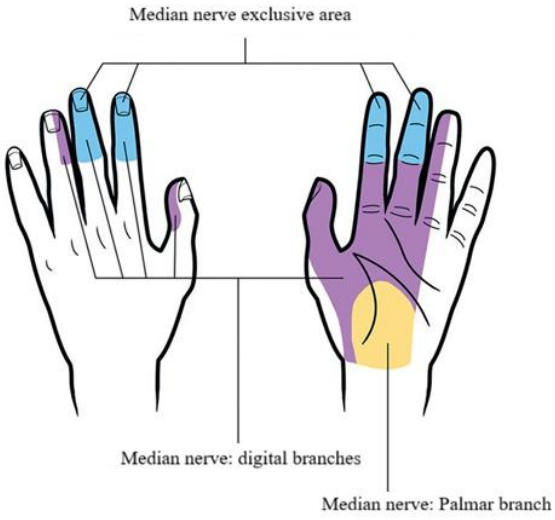


Figure 1.2 - Dermatomes innervated by median nerve and its sensory branches. Adapted from (13).

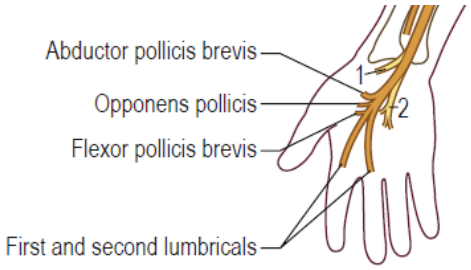


Figure 1.3 - Hand muscles innervated by the motor branches of the median nerve. Adapted from (4).

The clinical presentation of CTS is highly variable and depends on the degree and duration of median nerve compression. Although the combination of nocturnal paraesthesia, sensory disturbances within the median nerve territory and thenar weakness strongly suggests the diagnosis, symptom severity does not always correlate with the extent of electrophysiological impairment. Some patients with severe electrodiagnostic abnormalities may report relatively mild symptoms, whereas others with pronounced clinical complaints may demonstrate only minimal or even normal electrodiagnostic findings (1,11,13).

1.4 Diagnostic process

The diagnosis of carpal tunnel syndrome is primarily based on a thorough clinical history and physical examination. Characteristic symptoms, including nocturnal paraesthesia, numbness within the median nerve distribution, and progressive hand weakness, are often highly suggestive of CTS. However, because these manifestations may overlap with those of cervical radiculopathy, proximal median neuropathy, ulnar neuropathy, polyneuropathy and other musculoskeletal disorders, clinical assessment alone is insufficient to establish a definitive

diagnosis in all patients. Consequently, complementary investigations are frequently required to confirm median neuropathy at the wrist and exclude alternative diagnoses (1,11,13).

Several provocative manoeuvres have been proposed to reproduce median nerve compression symptoms and support the clinical diagnosis of CTS. The most performed tests include Phalen's test, Tinel's sign, the carpal compression test (Durkan's test) and the hand elevation test. Although these manoeuvres are simple, inexpensive and easily performed during routine clinical examination, their reported sensitivity and specificity vary considerably across studies. Earlier studies reported sensitivities ranging from 42% to 91% for Phalen's test and from 38% to 100% for the Hoffmann–Tinel sign, with corresponding specificities of 54% to 98% and 55% to 100%, respectively (14). More recently, a systematic review and meta-analysis reported pooled sensitivities and specificities of 68% and 71% for Phalen's test, 55% and 75% for Tinel's sign, 62% and 77% for Durkan's test, and 85% and 95% for the hand elevation test, respectively (15). However, substantial heterogeneity and methodological limitations across the included studies indicate that these estimates should be interpreted cautiously, particularly those concerning the hand elevation test, for which the pooled estimates were based on only five studies. Consequently, none of these tests should be used in isolation to confirm or exclude CTS; instead, their findings should always be interpreted in combination with the patient's clinical history and complementary investigations (3,11,13,16).

Imaging techniques, particularly high-resolution ultrasonography, have become increasingly useful as complementary diagnostic tools in CTS. Ultrasonography allows visualisation of median nerve enlargement, structural abnormalities and space-occupying lesions within the carpal tunnel. A meta-analysis including 19 studies and 3,131 wrists reported a pooled sensitivity of 77.6% and specificity of 86.8% for ultrasonography in the diagnosis of CTS (17). However, diagnostic performance depends on operator experience and methodological variability, including differences in measurement protocols and diagnostic thresholds. Magnetic resonance imaging is generally reserved for selected cases in which anatomical abnormalities or alternative pathologies are suspected. Therefore, despite these advances, imaging techniques complement rather than replace electrodiagnostic studies in the diagnostic evaluation of CTS (4,11,12).

As such, electrodiagnostic studies remain the reference standard for confirming median neuropathy at the wrist. Nerve conduction studies objectively demonstrate impaired median nerve conduction, quantify the severity of nerve dysfunction and assist in excluding alternative peripheral nerve disorders or cervical radiculopathy. Although a small proportion of patients with clinically suspected CTS may present normal electrodiagnostic findings, nerve conduction studies remain the most objective method for confirming the diagnosis and grading disease severity (1,11,13).

Overall, the diagnosis of CTS relies on integrating multiple demographic, anthropometric, clinical and electrodiagnostic findings rather than on any single variable. This complexity underscores the need for objective decision-support tools that combine information from multiple sources to improve diagnostic accuracy and support clinical decision-making.

1.5 Electrodiagnostic evaluation

Electrodiagnostic studies (EDX) are divided into nerve conduction studies (NCS) and needle electromyography (EMG), which serve as the reference standard for confirming median neuropathy at the wrist. They provide a measurable assessment of median nerve function, allowing confirmation of the diagnosis, exclusion of alternative or concomitant neurological disorders, and grading of disease severity. Although the diagnosis of CTS begins with clinical evaluation, electrodiagnostic testing is particularly valuable in patients with atypical symptoms, diagnostic uncertainty, persistent complaints despite conservative treatment, or before surgical decompression (1,11,13).

The electrophysiological abnormalities observed in CTS directly reflect the underlying pathophysiological changes occurring within the compressed median nerve. Early compression predominantly affects the myelin sheath, resulting in focal demyelination and slowing of nerve conduction across the carpal tunnel. As compression becomes prolonged or severe, axonal degeneration may develop, leading to reduced amplitudes of compound muscle action potential (CMAP) and sensory nerve action potential (SNAP). Consequently, electrodiagnostic abnormalities generally progress from isolated conduction slowing to more pronounced evidence of axonal dysfunction in advanced disease (1,4).

NCS assess the physiological integrity of both sensory and motor fibres of the median nerve. Sensory conduction studies are generally more sensitive for detecting early CTS, as sensory fibres are affected before motor fibres in most patients. Routine electrodiagnostic evaluation includes measurement of median sensory and motor distal latencies, conduction velocities and response amplitudes, often complemented by comparative studies with the ulnar or radial nerves to improve diagnostic sensitivity. Median–ulnar sensory latency comparisons, mixed palmar studies, and lumbrical–interosseous latency comparisons are among the most widely accepted techniques for detecting mild median neuropathy at the wrist. Interpretation of these parameters is based on established laboratory reference values and internationally accepted diagnostic criteria (1,4,13).

EMG is not routinely required for all patients with CTS, but it may provide additional diagnostic information in selected clinical situations. It is particularly useful when severe axonal loss is suspected, when symptoms suggest an alternative diagnosis such as cervical radiculopathy or proximal median neuropathy, or when concomitant neurological disorders cannot be excluded. In advanced CTS, needle EMG may demonstrate evidence of chronic denervation and reinnervation within the abductor pollicis brevis muscle, reflecting longstanding median nerve dysfunction (1,4).

Beyond confirming the diagnosis, EDX provide an objective method for classifying disease severity. Several classification systems have been proposed, most of which are based on progressive abnormalities in sensory and motor nerve conduction parameters. Among these, the classification proposed by Padua et al. in 1997 is one of the most widely adopted in both clinical practice and research. This system classifies CTS based on the progressive involvement of sensory and motor nerve conduction abnormalities, providing a standardised framework for assessing disease severity. These classifications are clinically relevant because they correlate with prognosis, assist treatment selection and facilitate comparison between studies (1,4,13,18).

Although EDX remain the gold standard for confirming CTS, they still have limitations. For example, mild or intermittent disease may occasionally produce normal electrophysiological findings, particularly during the early stages of nerve compression. In opposition, electrodiagnostic abnormalities may occasionally be detected in asymptomatic individuals. Therefore, EDX findings should always be interpreted within the context of the patient's clinical history and physical examination (11,13).

1.6 Risk factors

CTS is considered a multifactorial disorder resulting from the interaction of demographic, anthropometric, medical, occupational and anatomical factors. Although the exact mechanisms underlying disease development are not completely understood, numerous epidemiological studies have identified several factors consistently associated with an increased risk of CTS. These factors may contribute to elevated intracarpal pressure, impaired median nerve microcirculation, connective tissue remodelling or increased mechanical stress within the carpal tunnel (2,11,12).

CTS is usually bilateral, both clinically and electrically, although the dominant hand is more severely affected,

especially in idiopathic cases (4). Age is a well-established predictor of CTS, with prevalence increasing progressively from middle age onwards. Women are affected more frequently than men, with reported female-to-male ratios ranging, approximately, between 2:1 and 4:1 (19,20). Hormonal influences, smaller carpal tunnel dimensions and differences in connective tissue characteristics have been proposed to explain this increased susceptibility among women (11).

Obesity is another well-established risk factor for CTS. Several studies have demonstrated that increasing body mass index is associated with a higher risk of developing median nerve compression, possibly owing to increased adipose tissue deposition and elevated intracarpal pressure. Anatomical characteristics have also been implicated, particularly wrist morphology. Individuals with a relatively square-shaped wrist have been reported to exhibit increased susceptibility to CTS, although the strength of this association varies across studies (2,8,21,22).

Several systemic disorders have also been associated with CTS. Diabetes mellitus is considered one of the most important comorbidities because chronic hyperglycaemia may increase nerve susceptibility to compression through microvascular impairment and metabolic dysfunction. Other recognised risk factors include hypothyroidism, rheumatoid arthritis, pregnancy, chronic kidney disease and conditions associated with fluid retention or connective tissue disorders (2,11).

The systematic review and meta-analysis conducted by Kozak et al. (2015) revealed high-quality evidence that correlates biomechanical occupational factors with developing CTS; the greater the exposure, the greater the risk. Repetitive hand movements, forceful gripping, prolonged use of vibrating tools and sustained non-neutral wrist postures have all been associated with increased disease risk. Nevertheless, occupational exposure is generally considered to interact with individual susceptibility factors rather than acting as an isolated cause of CTS (9). El-Sherif et al. also showed that the total work time and the number of hours dedicated to repetitive hand movements were significantly higher among the patient group (8).

In addition to established risk factors, several clinical characteristics have been associated with electrodiagnostically confirmed CTS and increasing disease severity. Longer symptom duration, nocturnal awakenings, hand pain and subjective weakness have all been reported as indicators of more advanced median nerve dysfunction, although their independent contribution varies between studies. These clinical variables may therefore provide additional predictive information when combined with demographic and anthropometric factors (11,12).

Although numerous individual risk factors have been identified, no single variable is sufficiently accurate to predict the presence or severity of CTS (23,24).

1.7 Need for predictive models

The multifactorial nature of carpal tunnel syndrome presents a significant challenge for clinical decision-making. Age, sex, body mass index, anatomical characteristics, medical comorbidities, and symptom characteristics all contribute to disease development and progression, yet none alone provides sufficient diagnostic accuracy. Therefore, clinicians must consider multiple variables simultaneously when estimating the probability of CTS and determining the need for further investigation.

Traditional statistical approaches, particularly multivariable logistic regression, have been widely used to identify independent predictors of CTS and estimate disease probability (24,25). These methods provide valuable information regarding associations between risk factors and disease, however, conventional logistic regression does not automatically identify nonlinear relationships or interactions between predictors, as these must be explicitly incorporated into the model. So, they may not adequately capture the complex interactions frequently observed in

clinical practice (26). This limitation may be particularly relevant in CTS, where relationships between risk factors can vary according to other patient characteristics; for example, the association between BMI and CTS has been shown to differ according to age (27).

Recent advances in artificial intelligence (AI) and machine learning (ML) have enabled the development of predictive models that integrate multiple sources of clinical information by combining computational methods with large-scale clinical datasets, these models can identify patterns, predict outcomes, and support diagnostic and therapeutic decisions. Applications of AI have expanded rapidly across multiple medical specialties, including radiology, oncology, cardiology, neurology, and pathology, where these techniques have demonstrated the potential to improve diagnostic accuracy, optimize patient management, and facilitate personalized medicine (28,29).

ML focuses on developing algorithms capable of learning patterns directly from data without requiring explicit programming, they can model complex and non-linear interactions between multiple variables. Consequently, ML use for disease diagnosis, prognosis, risk stratification, and clinical decision support has increased over time (28,30).

Despite their high predictive performance, many ML algorithms, particularly deep learning models, operate as "black-box" systems, providing limited insight into how predictions are generated. This lack of interpretability represents an important limitation in healthcare, where understanding the reasoning underlying a prediction is often essential for clinician trust, model validation, and clinical implementation. As a result, there has been a growing interest in explainable AI approaches that combine predictive performance with transparency (29,30).

Probabilistic reasoning provides an interesting approach by explicitly modelling uncertainty and representing relationships between variables through probability theory. Rather than producing deterministic predictions, probabilistic models estimate the likelihood of different outcomes based on the available evidence while naturally accommodating incomplete or uncertain information. This characteristic is particularly valuable in clinical practice, where patient information is frequently heterogeneous, missing, or subject to uncertainty (31).

Among these approaches, Bayesian Networks offer several advantages, including the ability to represent probabilistic relationships between variables, explicitly model uncertainty and perform diagnostic inference even when some clinical information is unavailable. Furthermore, unlike many machine learning algorithms, Bayesian Networks provide transparent graphical representations of variable dependencies, making them particularly attractive for clinical applications where interpretability is essential (31–34).

The development of accurate and interpretable predictive models may assist clinicians in estimating the probability of CTS before electrodiagnostic testing, prioritising referrals, supporting diagnostic decision-making and optimising healthcare resources. These considerations provide the rationale for the present study, which aims to develop predictive models based on both conventional statistical methods and Bayesian Networks.

1.8 Bayesian Networks

Bayesian inference is based on Bayes' theorem, first described by the English mathematician Reverend Thomas Bayes in the eighteenth century and later formalised by Pierre-Simon Laplace. The theorem provides a mathematical rule for calculating the probability of an event after observing new evidence by combining prior knowledge with the likelihood of the observed data (35).

Bayesian networks (BNs) extend Bayes' theorem from a single probabilistic relationship to a multivariable framework capable of simultaneously modelling the conditional dependencies among numerous clinical variables. They allow efficient probabilistic inference while maintaining an interpretable representation of the relationships between predictors and clinical outcomes (34,35).

BNs are probabilistic graphical models that combine probability theory with graph theory to represent the conditional dependencies among a set of variables. They provide a compact and intuitive framework for modelling uncertainty by representing variables as nodes and their probabilistic relationships as directed edges within a directed acyclic graph (DAG). Unlike traditional statistical models, BNs not only estimate the probability of an outcome but also explicitly describe the relationships between predictor variables, allowing both prediction and probabilistic reasoning. Owing to their ability to integrate prior knowledge with observed data while maintaining model interpretability, BNs have become increasingly applied in clinical decision support, disease diagnosis and prognostic modelling (32,33,35).

Each node in a BN represents a random variable, which may correspond to a demographic characteristic, clinical symptom, laboratory measurement or disease outcome. The directed edges (arcs) connecting the nodes indicate conditional probabilistic dependencies between variables, with the direction of the edge representing the flow of probabilistic influence rather than necessarily implying causality. The resulting network forms a directed acyclic graph, meaning that all edges are directed and no variable can indirectly influence itself through a closed cycle (33,35).

One of the fundamental properties of BNs is conditional independence. The absence of an edge between two variables indicates that, given the values of their parent variables, they are conditionally independent. This property substantially simplifies the representation of complex multivariable systems by avoiding the need to estimate every possible joint probability directly. Consequently, BNs require considerably fewer parameters than complete probabilistic models while preserving the essential relationships between variables (32,35).

Once both the network structure and the associated conditional probability tables have been defined, BNs can perform probabilistic inference. This consists of updating the probability of one or more variables after new evidence has been introduced into the network. As additional clinical information becomes available, the posterior probabilities are automatically recalculated according to Bayes' theorem, allowing the probability of disease to be continuously refined. This capability closely resembles the clinical reasoning process: physicians progressively update their diagnostic hypothesis as new information is obtained during patient assessment (31,32).

Compared with many machine learning algorithms, BNs offer several characteristics that are particularly advantageous in healthcare. Their graphical representation facilitates model interpretation, enabling clinicians to visualise the relationships between variables and understand how individual predictors influence the estimated outcome. In addition, they can naturally accommodate incomplete or missing information without requiring imputation of every missing value and permit bidirectional probabilistic inference, allowing clinicians to estimate disease probabilities from symptoms or, on the contrary, infer the expected clinical manifestations associated with a given diagnosis. These characteristics have contributed to their increasing adoption in diagnostic support systems, prognostic prediction and personalised medicine (31,36).

The performance of a BN depends fundamentally on its graphical structure, which defines the conditional dependencies among variables. This process, known as structure learning, aims to identify the DAG that best represents the probabilistic relationships within a dataset. The resulting structure determines which variables are directly connected and, consequently, how information propagates throughout the network during probabilistic inference (32,35).

Network structures can be obtained using three main approaches: expert-driven, data-driven, or hybrid methods. In expert-driven approaches, the network topology is defined according to prior domain knowledge, relying on established causal or physiological relationships between variables. Although this strategy ensures clinically meaningful structures, it may overlook previously unknown associations present in the data. On the contrary, data-driven methods infer the network directly from observational data by identifying statistical dependencies among

variables. Finally, hybrid approaches combine expert knowledge with automated learning algorithms, allowing prior clinical information to guide the learning process while retaining the flexibility to discover novel relationships (34,35).

Several algorithms have been proposed for learning BN structures and are generally classified into constraint-based**,** score-based**,** and hybrid methods. Constraint-based algorithms construct the network by performing a sequence of conditional independence tests, while score-based algorithms evaluate multiple candidate network structures using a predefined scoring function and select the network that optimises this score. Hybrid methods integrate both strategies, typically using conditional independence tests to reduce the search space before applying score optimisation (34,35).

Among score-based methods, the hill-climbing algorithm is one of the most widely used approaches due to its computational efficiency and robustness. Hill-climbing begins with an initial network structure and iteratively improves it by adding, removing, or reversing individual edges. After each modification, the resulting network is evaluated using a scoring criterion, and only changes to improve the overall network score. This iterative process continues until no further improvement can be achieved, resulting in a locally optimal network structure (34).

The quality of candidate network structures depends on the selected scoring function. Commonly used scores include the Bayesian Information Criterion (BIC) and the Bayesian Dirichlet Equivalent (BDe) score. While the BIC penalises model complexity to reduce overfitting, the BDe score provides a fully Bayesian framework by incorporating prior assumptions regarding the distribution of network parameters. The BDe score is particularly suitable for discrete clinical variables because of its ability to balance model fit and complexity while accounting for prior information (34,35).

For classification tasks, specialised BN classifiers have also been developed. The simplest of these is the Naïve Bayes (NB) classifier, which assumes that all predictor variables are conditionally independent given the class variable. Although this assumption substantially simplifies model construction, it is often unrealistic in clinical datasets where risk factors frequently interact. The Tree-Augmented Naïve Bayes (TAN) classifier relaxes this assumption by allowing each predictor variable to have, in addition to the class node, at most one dependency on another predictor. This extension enables the model to capture important relationships among predictors while maintaining computational efficiency, often resulting in improved classification performance compared with the conventional Naïve Bayes classifier (37).

Once the network structure has been established, the next step is to estimate the network's parameters. In BNs, these parameters correspond to the conditional probability tables (CPTs), which quantify the probability distribution of each variable given the configurations of its parent nodes. Together with the network structure, the CPTs completely define the probabilistic model and enable inference to be performed (32,35).

Parameter learning can be performed using either maximum likelihood estimation (MLE) or Bayesian estimation. Maximum likelihood estimation derives the conditional probabilities directly from the observed frequencies in the available dataset and is computationally straightforward when complete data are available. However, MLE may produce unstable probability estimates when sample sizes are small or when some combinations of parent states occur infrequently, potentially resulting in zero probabilities that poorly affect probabilistic inference (35).

Bayesian parameter estimation addresses these limitations by combining the observed data with prior information regarding the expected parameter distributions. Rather than relying exclusively on the available observations, Bayesian estimation incorporates prior beliefs through a Dirichlet prior, resulting in posterior probability estimates that are generally more robust, particularly in scarce datasets. This approach reduces the risk of overfitting and prevents zero-probability estimates by smoothing the conditional probability distributions (32,35).

Although Bayesian parameter estimation partially mitigates this problem through prior distributions, model performance remains dependent on sample size and data quality. Reliable estimation of conditional probability tables requires an adequate number of observations for each combination of parent node configurations. As the number of variables and network complexity increase, data become increasingly sparse, potentially reducing the stability of parameter estimates (34,35).

BNs are also capable of handling incomplete or missing data without necessarily requiring imputation of all missing values. Since inference is based on the available evidence, probability estimates can still be generated when one or more predictor variables are unknown. Moreover, Bayesian networks support bidirectional inference, enabling clinicians not only to estimate the probability of a disease from observed clinical findings but also to explore the probability of individual clinical manifestations given a known diagnosis. This flexibility represents an important advantage in medical decision support systems (32,33).

A key component of Bayesian parameter estimation is the imaginary sample size (ISS), also referred to as the equivalent sample size. The ISS determines the relative influence of the prior distribution compared with the observed data. Lower ISS values allow the model to rely predominantly on available observations, whereas higher values increase the contribution of prior knowledge, resulting in smoother probability estimates. Consequently, selecting an appropriate ISS represents a balance between faithfully representing the observed data and maintaining stable parameter estimates (34).

Finally, many clinical variables are naturally continuous and must often be discretised before being incorporated into discrete Bayesian network models. Although discretisation simplifies probabilistic modelling and facilitates clinical interpretation, it may also result in some loss of information and predictive performance. Careful selection of clinically meaningful cut-off values is therefore essential to minimise this limitation (31,35).

Overall, the combination of probabilistic reasoning, model interpretability, and the ability to integrate multiple interacting clinical variables has made Bayesian networks one of the most widely applied probabilistic approaches for clinical decision support. Their strengths are particularly relevant in scenarios characterised by uncertainty, incomplete information, and complex multivariable relationships, making them well-suited for the development of predictive models in healthcare.

1.9 Clinical applications

BNs have become increasingly applied across a wide range of medical specialties because of their ability to integrate heterogeneous sources of clinical information, model uncertainty, and provide interpretable probabilistic predictions. Their flexibility enables the incorporation of demographic characteristics, clinical symptoms, laboratory findings, imaging results, and physiological measurements into a unified probabilistic framework, making them particularly suitable for clinical decision support systems (31,36).

One of the main applications of BNs is disease diagnosis. By combining multiple clinical variables, they estimate the probability of a disease while continuously updating this probability as new evidence becomes available. This dynamic reasoning process closely resembles clinical decision-making and has been successfully applied to support the diagnosis of several conditions, including cardiovascular diseases, neurological disorders, respiratory diseases, infectious diseases, and different types of cancer (31,36).

Beyond diagnosis, BNs have also been widely employed for prognostic prediction and risk stratification. In these settings, probabilistic models estimate the likelihood of future clinical outcomes, disease progression, treatment response, or complications by simultaneously considering multiple interacting risk factors. Their ability to quantify

uncertainty provides clinicians with probabilistic estimates rather than binary decisions, facilitating personalised risk assessment and supporting shared clinical decision-making (31).

Unlike many contemporary machine learning algorithms, BNs allow clinicians to visualise the probabilistic dependencies between predictors and outcomes, thereby facilitating model validation and improving confidence in clinical implementation. Furthermore, these networks remain functional even when some predictor variables are unavailable, making them particularly attractive for routine clinical practice, where complete patient information is not always accessible (31,32).

In recent years, predictive modelling has gained relevance in clinical medicine, offering tools to integrate multiple variables, estimate disease probability or outcome and guide clinical decision-making. Such models have demonstrated value in risk stratification, diagnostic support and resource optimisation across various medical fields. In the context of CTS, however, available predictive approaches are limited, often based on small samples, lack robust validation, or do not use electrodiagnostic findings as the reference outcome.

Therefore, there is a clear need for clinically applicable predictive models that integrate easily available risk factors and are validated against objective diagnostic standards. The development of such models may enhance diagnostic efficiency, improve patient selection for electrodiagnostic testing and support more personalised clinical decision-making in patients with suspected Carpal Tunnel Syndrome



Objectives

2. Objectives

Primary Objective

This project aims to develop a multivariable predictive model capable of (1) predicting the presence or absence of CTS confirmed by electrodiagnostic testing, (2) estimating the electrophysiological severity of the condition (Minimal / Mild / Moderate / Severe / Extreme) based on a set of variables recognised in the literature as risk factors. It also aims to (3) take the first step into designing a clinical decision support tool that enables physicians to prioritise patient access to the reference exam (NCS), considering both the probability of a CTS diagnosis and the predicted severity of the disease.

Secondary Objectives

Additionally, we aim to (4) compare the performance of logistic regression models with machine learning methods, (5) identify the key variables involved in the diagnostic prediction process, and (6) analyse the impact of each variable on syndrome severity.

Justification

3. Justification

Carpal Tunnel Syndrome is a frequent cause of referral for electrodiagnostic testing in the Neurophysiology Unit of Gaia Espinho Local Health Unit; yet, daily, patients do not meet the criteria for the diagnosis. This reflects the limited specificity of clinical assessment alone and contributes to increased diagnostic workload, prolonged waiting times and inefficient use of healthcare resources.

Although numerous risk factors for CTS have been described in the literature, they are often assessed independently and not integrated into a comprehensive predictive framework. As a result, health care workers currently lack validated tools to estimate an individual's disease probability or severity before electrodiagnostic testing.

The development of a predictive model that combines easily obtainable clinical and demographic information with established risk factors may support more informed clinical decision-making. Such a model has the potential to improve patient stratification, optimise referral pathways for electrodiagnostic studies, and enhance the overall efficiency of diagnostic services.

Furthermore, the use of electrodiagnostic studies as the reference standard ensures objective classification of outcomes and strengthens the clinical validity of the proposed model. By conducting this study in a real-world hospital setting and using consecutive patient inclusion, the findings are expected to reflect routine clinical practice and increase the applicability of the results.

In this context, the present study is justified by its potential to improve diagnostic accuracy, promote the rational use of electrodiagnostic, and advance the application of predictive modelling in the assessment of CTS.

Materials and Methods

4. Materials and Methods

4.1 Study Design

The present study is an observational, analytical, cross-sectional diagnostic and predictive study of consecutive patients referred for electrodiagnostic evaluation with clinical suspicion of CTS. Data collection will take place at the Neurophysiology Unit, integrated in the Neurology Department of the Gaia Espinho Local Health Unit (ULSGE), between January and April 2026.

Each study unit will correspond to a single patient or single hand, always considering the potential for unilateral or bilateral disease. When both hands are assessed in the same patient, each can be analysed as an independent observational unit, with appropriate statistical methods applied to account for intra-subject correlation. Considering this situation, two databases were created: one organised by patients and the other by hand.

4.2 Study Population

ULSGE provides primary healthcare services to the population of *Vila Nova de Gaia* and *Espinho,* which has approximately 335 thousand residents. We aim to study all patients referred to the Neurophysiology Unit for NCS to test the clinical hypothesis of CTS. A consecutive sampling strategy was used to minimise selection bias and reflect the real-world EDX referral population.

4.2.1 Inclusion and exclusion criteria

The inclusion criteria were:

- Age ≥18 years;
- Clinical suspicion of CTS;
- Submit to the full NCS protocol at the Neurophysiology Unit;
- Ability to understand the study and sign the informed consent form;
- Voluntary agreement to participate in the study.

The exclusion criteria were:

- Peripheral neuropathies of other aetiologies or Polyneuropathy;
- Cervical radiculopathy;
- Previous wrist or carpal tunnel surgery;
- Acute traumatic injury to the hand or wrist within the past 3 months;
- Incomplete clinical or electrophysiological data;

4.2.2 Sample size

No formal sample size calculation was performed. The sample size was determined by the number of consecutive patients referred to the Neurophysiology Unit with clinical suspicion of carpal tunnel syndrome during the study period. From a predictive modelling perspective, the available sample was deemed adequate for developing the proposed models. A total of 451 hands were included in the analysis, of which 313 (69.4%) had confirmed CTS.

This number exceeded commonly recommended thresholds for multivariable prediction modelling, ensuring an adequate number of outcome events relative to the number of candidate predictors and reducing the risk of overfitting. For the binary outcome (presence or absence of CTS), the number of events provided more than 30 events per variable included in the final logistic regression model, exceeding the minimum recommendations of 10–20 events per predictor. Likewise, the 313 confirmed CTS cases available for severity analysis were considered sufficient for the development of ordinal logistic regression and Bayesian network models. This approach is consistent with current recommendations for the development of clinical prediction models (38–40).

4.3 Variables

The variables collected were based on a literature search and day-to-day experience on the Neurophysiology Unit (see Table 4.1).

Table 4.1 - Variables collected.

Demographic	**Comorbidities**
Sex	Diabetes Mellitus
Age	Hypothyroidism
Dominant hand	Rheumatoid Arthritis
Occupational Factors	**Anthropometric measures**
Professional Occupation	Weight
Repetitive hand use	Height
Forceful hand use/gripping	BMI
	Hand length
Clinical History	Hand width
Affected side	Wrist diameter antero-posterior
Symptom duration	Wrist diameter medio-lateral
Paraesthesia	Wrist ratio*
Weakness	Grip strength
Pain	
Night awakenings	**Outcome in EDX**
Smoking	Presence/Absence of CTS
Pregnancy in the last year	CTS severity

*Wrist ratio = Wrist diameter antero-posterior/Wrist diameter medio-lateral

4.4 Data collection

All the information needed from the voluntary participants was collected on the day of their NCS appointment using a physical questionnaire. All data obtained in the paper were then entered into the digital database.

A Data Collection Form was used to gather all the information needed to build the database (see annex 10.1). Body weight was determined using a digital weighing scale (measurement uncertainty ± 0.05 kg; maximum of 180 kg), height was obtained using a height chart on the wall, grip strength was measured using a digital hand dynamometer (measurement uncertainty ± 0.1 kg; maximum of 180 kg) and hand measurements were attained with a digital calliper (measurement uncertainty ± 0.03 mm; maximum 250 mm).

The NCS were performed using the equipment Dantec Keypoint version 2.41.0.47 running Keypoint.NET software. The Neurophysiology Unit uses a standardised protocol for NCS, including a specific protocol for diagnosing CTS (see annex 10.2).

The severity of carpal tunnel syndrome was classified according to the criteria proposed by Padua et al. in 1997, which categorise CTS into six severity grades based on abnormalities detected in sensory and motor nerve conduction studies. The cut-off values for normality can be tailored to the realities of each Neurophysiology Unit. The classification includes minimal, mild, moderate, severe, and extreme CTS, reflecting the progressive deterioration of median nerve function (see Table 4.2).

Table 4.2 - CTS severity classification by Padua et al. in 1997.

Minimal	Mild	Moderate	Severe	Extreme
• Abnormal comparative or segmental sensory tests.	• Slow distal sensory latency (≥3.5 ms) • Normal distal motor latency (<4.4 ms)	• Slow distal sensory latency (≥3.5 ms) • Slow distal motor latency (≥4.4 ms)	• Absent distal sensory latency • Slow distal motor latency (≥4.4 ms)	• Absent distal sensory latency • Absent distal motor latency

The diagnosis and classification of CTS require the analysis of multiple electrodiagnostic parameters, including distal motor and sensory latencies, nerve conduction velocity, and the amplitude and morphology of the CMAP and SNAP. The Dantec Keypoint doesn't have a single, static table of reference values for these parameters. Instead, the software comes built with native multi-centre normative databases that automatically adjust based on your patient's age, height, and gender.

Furthermore, the interpretation of nerve conduction studies is supported by internationally recognised reference standards, including those described by Kimura, Preston, and Shapiro, as well as by the American Association of Electrodiagnostic Medicine (AAEM).

Ultimately, reference values should never be interpreted in isolation. NCS findings must always be considered within the individual clinical context, taking into account the patient's symptoms, physical examination, and overall clinical presentation.

4.5 Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics version 31.0.2.0 (126) and R software version 4.6.0. (41,42) A two-sided p-value < 0,05 was considered statistically significant.

Continuous variables were described as mean ± standard deviation (SD) or median and interquartile range (IQR), according to their distribution, whereas categorical variables were presented as absolute and relative frequencies. Between-group comparisons were performed using the independent samples t-test or the Mann–Whitney U test for continuous variables and using Pearson's chi-square test or Fisher's exact test for categorical variables, as appropriate.

To identify factors associated with EDX confirmed CTS, univariable and multivariable binary logistic regression analyses were performed. Variables considered clinically relevant or statistically significant in the univariable analysis were used in the multivariable model. Results were expressed as odds ratios (OR) with corresponding 95% confidence intervals (95% CI).

In parallel, BN models were developed to estimate the probability of EDX-confirmed CTS. Network structure learning was performed using the hill-climbing algorithm and the Bayesian Dirichlet equivalent (BDe) score. Continuous variables were categorised when necessary to avoid sparse conditional probability tables and excessive model complexity.

Model performance was evaluated using confusion matrices, overall accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and balanced accuracy. Receiver operating characteristic (ROC) curves and the area under the curve (AUC) were used to assess discriminative performance. Structural robustness of the Bayesian network was investigated using bootstrap resampling with 500 iterations, and arc strength and direction probabilities were calculated.

In the present study, the conditional probability tables were estimated using Bayesian parameter estimation with an imaginary sample size of 10, as implemented in the bnlearn package. This approach was selected because it provides stable probability estimates while reducing the influence of sparse observations, making it particularly suitable for clinical datasets in which certain combinations of predictor variables occur infrequently (34).

Severity analyses were restricted to patients with CTS diagnoses confirmed in the electrodiagnostic evaluation. CTS severity represents an ordered outcome, so ordinal logistic regression was used to identify factors associated with increasing disease severity. The results were expressed as odds ratios with 95% confidence intervals.

CTS cases were initially classified into five categories (minimum, mild, moderate, severe, and extreme) as this is the classification used at our Neurophysiology Unit. For predictive modelling purposes, these categories were subsequently collapsed into three ordered groups (mild, moderate and severe). Minimum and mild CTS were combined into a single mild category, whereas severe and extreme CTS were grouped into a severe category. This approach was adopted to increase the number of observations per category, improve model stability and reduce sparsity in conditional probability tables (43,44).

Three models with increasing complexity were subsequently developed to predict CTS severity: a multivariable ordinal logistic regression, a Tree-Augmented Naive Bayes and the last using the hill-climbing algorithm. Network structure learning was performed using the hill-climbing algorithm with the BDe score, and parameter estimation was carried out using Bayesian estimation with an imaginary sample size of 10.

Predictive performance of the different models was assessed by confusion matrices, overall accuracy,

Cohen's kappa coefficient, sensitivity, specificity, PPV, NPV and balanced accuracy. Bootstrap analysis with 500 resamples was used to evaluate the stability and reproducibility of the final BN structure.

4.6 Ethical considerations

The study will fully comply with the principles of the Declaration of Helsinki and the General Data Protection Regulation (GDPR). Data was coded and treated confidentially, exclusively for research purposes. Informed consent was obtained from all participants (see annex 10.3), and the protocol was submitted to the Ethics Committee of the Gaia Espinho Local Health Unit for prior approval (document number I16008-202603).

Results

5. Results

5.1 Patient Inclusion

We collected data from 256 patients considered for inclusion; 9 were excluded for the following reasons: 2 due to polyneuropathy, 2 due to cervical radiculopathy, and 5 due to a history of bilateral carpal tunnel surgery. Of the remaining 247 patients, 43 were excluded from the analysis: 20 due to previous unilateral carpal tunnel surgery, another 20 did not report symptoms on that side, and 3 had history of trauma to the hand, wrist or arm. So, of the 494 potentially eligible hands, a total of 451 hands were included in the final analysis (see figure 5.1).

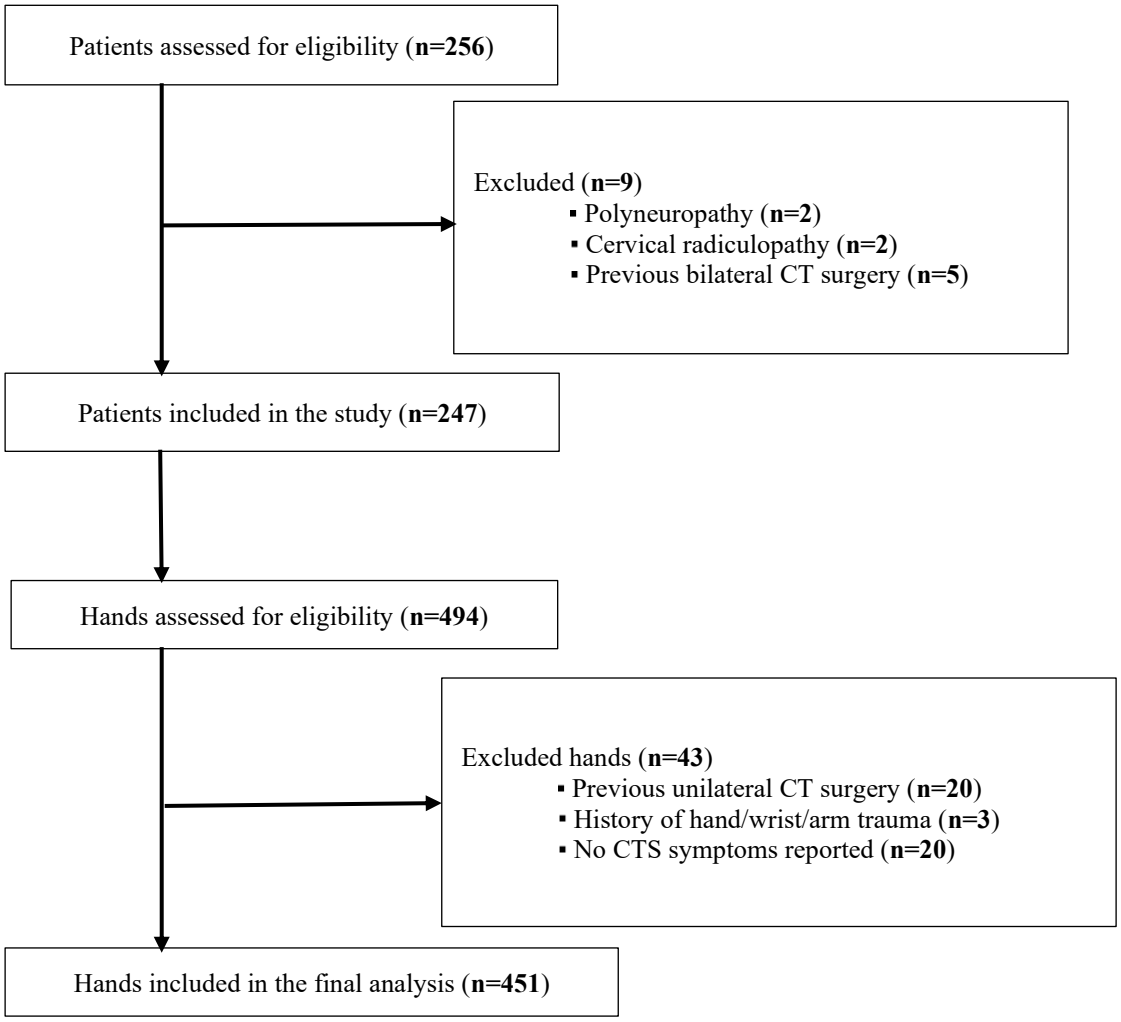


Figure 5.1 - Flowchart of patient and hand selection for inclusion in the study.

5.2 Study Population

The descriptive characteristics of the study population are presented in Table 5.1. Normality was assessed using the Shapiro–Wilk test and visual inspection of histograms and Q–Q plots. Given the relatively large sample size, graphical methods were also used to examine the distributions of continuous variables.

The final cohort consisted of 247 patients with a mean age of approximately 57 years, of whom 194 (78.5%) were female, none were pregnant or had a history of pregnancy in the last year. The median body mass index was 28.0 kg/m² (IQR 25.4 – 31.8). Additional demographic, anthropometric, clinical and electrophysiological characteristics are summarised in Table 5.1.

Table 5.1 - Descriptive characteristics of the study population.

Variable	n (%) or Mean ± SD or median (IQR)
Demographic	
Sex	
Male	53 (21.5)
Age	57 ± 13
Dominant hand	
Right	235 (95.1)
Left	8 (3.2)
Ambidextrous	4 (1.6)
Occupational Factors	
Professional Occupation	
Employed	181 (73.3)
Unemployed	48 (19.4)
Retired	18 (7.3)
Repetitive hand use	157 (63.6)
Forceful hand use/gripping	137 (55.5)
Comorbidities	
Diabetes Mellitus	38 (15.4)
Hypothyroidism	15 (6.1)
Rheumatoid Arthritis	12 (4.9)
Clinical History	
Affected side	
Bilateral	192 (77.7)
Right	29 (11.7)
Left	26 (10.5)
Symptom duration	
<6 months	6 (2.4)
6 – 12 months	36 (14.6)
>12 months	205 (83.0)
Paraesthesia	238 (96.4)

Weakness	151 (61.1)
Pain	151 (61.1)
Night awakenings	186 (75.3)
Smoking	43 (17.4)
Anthropometric measures	
Weight (kg)	72.9 (65.2 – 83.7)
Height (m)	1.61 ± 0.08
BMI (kg/m²)	28.0 (25.4 – 31.8)
Normal weight (18.5 ≤ BMI < 25)	54 (21.9)
Overweight (25 ≤ BMI < 30)	104 (42.1)
Obesity (BMI ≥ 30)	89 (36.0)
Hand length (mm)	RH: 170.70 ± 11.35 LH: 171.22 ± 11.80
Hand width (mm)	RH: 91.74 ± 8.53 LH: 91.32 ± 8.69
Wrist diameter antero-posterior (mm)	RH: 39.79 (37.81 – 43.17) LH: 39.80 (37.60 – 43.48)
Wrist diameter medio-lateral (mm)	RH: 57.10 ± 4.94 LH: 56.91 ± 4.93
Wrist ratio	RH: 0.71 ± 0.04 LH: 0.72 ± 0.04
Grip strength (kg)	RH: 16.60 (11.50 – 22.70) LH: 15.80 (10.90 – 21.20)
Wrist morphology	
Square wrist (wrist ratio > 0.7)	RH: 153 (61.9) LH: 164 (66.4)
Non-square wrist (wrist ratio ≤ 0.7)	RH: 94 (38.1) LH: 83 (33.6)

SD standard deviation | *IQR* interquartile range | *kg* kilograms | *m* meters | *kg/m²* kilograms per square meter | *mm* millimetres | *LH* Left Hand | *RH* Right Hand

5.3 Electrophysiological findings

Subsequent analyses were performed at the hand level (n=451), since each hand was considered an independent observation. As shown in Table 5.2, of the 451 hands included in the study, 313 (69.4%) were diagnosed with CTS, while 138 (30.6%) had normal electrophysiological findings. Among the CTS cases (313), mild and moderate forms were the most frequent, representing 198 hands (63.3%), whereas minimum, severe and extreme forms accounted for the remaining cases.

Table 5.2 – Carpal Tunnel Syndrome (CTS) presence and severity in Electrodiagnostic studies (EDX).

Outcome in EDX	**n (%)**		
CTS		Right Hand	Left Hand
Present	313 (63.4)	156 (63.2)	157 (63.6)
Absent	138 (27.9)	65 (26.3)	73 (29.6)
Non-evaluated	43 (8.7)	26 (10.5)	17 (6.9)
CTS severity		Right Hand	Left Hand
Minimum	60 (12.2)	26 (10.5)	34 (13.8)
Mild	110 (22.3)	49 (19.8)	61 (24.7)
Moderate	88 (17.8)	49 (19.8)	39 (15.8)
Severe	49 (9.9)	29 (11.7)	20 (8.1)
Extreme	6 (1.2)	3 (1.2)	3 (1.2)

5.4 Univariate analysis of factors associated with CTS

Univariate analyses were performed to identify variables associated with the electrophysiological diagnosis of CTS.

In Table 5.3, patients with CTS were significantly older than those without CTS ($p = 0.002$) and presented significantly higher BMI values ($p < 0.001$). Similarly, obesity was more frequent among CTS cases when BMI was analysed categorically ($p = 0.007$). Diabetes mellitus was also significantly associated with CTS ($p = 0.026$).

Regarding clinical characteristics, longer symptom duration ($p = 0.019$), self-reported weakness ($p = 0.007$), pain ($p = 0.012$), and nocturnal awakenings ($p < 0.001$) were significantly associated with CTS. No significant association was found for paraesthesia ($p = 0.086$).

Anthropometric analysis demonstrated a significant association between CTS and wrist morphology. Hands diagnosed with CTS showed larger antero-posterior wrist diameters ($p < 0.001$), higher wrist ratios ($p < 0.001$), and a higher prevalence of square wrist morphology ($p = 0.001$). In contrast, hand length, hand width, mediolateral wrist diameter, and grip strength were not significantly associated with CTS.

No significant associations were observed for sex, smoking status, hypothyroidism, rheumatoid arthritis, repetitive hand use, forceful hand use, or occupational status.

Variables demonstrating significant associations in the univariate analysis were subsequently considered for multivariable modelling and Bayesian network development.

Table 5.3 – Comparison and univariate analysis of demographic, occupational, clinical and anthropometric characteristics between hands with and without carpal tunnel syndrome.

Variable	Total (n=451)	CTS Present (n=313)	CTS Absent (n=138)	p-value
Sex				0.204
Female	356 (78.9)	242 (77.3)	114 (82.6)	
Male	95 (21.1)	71 (22.7)	24 (17.4)	
Age	56.47 (± 12.65)	57.66 (± 13.10)	53.76 (± 11.14)	**0.002**
Professional Occupation				0.067
Employed	332 (73.6)	223 (71.2)	109 (79.0)	
Retired	88 (19.5)	70 (22.4)	18 (13.0)	
Unemployed	31 (6.9)	20 (6.4)	11 (8.0)	
Repetitive hand use	288 (63.4)	198 (63.3)	88 (63.8)	0.918
Forceful hand use/gripping	253 (56.1)	172 (55.0)	81 (58.7)	0.460
Diabetes	68 (15.1)	55 (17.6)	13 (9.4)	**0.026**
Hypothyroidism	27 (6.0)	20 (6.4)	7 (5.1)	0.587
Rheumatoid arthritis	24 (5.3)	16 (5.1)	8 (5.8)	0.765
Smoking	82 (18.2)	53 (16.9)	29 (21.0)	0.516
Symptom duration				**0.019**
< 6 months	9 (2.0)	7 (2.2)	2 (1.4)	--
6 – 12 months	67 (14.9)	56 (17.9)	11 (8.0)	--
> 12 months	375 (83.1)	250 (79.9)	125 (90.6)	--
Paraesthesia	435 (96.5)	305 (97.4)	130 (94.2)	0.086
Weakness	278 (61.6)	180 (57.5)	98 (71.0)	**0.007**
Pain	278 (61.6)	181 (57.8)	97 (70.3)	**0.012**
Night awakenings	347 (76.9)	263 (84.0)	84 (60.9)	**<0.001**
BMI category				**0.007**
Normal	98 (21.7)	57 (18.2)	41 (29.7)	
Overweight	193 (42.8)	133 (42.5)	60 (43.5)	
Obesity	160 (35.5)	123 (39.3)	37 (26.8)	
BMI, kg/m²	28.60 (± 4.45)	29.10 (± 4.32)	27.46 (± 4.54)	**<0.001**
Hand length, mm	170.75 (± 11.53)	170.72 (± 11.72)	170.80 (± 11.11)	0.953

Hand width, mm	91.23 (± 8.58)	91.38 (± 8.48)	90.88 (± 8.82)	0.566
Wrist diameter ML, mm	56.04 (43.45 – 60.04)	56.50 (53.70 – 60.44)	55.64 (53.09 – 59.14)	0.094
Wrist diameter AP, mm	39.71 (37.63 – 43.17)	40.30 (38.02 – 43.96)	38.77 (36.90 – 41.97)	**<0.001**
Wrist ratio	0.71 (± 0.04)	0.72 (± 0.04)	0.70 (± 0.04)	**<0.001**
Square wrist morphology	288 (63.9)	215 (68.7)	73 (52.9)	**0.001**
Grip strength, kg	16.40 (11.30 – 22.10)	16.50 (11.35 – 22.00)	15.95 (11.20 – 22.45)	0.818

Frequencies are presented: n (%); Means are presented: mean (± SD); Medians are presented: median (IQR);
SD standard deviation | *IQR* interquartile range *kg* kilograms | *m* meters | *kg/m²* kilograms per square meter | *mm* millimetres | *LH* Left Hand | *RH* Right Hand | *ML* Medio-Lateral | *AP* Antero-Posterior

5.5 Models for CTS diagnosis

5.5.1 Initial multivariate logistic regression model (LR1)

We identified 11 variables significantly associated with CTS in the univariate analysis (see Table 5.3) and used them in the development of the first model. Since 3 of those variables were related to the wrist and overlapped (wrist diameter AP, wrist ratio, and square wrist morphology), we chose to use only wrist ratio in this model.

Hence, a multivariable binary logistic regression analysis was performed using 9 variables (Table 5.4) to identify independent predictors of CTS. The overall model was statistically significant ($\chi^2 = 85.247$, $p < 0.001$), indicating that the included variables improved the prediction of CTS compared with the null model.

According to the Nagelkerke R^2, the model explained 24.3% of the variance in CTS occurrence. The Hosmer–Lemeshow goodness-of-fit test showed no evidence of lack of fit ($\chi^2 = 2.631$, $p = 0.955$), indicating good calibration. Overall, the model correctly classified 72.7% of the hands, with a sensitivity of 92.7% and a specificity of 27.5%.

After adjustment for the remaining covariates, increasing age (OR = 1.028, 95% CI 1.009–1.048; p = 0.004), higher BMI (OR = 1.084, 95% CI 1.028–1.143; p = 0.003), the presence of nocturnal awakenings (OR = 4.361, 95% CI 2.607–7.295; p < 0.001), and wrist ratio (OR = 2.189, 95% CI 1.377–3.479; p < 0.001) remained independently associated with CTS.

Sex, diabetes mellitus and self-reported weakness were not independently associated with CTS after adjustment for the remaining variables. Symptom duration contributed significantly to the model (p = 0.023), although none of its categories reached statistical significance.

Interestingly, pain remained independently associated with CTS after adjustment, although the direction of the association (OR < 1) suggests a complex relationship with the remaining predictors and should be interpreted cautiously.

Table 5.4 – Initial multivariable logistic regression analysis of factors associated with CTS.

Variable	OR	95% CI	p-value
Sex	1.112	0.608 – 2.034	0.730
Age	1.028	1.009 – 1.048	**0.004**
Diabetes mellitus	1.669	0.828 – 3.486	0.148
Symptom duration	----	----	**0.023***
Weakness	0.641	0.389 – 1.054	0.080
Pain	0.556	0.343 – 0.901	**0.017**
Night awakenings	4.361	2.607 – 7.295	**<0.001**
BMI, kg/m²	1.084	1.028 – 1.143	**0.003**
Wrist ratio (square wrist)	2.189	1.377 – 3.479	**<0.001**

*Overall effect of symptom duration

OR Odds Ratio | *CI* Confidence Interval | *kg/m²* kilograms per square meter

5.5.2 Final multivariate logistic regression model (LR2)

Variables that did not retain statistical significance in the initial model (sex, diabetes and weakness) were removed to obtain a more parsimonious model while preserving predictive performance (Table 5.5).

The reduced model remained statistically significant ($\chi^2 = 79.927$, $p < 0.001$), with a Nagelkerke R^2 of 0.229, and calibration was also adequate according to the Hosmer–Lemeshow goodness-of-fit test ($\chi^2 = 4.817$, $p = 0.777$). The model correctly classified 72.9% of the cases, with a sensitivity of 91.4% and a specificity of 31.2%.

Increasing age (OR 1.032, 95% CI 1.014–1.051; $p < 0.001$), higher BMI (OR 1.088, 95% CI 1.032–1.146; $p = 0.002$), presence of nocturnal awakenings (OR 4.284, 95% CI 2.580–7.114; $p < 0.001$) and square wrist morphology (OR 2.257, 95% CI 1.427–3.568; $p < 0.001$) were independently associated with CTS. Symptom duration showed a significant overall effect ($p = 0.013$), and pain also remained independently associated with the outcome (OR 0.551, 95% CI 0.344–0.882; $p = 0.013$).

Table 5.5 - Final multivariable logistic regression analysis.

Variable	OR	95% CI	p-value
Age	1.032	1.014 – 1.051	**<0.001**
Symptom duration	----	----	**0.013***
Pain	0.551	0.344 – 0.882	**0.013**
Night awakenings	4.284	2.580 – 7.114	**<0.001**
BMI, kg/m²	1.088	1.032 – 1.146	**0.002**
Wrist morphology (square wrist)	2.257	1.427 – 3.568	**<0.001**

*Overall effect of symptom duration.

OR Odds Ratio | *CI* Confidence Interval | *kg/m²* kilograms per square meter

5.5.3 Tree-Augmented Naïve Bayes (TAN3)

The development of the Bayesian networks was made considering the variables identified by the univariate and multivariate analyses as associated with the diagnosis of CTS. To reduce model complexity and avoid sparse conditional probability tables, age was categorised into three groups (<50 years, 50–64 years and ≥65 years), and BMI was used in its categorical form (Normal weight, Overweight and Obesity). (45) We also used wrist morphology (square vs non-square wrist) over wrist ratio because the former is a categorical variable.

A TAN model was developed as an intermediate Bayesian classifier, allowing one additional dependency between predictor variables while maintaining the CTS diagnosis as the class node. The resulting network included direct arcs from CTS diagnosis to all predictor variables, along with additional dependencies between age and sex, BMI, diabetes, nocturnal awakenings and wrist morphology, as well as between sex and pain and between BMI and symptom duration (Figure 5.2).

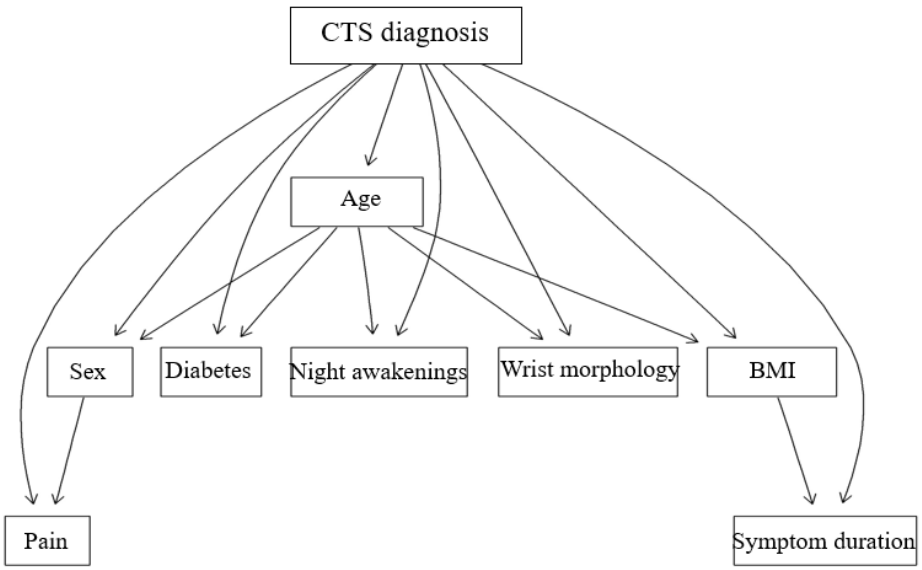


Figure 5.2 – Structure of the TAN3 with 8 variables.

The TAN model correctly classified 335 of 451 hands, corresponding to an overall accuracy of 74.3%. Sensitivity was 87.2%, specificity 44.9%, positive predictive value 78.2%, negative predictive value 60.8%, and balanced accuracy 66.1%. Cohen's kappa coefficient was 0.347, indicating fair agreement beyond chance. The model showed good discriminative ability, with an AUC of 79.1%.

5.5.4 Hill-climbing Bayesian Network (BN4)

A clinically oriented BN was developed using the same variables as in the initial multivariable logistic regression model, while allowing additional dependencies between predictor variables. The network structure was learned using the hill-climbing algorithm with the Bayesian Dirichlet equivalent (BDe) score. Parameter estimation was performed using Bayesian estimation with an imaginary sample size of 10.

The BN4, as shown in Figure 5.3, included age, BMI, symptom duration, pain, nocturnal awakenings and wrist morphology as direct parent nodes of electrodiagnostic confirmed CTS. Additional dependencies between predictors were identified, including directed associations between age and sex, age and diabetes, diabetes and BMI, and sex and pain.

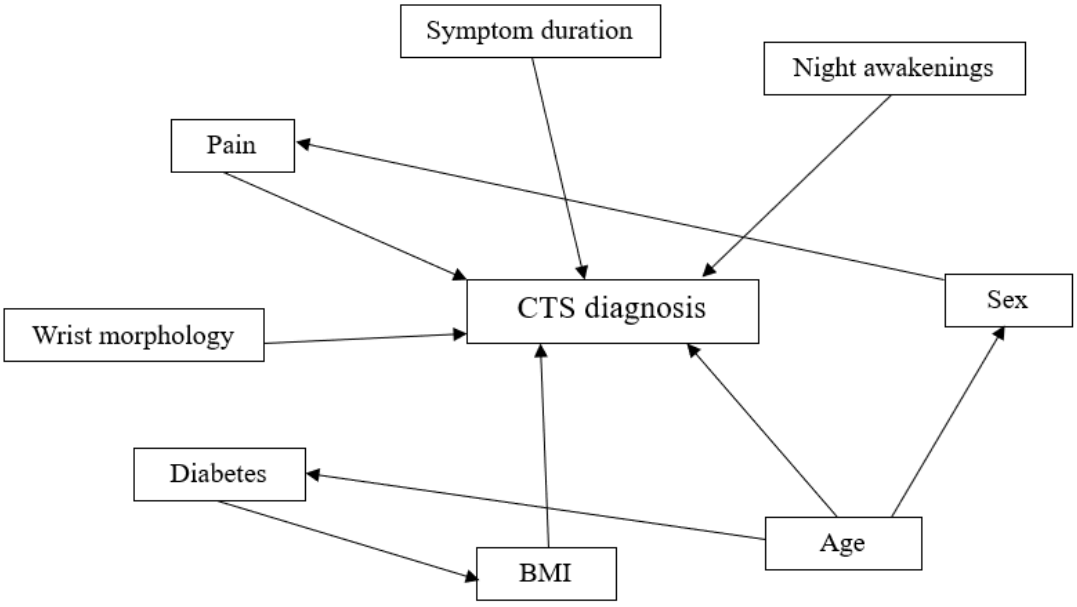


Figure 5.3 - Structure of the BN4 model with 8 variables.

The resulting model correctly classified 364 of 451 hands, corresponding to an overall accuracy of 80.7%. Sensitivity was 91.1%, whereas specificity was 57.3%. Positive and negative predictive values were 82.9% and 73.8%, respectively. The balanced accuracy was 74.2%, and Cohen's kappa coefficient was 0.515. The discriminative performance of the BN4 was good, with an area under the receiver operating characteristic curve (AUC) of 88.3%.

The stability of the BN structure was assessed using bootstrap resampling with 500 iterations. Three arcs linking symptom duration, nocturnal awakenings and wrist morphology to CTS demonstrated good structural robustness, being identified in more than 70% of bootstrap samples. In particular, the association between nocturnal awakenings and CTS was highly stable, observed in 99.8% of bootstrap samples. Additional dependencies among predictors, including relationships between age and sex, age and diabetes, diabetes and BMI, and sex and pain, also demonstrated strengths above 0.80. However, the directionality of most arcs was less stable, with directional probabilities close to 0.5, indicating that the presence of these associations was more robust than their orientation. Overall, bootstrap resampling supported the reproducibility of the main network relationships while suggesting some uncertainty regarding arc direction.

5.5.5 Final Hill-climbing Bayesian Network (BN5)

A second BN was developed using the variables retained in the final multivariable logistic regression model under the same conditions as the first network.

The BN5 included age, BMI, symptom duration, pain, nocturnal awakenings and wrist morphology as direct parent nodes of electrodiagnostic confirmed CTS, as shown in Figure 5.4.

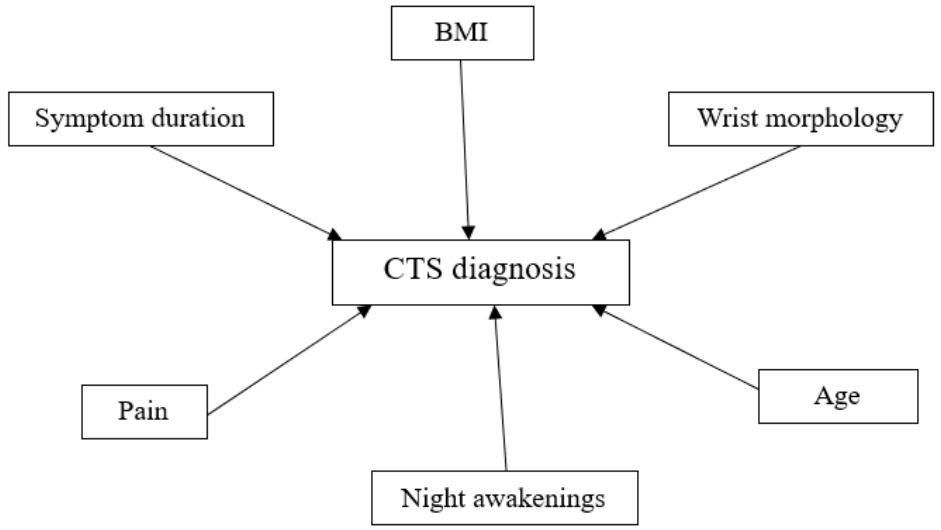


Figure 5.4 - Structure of the BN5 model with 6 variables.

The resulting model correctly classified 360 of 451 hands, corresponding to an overall accuracy of 79.8%. Sensitivity was 91.1%, and specificity was 54.4%, while positive and negative predictive values were 81.9% and 72.8%, respectively. The balanced accuracy was 72.7%, and Cohen's kappa coefficient was 0.489. The discriminative performance was good, with an AUC of 88,0%.

The evaluation of the BN structure stability using bootstrap resampling with 500 iterations demonstrated excellent stability of the network structure. All arcs connecting age, BMI, symptom duration, pain, nocturnal awakenings and wrist morphology to electrodiagnostic confirmed CTS were identified in 100% of bootstrap samples, with complete directional consistency.

5.5.6 Performance of predictive models

The predictive performance of the five developed models (LR1, LR2, TAN3, BN4, and BN5) is summarised in Table 5.6 and illustrated by the ROC curves in Figure 5.5.

The LR1 model achieved an AUC of 73.2%. After variable selection, the LR2 model demonstrated a modest improvement in discriminative performance, with an AUC of 74.88%.

The TAN3 model was developed as an intermediate Bayesian classifier, achieving 74.3% accuracy and an AUC of 79.1%. Although this model outperformed both logistic regression models, its predictive performance remained lower than that of the unrestricted Bayesian network models.

Both BN4 and BN5 models outperformed the previous ones. The BN4 achieved the highest discriminative ability (AUC = 88.3%), correctly classifying 364 of 451 hands (accuracy = 80.7%), with a sensitivity of 91.1% and a specificity of 57.3%.

The BN 5, developed using only the predictors retained in the LR 2 model, showed very similar performance (AUC = 88.0%; accuracy = 79.8%). Although its specificity was slightly lower (54.4%), sensitivity remained unchanged at 91.1%.

Table 5.6 – Performance of the predictive models.

	Accuracy (%)	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*	*NPV (%)*	*Balanced Accuracy (%)*	*Cohen's kappa*	*AUC (%)*
LR1	72.7	**92.7**	27.5	74.4	62.3	60.1	0.239	73.2
LR2	72.9	91.4	31.2	75.1	61.4	61.3	0.261	74.8
TAN3	74.3	87.2	44.9	78.2	60.8	66.1	0.347	79.1
BN4	**80.7**	91.1	**57.3**	**82.9**	**73.8**	**74.2**	**0.515**	**88.3**
BN5	79.8	91.1	54.4	81.9	72.8	72.7	0.489	88.0

CI=95%

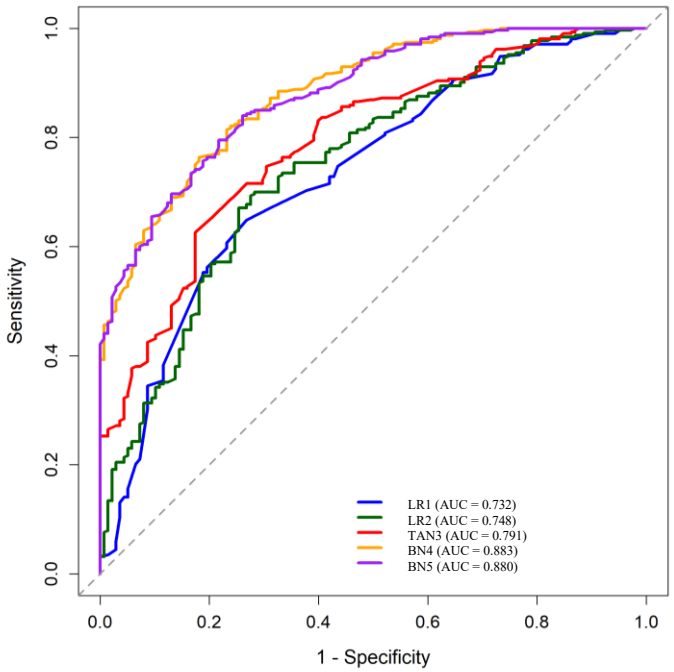


Figure 5.5 - Receiver operating characteristic curves for LR, TAN and BN models.

5.6 Analysis of CTS severity

Among the 313 CTS cases, severity was initially distributed as follows: minimum (n = 60), mild (n = 110), moderate (n = 88), severe (n = 49) and extreme (n = 6). Because only six hands were classified as extreme CTS, and to improve model stability, minimum and mild cases were grouped into a single mild category, whereas severe and extreme cases were combined into a severe category. Thus, severity prediction analyses were performed using three ordered categories (mild, moderate and severe). After regrouping, 170 cases were classified as mild, 88 as moderate and 55 as severe.

5.6.1 Multivariable ordinal logistic regression (LR6)

A multivariable ordinal logistic regression was performed to identify factors associated with increasing CTS severity. The model included variables previously identified as independent predictors of CTS diagnosis (Table 5.7), along with sex, which was retained due to its established clinical relevance.

Age, BMI and nocturnal awakenings were independently associated with greater CTS severity. The metrics (see Table 5.7) show that each additional year of age increased the odds of belonging to a higher severity category by approximately 5.4%, while each 1 kg/m² increase in BMI increased these odds by approximately 7.2%. Patients reporting nocturnal awakenings had nearly twice the odds of presenting more severe CTS.

In contrast, symptom duration showed no significant overall association with CTS severity (likelihood ratio test, p=0.193). Likewise, sex, weakness, pain, wrist morphology and diabetes were not independently associated with CTS severity after adjustment for the remaining covariates.

Nevertheless, these variables were retained in subsequent Bayesian network development due to their established clinical relevance and predictive value for CTS diagnosis.

Table 5.7 - Multivariable ordinal logistic regression model for the prediction of CTS severity.

Variable	OR	95% CI	p-value
Sex	1.42	0.645 – 2.000	0.644
Age	1.054	1.034 – 1.076	**<0.001**
Diabetes mellitus	1.111	0.601 – 2.035	0.733
Symptom duration	----	----	0.193*
Weakness	1.183	0.739 – 1.903	0.485
Pain	0.826	0.513 – 1.333	0.433
Nocturnal awakenings	1.954	1.042 – 3.787	**0.041**
BMI, kg/m²	1.072	1.015 – 1.133	**0.013**
Wrist morphology (square wrist)	1.373	0.834 – 2.286	0.217

*Overall effect of symptom duration

OR Odds Ratio | *CI* Confidence Interval | *kg/m²* kilograms per square meter

5.6.2 Tree-Augmented Naïve Bayes (TAN7)

A TAN model was developed to classify CTS severity. The resulting network retained CTS severity as the class node and incorporated additional dependencies among predictor variables identified by the TAN algorithm (Figure 5.6).

The TAN7 model correctly classified 193 of 313 hands, yielding an overall accuracy of 61.7%. The model achieved a Cohen's kappa coefficient of 0.297, indicating fair agreement beyond chance. Sensitivity was 85.9% for mild CTS, 28.4% for moderate CTS, and 40.0% for severe CTS, while the corresponding specificities were 46.2%, 88.9%, and 93.0%, respectively. Balanced accuracy ranged from 58.6% to 66.6% across the three severity categories.

Given the superior flexibility of unrestricted Bayesian networks for modelling complex probabilistic dependencies among clinical variables, a more comprehensive Bayesian network was subsequently developed using hill-climbing structure learning.

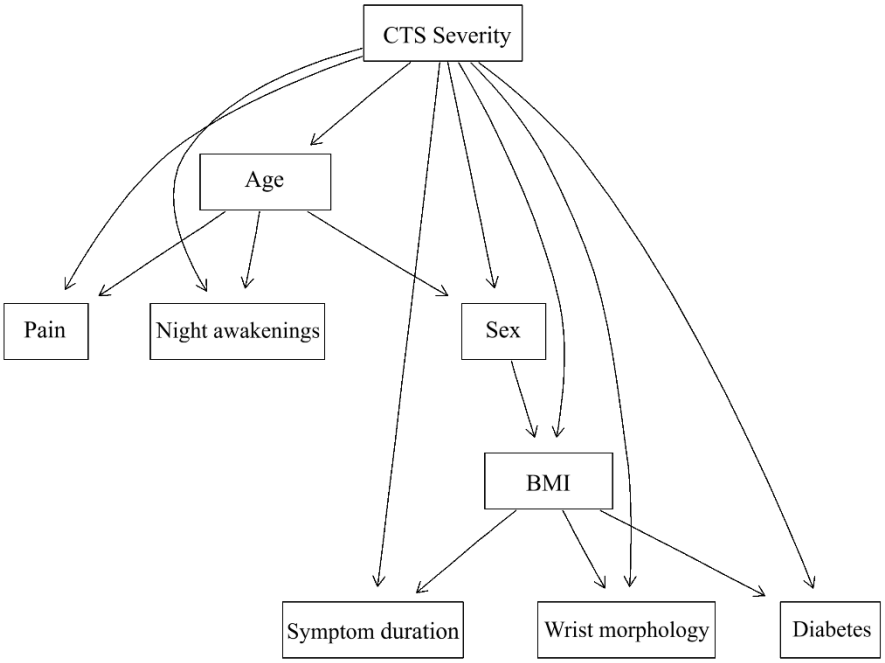


Figure 5.6 – Structure of the TAN 7 model for the classification of CTS severity with 8 variables.

5.6.3 Hill-climbing Bayesian Network (BN8)

A BN was developed to predict CTS severity using the previous variables as direct parent nodes of the outcome, while allowing additional dependencies between them. The final network included two additional relationships between predictors: age/sex, sex/pain and diabetes/BMI (Figure 5.7).

The model correctly classified 73.5% of the observations, corresponding to an overall accuracy of 73.5% (Cohen's $\kappa = 0.537$). Sensitivity was 87.1% for mild CTS, 61.4% for moderate CTS and 50.9% for severe CTS. Balanced accuracy ranged from 73.3% to 78.8% across severity categories, indicating good overall discriminative performance.

BN evaluation using 500 bootstrap resamples demonstrated excellent structural stability. All direct arcs connecting the predictor variables to CTS severity were identified in 100% of bootstrap samples. In addition, the relationships between age group and sex (94.2%) and between sex and pain (83.2%) were consistently reproduced, supporting the robustness of the learned network structure.

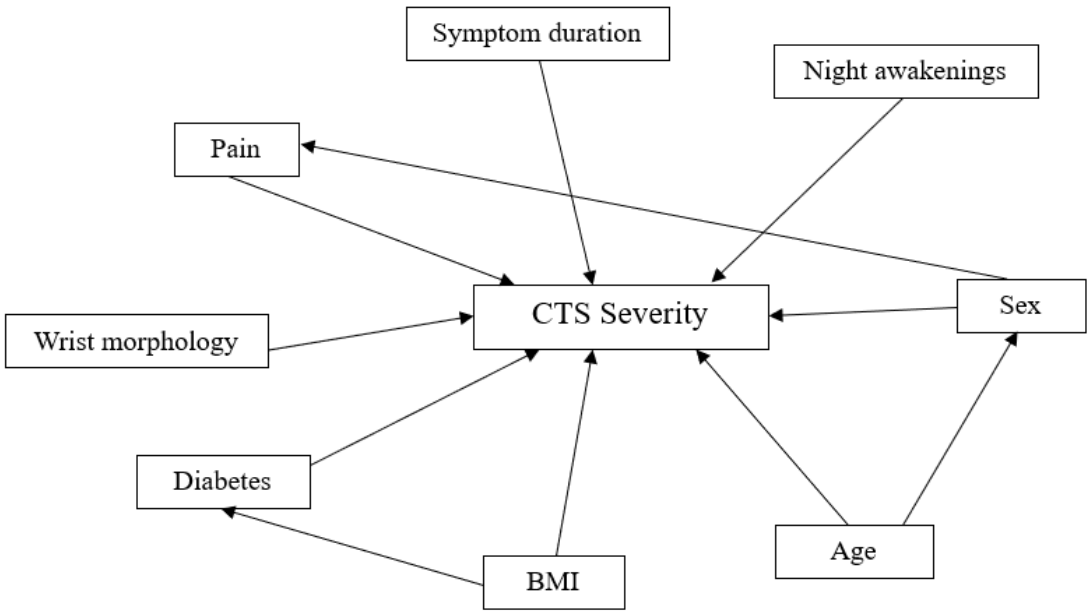


Figure 5.7 - Structure of the BN8 model for CTS severity prediction with 8 variables.

We attempted to develop a model using only the variables identified as independent predictors by ordinal logistic regression (age, nocturnal awakenings and BMI). Unlike the diagnosis model, restricting the severity of the BN resulted in a substantial reduction in predictive performance. Therefore, the expanded BN8 was retained as the final model for CTS severity classification.

5.6.4 Performance of predictive models

The predictive performance of the 3 models (LR6, TAN7 and BN8) was subsequently compared as shown in Table 5.8. The LR6 achieved an overall accuracy of 55.6% (Cohen's $\kappa = 0.136$), correctly identifying most mild CTS cases (sensitivity 91.2%) but showing poor discrimination for moderate (11.4%) and severe CTS (16.4%). Compared with ordinal logistic regression, the TAN7 model improved the overall classification accuracy from 55.6% to 61.7% and increased the kappa coefficient from 0.136 to 0.297. Sensitivity improved for moderate (28.4% vs. 11.4%) and severe CTS (40.0% vs. 16.4%).

In contrast, the BN8 substantially improved classification performance, increasing the overall accuracy to 73.5% ($\kappa = 0.537$). Sensitivity increased to 61.4% for moderate CTS and 50.9% for severe CTS, while maintaining high sensitivity for mild CTS (87.1%). Balanced accuracy was consistently higher across all severity categories, supporting the BN's superior predictive performance for CTS severity classification.

Table 5.8 - Comparison of predictive performance between LR8, TAN7 and BN8 models for CTS severity classification.

	Accuracy (%)	***Cohen's k***	***Sensitivity (%)***			***Specificity (%)***			***Balanced accuracy (%)***		
			Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe
LR 6	55.6	0.136	**91.2**	11.4	16.4	30.8	88.4	94.6	61.0	49.9	55.5
TAN7	61.7	0.297	85.9	28.4	40.0	46.2	**88.9**	93.0	66.0	58.7	66.5
BN8	**73.5**	**0.537**	87.1	**61.4**	**50.9**	**70.6**	86.7	**95.7**	**78.8**	**74.0**	**73.3**

CI=95%

Discussion

6. Discussion

This study developed and compared several predictive models for the diagnosis and severity of CTS using demographic, anthropometric and clinical variables collected before electrodiagnostic testing. We used two distinct approaches: LR and BN. Among them, BNs consistently demonstrated superior predictive performance when compared with LR models. While LR2 only attained an AUC of 74.8%, BN4 achieved the highest discriminative ability for CTS diagnosis, with an AUC of 88.3%, even BN5 showed comparable performance using fewer predictors. When predicting CTS severity, BN8 also outperformed the LR6, presenting sensitivities approximately three to five times higher for moderate and severe cases: 61.4% versus 11.4% for moderate CTS and 50.9% versus 16.4% for severe CTS, respectively.

Across all models, increasing age, higher BMI, longer symptom duration, nocturnal awakenings and wrist morphology emerged as the most consistent predictors of CTS. For disease severity, age, BMI, and nocturnal symptoms remained independently associated with more advanced electrodiagnostic involvement.

Age was a consistent predictor across all models developed in this study. Increasing age was independently associated with both the presence and severity of CTS, a finding consistent with previous epidemiological studies that have identified age as a major risk factor for median nerve compression (3,6,46). Several mechanisms may explain this association, including age-related degenerative changes in connective tissues, reduced nerve regenerative capacity, and the cumulative effect of lifelong exposure to biomechanical stress. In addition, older individuals are more likely to present with systemic conditions that may further predispose them to median nerve dysfunction. The association between age and disease severity is also biologically plausible. Prolonged compression of the median nerve may lead to progressive demyelination and secondary axonal loss, resulting in more severe electrodiagnostic abnormalities. This is reflected in the present study, where increasing age remained an independent predictor of greater CTS severity after adjustment for other clinical and anthropometric variables (2,3,6,27,47).

BMI was another consistent predictor across the developed models, being independently associated with both the presence and severity of CTS. Obesity is one of the best-established risk factors for CTS and has been consistently identified in epidemiological studies and systematic reviews. Although the underlying mechanisms are not fully understood, several explanations have been proposed. Increased adipose tissue within and around the carpal tunnel may elevate intracarpal pressure, while obesity is also associated with chronic low-grade inflammation, metabolic dysfunction, and structural changes in connective tissues that may increase susceptibility to median nerve compression. The relationship between obesity and CTS severity observed in this study further supports the hypothesis that excess body weight not only contributes to disease development but may also influence its progression (3,6,22,27).

Nocturnal awakenings emerged as one of the strongest clinical predictors of both CTS diagnosis and disease severity. This finding is consistent with the clinical presentation of CTS, in which nocturnal symptoms are considered a hallmark of median nerve compression. Increased intracarpal pressure during sleep, particularly when the wrist is flexed, has been proposed as the main mechanism underlying nocturnal symptom exacerbation. Sustained

compression compromises intraneural blood flow and axonal transport, leading to transient ischaemia and increased nerve irritability, which may explain the characteristic night-time pain and paraesthesia experienced by many patients. The persistence of nocturnal awakenings as an independent predictor after multivariable adjustment suggests that this symptom provides clinically relevant information beyond that captured by demographic and anthropometric factors alone. This observation aligns with previous studies and clinical guidelines, which consistently identify nocturnal symptoms as among the most discriminative clinical features of CTS. Although individual symptoms should not be used in isolation to establish the diagnosis, the present findings support their value when incorporated into multivariable predictive models alongside established risk factors (3,11,47,48).

Symptom duration was independently associated with CTS but did not remain a significant predictor of electrodiagnostic severity after multivariable adjustment. This finding suggests that patients with longer-lasting symptoms are more likely to have CTS; however, symptom duration alone may not accurately reflect the extent of median nerve dysfunction. The relationship between symptom duration and disease severity is complex and may be influenced by considerable inter-individual variability, including disease progression, symptom perception, and healthcare-seeking behaviour. Previous studies have reported inconsistent associations between symptom duration and electrodiagnostic severity. While some authors have described a positive correlation between longer symptom duration and more advanced nerve impairment, others have found that clinical symptoms do not necessarily imply electrophysiological findings. Patients may tolerate symptoms for prolonged periods before seeking medical attention, while others present early despite relatively mild complaints. These findings highlight the importance of combining symptom duration with demographic, anthropometric and clinical variables when estimating the probability of CTS. The absence of an independent association between disease severity and symptom duration in the present study also supports the concept that symptom progression and nerve dysfunction do not always occur in parallel, reinforcing the need for electrodiagnostic evaluation to accurately assess the extent of median nerve involvement (3,11,13,48).

Wrist morphology was consistently associated with CTS diagnosis across the predictive models developed in this study, supporting previous evidence that wrist anatomical characteristics contribute to median nerve compression. Individuals with a relatively square-shaped wrist have been reported to be at increased risk of CTS, presumably because a reduced carpal tunnel cross-sectional area limits the available space for the median nerve and flexor tendons. Consequently, even modest increases in tunnel contents or intracarpal pressure may be sufficient to produce symptomatic nerve compression. The association between wrist morphology and CTS has been reported in several anthropometric studies, although the magnitude of its effect has varied across populations. Differences in measurement techniques, diagnostic criteria and patient characteristics may partly explain these inconsistencies. In the present study, wrist morphology remained an important predictor even after adjustment for age, BMI and symptom duration, suggesting that anatomical factors provide complementary information beyond traditional demographic and clinical variables. Interestingly, wrist morphology was associated with CTS diagnosis but not with electrodiagnostic severity. This finding suggests that anatomical characteristics may primarily influence an individual's susceptibility to developing median nerve compression rather than determining the extent of nerve damage once the disease is established. Disease progression is likely to depend on additional factors, including the duration and magnitude of compression, metabolic comorbidities and individual biological variability (3,21,49).

Female sex and diabetes are widely recognised risk factors for CTS and were therefore included in the BN4 based on their established clinical relevance. Although both variables contributed to the overall predictive model, neither emerged as a strong independent predictor in the multivariable analyses. This finding does not contradict the existing literature but rather suggests that part of their effect may be mediated through or shared with other

demographic and clinical variables included in the models (3,6,22).

The higher prevalence of CTS among women has been consistently reported in epidemiological studies and is generally attributed to a combination of anatomical, hormonal and occupational factors. Women typically have smaller carpal tunnel dimensions relative to tendon volume, which may increase the median nerve susceptibility to compression. Hormonal influences, particularly during pregnancy and menopause, have also been proposed as contributing mechanisms, although their precise role remains incompletely understood. In the present study, however, the predictive contribution of sex was modest after adjustment for age, BMI, wrist morphology and clinical symptoms, suggesting that these variables may account for much of the observed sex-related difference. On the other hand, the predominance of female participants in the present cohort may also have limited the ability to detect sex-related differences; this distribution reflects the well-established epidemiology of CTS in clinical practice (3,6,47).

Diabetes has similarly been associated with an increased risk of CTS through mechanisms including peripheral nerve vulnerability, connective tissue glycation and chronic microvascular dysfunction. Nevertheless, its independent predictive value was limited in the present study. One possible explanation is the relatively low prevalence of diabetes in the study population, which reduces its statistical contribution after adjustment for other predictors. Moreover, diabetes may increase susceptibility to nerve compression without necessarily being a major determinant of electrodiagnostic severity once CTS has developed. These findings highlight that well-established epidemiological risk factors do not always retain strong independent predictive value when evaluated alongside multiple correlated clinical variables (3,6,50).

No significant associations were observed for smoking status, hypothyroidism or rheumatoid arthritis. The absence of an association with smoking is consistent with a recent meta-analysis, in which cohort and case–control studies did not support smoking as an independent risk factor for CTS after accounting for study quality, bias and confounding (51). Evidence regarding hypothyroidism is also relatively weak, with a previous meta-analysis reporting only a modest association that was partly attenuated after adjustment for confounding and publication bias (52). In contrast, rheumatoid arthritis has been associated with an increased risk of CTS in previous studies (53). Its lack of significance in the present analysis may reflect the limited number of participants with this condition and the use of a binary comorbidity variable, which did not account for disease duration, inflammatory activity or treatment.

The absence of significant associations for repetitive hand use, forceful hand use and occupational status should be interpreted cautiously. Previous evidence supports a dose–response relationship between occupational biomechanical exposure and CTS, particularly when repetition and forceful exertion are combined (9). In the present study, however, these exposures were recorded as self-reported binary variables and did not quantify their intensity, frequency, duration or cumulative exposure. This relatively broad classification may have resulted in exposure misclassification and reduced the ability to detect associations. Similarly, occupational status is only an indirect indicator of biomechanical exposure and may not adequately represent the specific physical demands of each occupation or previous occupational exposure, particularly among retired or unemployed participants.

Furthermore, the study population consisted exclusively of individuals referred for electrodiagnostic evaluation because of suspected CTS. Consequently, hands without electrodiagnostically confirmed CTS were not asymptomatic population controls but belonged predominantly to symptomatic individuals with normal nerve conduction findings. Established population-level risk factors may therefore have had limited ability to discriminate between these two clinically selected groups. Overall, these findings indicate limited independent diagnostic contribution within the present sample rather than the absence of an etiological role.

The most influential variables identified in this study are consistent with the current understanding of CTS

pathophysiology and epidemiology. Age, obesity, symptom duration and nocturnal symptoms have repeatedly been recognised as important determinants of both disease occurrence and severity, although the strength and consistency of these associations vary across factors and studies (3,6,11,22,27,47).

Interestingly, some variables previously associated with CTS, namely pain and wrist morphology, did not retain statistical significance when severity was the outcome. This suggests that certain factors may contribute to the occurrence of CTS but not necessarily to progression towards more severe electrodiagnostic forms (46).

For the CTS diagnosis, LRs have very low specificity (27.5 – 31.2%), while BNs almost duplicate that value (44.9 – 57.3%) without compromising sensitivity (87.2 – 91.1%). So, it is not only the AUC that improves; BNs maintain high sensitivity to identify cases with CTS while improving the ability to detect cases without CTS.

Additionally, although LR identified only age, BMI and nocturnal awakenings as significant predictors of increasing CTS severity, the BN approach demonstrated that additional variables, such as symptom duration, wrist morphology, pain, sex, and diabetes, contributed to improved classification accuracy.

LR's ability to correctly classify severity categories was limited, with a marked tendency to assign observations to the mild category. In contrast, the BN provided a substantially more balanced classification across all severity categories, resulting in higher overall accuracy and balanced accuracy.

The present findings, therefore, support existing evidence and demonstrate that modelling the relationships among these variables using BN may improve predictive performance beyond conventional regression-based approaches (36,54,55).

6.1 Predictive models

One of the principal findings of this study was the superior predictive performance of BN compared with conventional LR models. Although LR identified several significant predictors of CTS and disease severity, the BN consistently achieved higher discriminative ability for CTS diagnosis while simultaneously providing a graphical representation of the probabilistic relationships between variables. These findings suggest that BN may represent a valuable alternative for modelling complex clinical conditions in which multiple demographic, anthropometric and symptomatic factors interact.

Unlike LR, which assumes a direct independent relationship between each predictor and the outcome, BN explicitly models conditional dependencies among variables. This characteristic is particularly relevant in CTS, where several predictors are biologically and clinically interrelated. For example, increasing age is associated with a higher prevalence of diabetes, obesity and other comorbidities, while BMI may influence metabolic status (22,27). By incorporating these dependencies, BN provides a more realistic representation of the underlying mechanisms contributing to median nerve compression.

The BN4 developed in the present study demonstrated the highest diagnostic performance, achieving an AUC of 88.3% while maintaining excellent sensitivity. Notably, the simpler network (BN5), based on only five directly connected predictors, achieved comparable diagnostic performance, suggesting that clinically meaningful models can be developed without requiring many variables. This characteristic may facilitate implementation in routine clinical practice, where rapid assessment based on a limited number of readily available variables is desirable.

The diagnostic performance of BN4 may also be considered in relation to commonly used provocative tests. In a meta-analysis of 67 studies, the Phalen test showed a median sensitivity of 70% and specificity of 80%, while the corresponding values were 59% and 80% for Tinel's sign and 67% and 74% for the Durkan test (56). Compared with these estimates, BN4 demonstrated substantially higher sensitivity (91.1%), although its specificity was lower

(57.3%). This performance profile may be advantageous for referral prioritisation, where minimising missed CTS cases is particularly important. Nevertheless, these comparisons are indirect because the studies differed in population characteristics, test execution and reference standards. Moreover, the performance of BN4 was measured in its development sample and may be optimistic until confirmed through internal and external validation.

An additional advantage of BN is its ability to estimate individual probabilities rather than simply generating binary classifications. This allows clinicians to explore how changes in specific patient characteristics influence the estimated probability of CTS and provides a transparent framework for clinical decision support. Furthermore, BN can accommodate incomplete information by updating probability estimates as new clinical data become available, a feature that may be particularly useful in real-world clinical settings where not all variables are immediately available (36).

Despite these advantages, BNs should not be viewed as a replacement for electrodiagnostic testing. Instead, they should be considered complementary decision-support tools that can improve patient stratification before referral for nerve conduction studies.

Several ML approaches have recently been investigated for this purpose. Artificial neural networks (ANNs), support vector machines (SVMs), random forests (RFs) and other supervised learning algorithms have generally demonstrated good diagnostic performance when trained on clinical, electrophysiological or ultrasound data. However, many of these approaches rely on complex computational models that provide limited insight into how individual predictors contribute to the final prediction, reducing their interpretability in routine clinical practice (43,57–59).

In contrast, BNs combine competitive predictive performance with a transparent probabilistic structure that explicitly represents dependencies between variables. This interpretability represents a significant advantage in clinical practice, where understanding how individual patient characteristics contribute to the predicted outcome is often as important as the prediction itself. Furthermore, BNs naturally accommodate missing information and can continuously update probability estimates as additional clinical data become available, making them particularly suitable for decision-support applications in healthcare (36).

Park et al. compared seven supervised ML algorithms for predicting electrodiagnostic CTS severity using demographic, clinical, ultrasonographic and electrophysiological variables. Among the evaluated models, XGB achieved the highest external validation accuracy (76.6%), closely followed by RF and KNN (75.6%). The most influential predictors included pain intensity, BMI, symptom duration, thenar weakness, palmar bowing, median nerve cross-sectional area and age, highlighting the value of combining multiple clinical and imaging parameters to improve predictive performance (43).

Similarly, Yetiş et al. demonstrated that ML algorithms based exclusively on anthropometric measurements and hand strength assessments could accurately identify CTS. RF achieved the highest diagnostic accuracy (89.5%), followed by XGB (86.8%), supporting the feasibility of using readily obtainable clinical variables for non-invasive CTS screening without requiring imaging or electrodiagnostic data (59).

Also, Elseddik et al. expanded the scope of ML applications by integrating demographic characteristics, clinical history, patient-reported outcome measures, ultrasonographic findings and electrodiagnostic parameters into ensemble learning models. Their approach achieved diagnostic accuracies between 90 and 95.5% for the different models used. They also developed models for predicting treatment outcomes following ultrasound-guided hydrodissection injection. However, these models relied on information that is typically only available after specialist assessment, potentially limiting their applicability during the initial clinical evaluation (57).

In another perspective, Inui et al. extended the application of ML beyond diagnosis by developing models to

predict postoperative electrophysiological severity and patient-reported outcomes following carpal tunnel release. Using LR, SVM, RF and Light Gradient Boosting Machine (LGBM), the authors reported the best classification performance with LGBM (AUC = 80.2%), while RF achieved the best results for predicting postoperative symptom improvement. These findings further illustrate the expanding role of ML across different stages of CTS management, from diagnosis to prognostic prediction (58).

To our knowledge, very few studies have explored BNs for predicting CTS diagnosis or severity using routinely available demographic and clinical variables. We identified one application that involved modelling treatment outcomes following conservative and surgical interventions rather than diagnostic prediction (60).

Collectively, these studies demonstrate the growing potential of ML for CTS diagnosis and management. Nevertheless, most published models prioritise predictive performance and rely on discriminative algorithms that provide limited insight into the relationships between predictors. In contrast, the BN developed in the present study was designed to provide both accurate prediction and clinical interpretability. The BN4 achieved excellent discrimination (AUC = 88.3%), while explicitly representing the conditional dependencies between demographic, anthropometric and clinical variables. Furthermore, unlike many previously published models, the proposed network estimates the probability of both CTS diagnosis and electrodiagnostic severity using information routinely available before nerve conduction studies, making it particularly suitable as a clinical decision-support tool for patient triage and prioritisation.

6.2 Study limitations

This study has several limitations that should be considered when interpreting its findings. First, it was conducted at a single centre and included only individuals referred for electrodiagnostic evaluation because of suspected CTS. Consequently, the sample represents a clinically selected population rather than the general population, and the findings may not be directly generalisable to primary care settings, asymptomatic individuals or populations with different referral practices. Moreover, the cross-sectional design allowed the identification of associations and predictive relationships but did not permit causal inferences or assessment of the temporal relationship between risk factors and CTS development or progression.

Second, both hands from the same participant could be included in the analysis. Although this increased the number of observations available for model development, observations from the same individual may not be completely independent because both hands share demographic, metabolic and occupational characteristics. This within-participant correlation may therefore have influenced the precision of the estimates. Several clinical and occupational variables were also self-reported and recorded using relatively broad categories. In particular, repetitive and forceful hand use was not quantified by intensity, frequency, duration or cumulative exposure, potentially leading to exposure misclassification. Similarly, symptom characteristics may have been affected by recall and reporting bias.

Continuous and ordinal variables, including age, BMI, symptom duration and electrodiagnostic severity, were categorised for some analyses. Although categorisation facilitated the development and interpretation of the discrete BNs and reduced sparsity within the conditional probability tables, it inevitably resulted in some loss of information and introduced data-dependent or clinically defined thresholds. In addition, the smaller number of observations in some severity categories may have limited the models' ability to distinguish moderate and severe CTS.

Finally, model performance was evaluated using the same clinical setting from which the models were

developed. Therefore, the reported results should be interpreted as estimates of performance within the development population and may be optimistic when applied to new patients. Although internal validation can assess model stability and optimism, external validation in independent and more diverse populations remains necessary before clinical implementation. In the absence of internal and external validation, the models should therefore be regarded as exploratory tools requiring further validation, calibration assessment and evaluation of their clinical utility.

Conclusion

7. Conclusion

This study developed and compared LR and BN models for predicting the presence and electrodiagnostic severity of CTS using routinely available demographic, anthropometric and clinical information. Age, BMI, symptom duration, nocturnal awakenings and wrist morphology emerged as relevant predictors of CTS diagnosis, while age, BMI and nocturnal awakenings were independently associated with increasing electrodiagnostic severity.

The BNs demonstrated better diagnostic performance than conventional logistic regression, particularly through their greater ability to identify hands without CTS while maintaining high sensitivity for confirmed cases. Their graphical structure also provided a clinically interpretable representation of the probabilistic dependencies among predictors. For severity prediction, progressively expanded networks improved the classification of moderate and severe CTS, although these categories remained more difficult to identify than mild disease.

Overall, these findings suggest that BNs represent a promising approach for modelling CTS, as they combine predictive ability with an intuitive representation of the complex relationships between demographic, anthropometric and symptomatic factors. Following external validation, such models could support clinical assessment and prioritisation of electrodiagnostic testing referrals. Nevertheless, they should be regarded as decision-support tools rather than replacements for clinical examination or electrodiagnostic confirmation.



Future Work

8. Future Work

Future research should focus primarily on the internal validation using k-fold cross validation and then external validation of the proposed models in larger and more diverse populations. Multicentre prospective studies involving different clinical settings and referral pathways are needed to determine whether model performance is maintained beyond the population in which the models were developed. These studies should also account for the correlation between hands from the same participant by using appropriate statistical methods.

Further model development could incorporate additional clinically relevant variables, such as detailed occupational exposure, symptom distribution, physical examination findings and validated clinical questionnaires. Whenever possible, continuous variables such as age and BMI should be retained in their original form, to avoid information loss associated with categorisation. Alternative BN structures and parameter-learning methods could also be investigated, particularly approaches that can handle both continuous and categorical variables.

Future validation should extend beyond discrimination and classification measures to include calibration, clinical utility and comparison with existing diagnostic approaches. Decision-curve analysis may help determine whether the models provide a meaningful clinical benefit at different probability thresholds. The models could subsequently be translated into an accessible clinical decision-support tool and evaluated prospectively to determine whether they improve referral prioritisation, reduce unnecessary electrodiagnostic examinations and support the earlier identification of patients at risk of more severe CTS.

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Annexes

10. Annexes

10.1 Annex 1 – Clinical Information Form

Modelo preditivo da Síndrome do Túnel Cárpico
Formulário para recolha de dados

Código do participante: _____ Data: ___/___/_____

1. Dados Demográficos

Idade: _____ anos

Sexo: ☐ M ☐ F

Mão dominante: ☐ Direita ☐ Esquerda ☐ Ambidestro

2. Ocupação profissional

Profissão: _____

Movimentos repetitivos da (s) mão(s): ☐ Sim ☐ Não

Uso de força/preensão manual: ☐ Sim ☐ Não

Força de preensão manual: Direita_____ kg Esquerda_____ kg

3. História clínica

Diabetes: ☐ Sim ☐ Não

Hipotiroidismo: ☐ Sim ☐ Não

Gravidez (no último ano): ☐ Sim ☐ Não ☐ N/A

Tabagismo: ☐ Sim ☐ Não ☐ Ex-fumador (>1 ano)

Artrite reumatoide: ☐ Sim ☐ Não

Outras comorbilidades relevantes: _____

Medicação relevante: _____

4. Sintomas

Lado afetado: ☐ Direito ☐ Esquerdo ☐ Bilateral

Duração dos sintomas: ☐ < 6 meses ☐ 6 -12 meses ☐ > 12 meses

Parestesias: ☐ Sim ☐ Não

Fraqueza: ☐ Sim ☐ Não

Dor: ☐ Sim ☐ Não

Despertares noturnos devido aos sintomas: ☐ Sim ☐ Não

5. Medidas Antropométricas

Altura: _____ cm

Peso: _____ kg

IMC: _____ kg/m^2

Mão Direita

A - Comprimento da mão: _____ mm

B - Largura da mão: _____ mm

C - Largura medio-lateral do punho (2) _____ mm

D - Largura ântero-posterior do punho (1) _____ mm

- Índice do punho (1/2): _____

Mão Esquerda

A - Comprimento da mão: _____ mm

B - Largura da mão: _____ mm

C - Largura medio-lateral do punho (2) _____ mm

D - Largura ântero-posterior do punho (1) _____ mm

- Índice do punho (1/2): _____

6. Estudo Neurofisiológico

Mão Direita: STC: ☐ Presente ☐ Ausente

Se Presente:

Grau de severidade: ☐ Mínimo ☐ Ligeiro ☐ Moderado ☐ Severo ☐ Extremo

Mão Esquerda: STC: ☐ Presente ☐ Ausente

Se Presente:

Grau de severidade: ☐ Mínimo ☐ Ligeiro ☐ Moderado ☐ Severo ☐ Extremo

7. Observações e Assinatura

Observações: _____

_____

Investigador: _____ Data: ___/___/_____

10.2 Annex 2 - Neurophysiology Unit Protocol for NCS in suspected cases of CTS

1- Explain the procedure to the patient.

2- The evaluation begins with motor nerve conduction studies of the median nerve. Surface recording electrodes are placed over the *abductor pollicis brevis* (APB) muscle, with the active electrode positioned over the muscle belly and the reference electrode in the first metacarpal-phalangeal joint. The ground electrode is positioned between the active and the stimulation site: distally, 8 cm from the APB, slightly lateral to the mid wrist between the tendons to the flexor carpi radialis and palmaris longus; proximally, at the antecubital fossa, just medial to the brachial artery. The distance between both stimulation sites is measured to calculate nerve conduction velocity.

3- Next step is the motor nerve conduction study of the cubital nerve. The active electrode is placed over the muscle belly of the *abductor digiti minimi* (ADM) and the reference electrode in the fifth metacarpal-phalangeal joint. The ground electrode is positioned between the active and the stimulation site: distally, 8 cm from the ADM, medial wrist adjacent to the *flexor carpi ulnaris tendon.*

4- At this point starts the evaluation of mixed conduction studies, for both median and cubital nerve. The active and reference electrodes are placed at the wrist, first over the median nerve then on the cubital nerve, at an interelectrode distance of 2,5 – 4 cm, with the active electrode closest to the stimulator. The stimulation site is the palm of the hand, at exactly 8 cm from the active electrode, the stimulator is placed laterally when evaluating the median nerve and medially for the cubital nerve.

5- Finally, sensory nerve conduction studies are performed on digit 4, which has dual innervation, from both median and cubital nerve. Active and reference electrodes are placed on the finger, at an interelectrode distance of 2,5 – 4 cm, the first just above the metacarpal-phalangeal joint and the second over the distal interphalangeal joint. The stimulation sites are on the wrist, the same ones used to study the motor potentials for median and cubital nerves. The distance between the active electrode and stimulator depends on hand length and varies between 12 and 15 cm, same distance must be used for both studies.

6- If needed, to better characterize CTS' severity, sensory nerve conduction studies of digit 2 (median nerve) and digit 5 (cubital nerve) can also be performed.

Additionally, in severe cases, when the APB muscle is completely atrophied and no motor response can be elicited, the second lumbrical muscle may be evaluated. If this response is also absent, additional studies are necessary to ensure that the underlying pathology is confined to the carpal tunnel. In these situations, the palmar cutaneous branch of the median nerve can be examined. As this branch originates proximally to the carpal tunnel and does not pass through it, sensory conduction should remain preserved in isolated CTS, thereby helping to distinguish it from more proximal median neuropathies or generalized peripheral nerve disorders.

These steps allowed us to determine the main outcome: presence or absence of CTS and, if present, its severity.

10.3 Annex 3 – Informed Consent

UNIDADE LOCAL DE SAÚDE GAIA E ESPINHO — CONSENTIMENTO INFORMADO ESCLARECIDO E LIVRE CIEL

Por favor, leia com atenção a seguinte informação. Se achar que algo está incorreto ou que não está claro, não hesite em solicitar mais informações. Se concorda com a proposta que lhe foi feita, queira assinar este documento.

Título do estudo:

"A Predictive Model for Detecting and Grading Carpal Tunnel Syndrome Using Known Risk Factors"

Enquadramento:

O presente estudo insere-se no âmbito do Mestrado de Informática Médica da Faculdade de Medicina da Universidade do Porto. Pretende-se recolher e analisar dados clínicos e demográficos de doentes submetidos a estudos de condução nervosa, realizados por suspeita de Síndrome do Túnel do Carpo, com o objetivo de desenvolver um modelo preditivo que auxilie no diagnóstico e estratifique a gravidade da doença.

Explicação do estudo / Objetivos:

Este estudo tem como objetivo principal desenvolver e validar um modelo preditivo capaz de estimar a probabilidade de um doente apresentar STC, e, nos casos positivos, prever a respetiva gravidade, com base em características clínicas, antropométricas e ocupacionais (como idade, sexo, índice de massa corporal, medidas da mão, profissão, etc).

Não haverá qualquer intervenção adicional nem alteração ao procedimento habitual adotado na realização do eletrodiagnóstico. O estudo baseia-se exclusivamente na recolha e análise de dados obtidos no decurso da prática clínica habitual.

Condições e financiamento:

Este estudo não possui financiamento externo e é conduzido exclusivamente por profissionais da ULSGE. Não existe qualquer benefício económico direto para os investigadores ou para a instituição decorrente da realização do estudo.

Informar sobre riscos e/ou benefícios decorrentes do estudo:

A participação não acarreta riscos adicionais para o participante, uma vez que não são realizados procedimentos ou exames fora da prática clínica de rotina. Embora não existam benefícios diretos para o participante, espera-se que os resultados contribuam para o aperfeiçoamento dos métodos diagnósticos e para uma melhor orientação clínica de futuros doentes com STC.

Informação sobre custos para o próprio decorrente da participação e se está previsto ressarcimento ou não e quem suporta os referidos custos

A participação não implica quaisquer custos adicionais para o participante, nem está previsto qualquer ressarcimento. Todos os procedimentos incluídos fazem parte da prática clínica habitual.

O propósito da recolha de dados/ constituição da base de dados

Os dados recolhidos servirão para criar uma base de dados de investigação destinada exclusivamente ao desenvolvimento e validação do modelo preditivo referido. Esta base de dados será utilizada apenas para fins científicos e de investigação clínica, de acordo com o protocolo aprovado pela Comissão de Ética da ULSGE.

Garantia que os dados recolhidos e tratados são necessários (minimização dos dados)

Serão recolhidos apenas os dados estritamente necessários à concretização dos objetivos do estudo, garantindo a aplicação do princípio da minimização de dados previsto no RGPD.

Garantia que os dados serão usados exclusivamente para os fins específicos (limitação dos dados) e que para efeitos de investigação serão submetidos a análise por uma comissão de ética

Os dados recolhidos serão utilizados exclusivamente para os fins científicos descritos neste documento.

As medidas de segurança que serão adotadas para proteger os dados (segurança dos dados)

Os dados serão codificados (isto é, substituídos por um código numérico) de modo a impedir a identificação direta dos participantes. A base de dados será armazenada em sistema informático protegido com palavra-passe e acesso restrito à investigadora. Serão adotadas medidas técnicas e organizativas adequadas à proteção contra acesso, modificação ou destruição não autorizados.

Identificação dos responsáveis pela base de dados

O Investigador Principal é responsável pela criação, gestão e manutenção da base de dados de investigação, garantindo o cumprimento de todas as normas éticas e legais aplicáveis.

Garantia que os dados não são partilhados com terceiros (se existir partilha de dados a terceiros, especificar detalhadamente)

Os dados não serão partilhados com terceiros fora da ULSGE.

O prazo de conservação dos dados

Os dados serão conservados por um período máximo de 5 anos após a conclusão do estudo. Após esse prazo, serão eliminados de forma segura.

Como serão eliminados os dados quando ultrapassado o prazo de conservação

Findo o período de conservação, os dados eletrónicos serão eliminados permanentemente dos sistemas informáticos através de métodos de destruição segura, garantindo a impossibilidade de recuperação.

Confidencialidade e anonimato:

Todas as informações recolhidas são estritamente confidenciais. Nenhum participante será identificado em publicações, apresentações ou relatórios. Os dados serão analisados de forma codificada e sem referência direta à identidade dos doentes.

Reconhecer a possibilidade do participante retificar, consultar ou retirar os dados a qualquer momento (direito ao esquecimento)

O participante tem o direito de aceder, corrigir ou solicitar a eliminação dos seus dados pessoais a qualquer momento, sem qualquer prejuízo. Para exercer este direito, poderá contactar a equipa de investigação ou o Encarregado de Proteção de Dados da ULSGE.

Garantia da liberdade de participação no estudo e de desistir a qualquer momento sem consequências decorrentes dessa decisão

A participação é totalmente voluntária. O participante pode recusar-se a participar ou desistir a qualquer momento, sem qualquer impacto no tratamento, acompanhamento ou relação com a instituição.

E-mail do EPD da ULSGE, para o participante apresentar dúvidas/reclamação sobre recolha e tratamento dos dados

Para esclarecimento de dúvidas ou apresentação de reclamações sobre o tratamento dos dados pessoais, o participante poderá contactar o Encarregado de Proteção de Dados da ULSGE através do seguinte e-mail: dpo@ulsge.min-saude.pt.

Pedir consentimento para publicação do estudo:

Autorizo que os resultados deste estudo possam ser publicados em revistas científicas ou apresentados em congressos, desde que não contenham qualquer dado identificativo dos participantes.

Identificação Investigador

Nome: Diana Patrícia Oliveira Miller

Contacto: 916933028

N.º Cédula Profissional: C-050124102

Assinatura: _____

Declaro ter lido e compreendido este documento, bem como as informações verbais que me foram fornecidas pela/s pessoas/s que acima assina/m. Foi-me garantida a possibilidade de, em qualquer altura, recusar participar neste estudo sem qualquer tipo de consequências. Desta forma, aceito participar neste estudo e permito a utilização dos dados que de forma voluntária forneço, confiando em que apenas serão utilizados para esta investigação e nas garantias de confidencialidade e anonimato que me são dadas pelo/a investigador/a.

Nome: _____ Processo Clínico n.º _____

Assinatura: _____ Data: __ /__ /_____

Se não for o próprio a assinar por idade ou incapacidade

(se o menor tiver discernimento deve também assinar em cima)

Nome:

Identificação N.º: Validade:

Grau de parentesco ou tipo de representação:

Assinatura: _____

ESTE DOCUMENTO, COMPOSTO DE 3 PÁGINA/S, É FEITO EM DUPLICADO:
UMA VIA PARA O/A INVESTIGADOR/A, OUTRA PARA A PESSOA QUE CONSENTE[1]

[1] De acordo com a Declaração de Helsínquia e a Convenção de Oviedo