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SERGIO MURILO GEORGETO

**SÍNDROME DO TÚNEL DO CARPO BILATERAL E
IDIOPÁTICA: CARACTERIZAÇÃO CLÍNICO-FUNCIONAL E
EFICÁCIA DE DOIS TRATAMENTOS FISIOTERAPÊUTICOS
COMBINADOS PARA REABILITAÇÃO DE PACIENTES
CLÍNICOS E CIRÚRGICOS**

Londrina
2022

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Tese apresentada ao Programa de Pós-Graduação em Ciências da Reabilitação programa associado entre a Universidade Estadual de Londrina e a Universidade Pitágoras Unopar, como requisito parcial para a obtenção do título de Doutor em Ciências da Reabilitação.

Orientador: Profa. Dra. Karen Barros Parron Fernandes

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Londrina, 16 de fevereiro de 2022

Aos meus pais, irmã, sobrinha, filhos, genro e neto,
bem como aos amigos, pelo apoio, compreensão
e incentivo, compartilhando das alegrias e das tristezas.

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“A ciência é a confrontação das hipóteses”
(Aristóteles)

GEORGETO, Sérgio Murilo. **Síndrome do Túnel do Carpo Bilateral e Idiopática: Caracterização Clínico-Funcional e a Eficácia da Combinação de Diferentes Técnicas de Fisioterapia para Reabilitação de Pacientes Clínicos e Cirúrgicos.** 2022.165 páginas. Tese (Doutorado em Ciências da Reabilitação) - programa associado entre a Universidade Estadual de Londrina - UEL - e a Universidade Pitágoras Unopar [UNOPAR] – Universidade Pitágoras Unopar, Londrina, 2022.

RESUMO

Introdução: A presente tese realizou um estudo sobre a síndrome do túnel do carpo (STC) bilateral idiopática que é a neuropatia compressiva mais frequente na população mundial adulta. Apesar da alta prevalência, há controvérsias na literatura quanto a melhor forma de conduzir esses casos. **Objetivos:** O primeiro estudo pretendeu atualizar os aspectos clínico-funcionais da STC e discorreu sobre as algumas opções de tratamento; o segundo estudo objetivou avaliar o uso combinado do alongamento com a mobilização miofascial com instrumentos (*instrument-assisted soft tissue mobilization* ou IASTM) no tratamento clínico de STC bilateral idiopática leve e moderada; no terceiro estudo analisou o efeito da gabapentina como medicação preemptiva na dor pós-cirúrgica de STC bilateral idiopática; o quarto estudo verificou o efeito da mesma combinação de técnicas utilizadas no segundo artigo, na reabilitação pós-cirúrgica da STC, averiguando a diferença de resposta entre a mão operada e a mão não operada. **Métodos:** No primeiro estudo foi realizada uma revisão de literatura atualizada sobre o tema proposto. Para o segundo estudo realizou-se um ensaio clínico randomizado (ECR) *cross-over* com portadores de STC bilateral idiopática leve e moderada, a fim de avaliar a resposta para combinação terapêutica alongamento/IASTM ou IASTM/alongamento durante o seguimento de seis meses. No terceiro e quarto estudo participaram indivíduos com STC bilateral idiopática com pelo menos uma das mãos apresentando comprometimento severo. No terceiro estudo, analisou-se o efeito analgésico preventivo da gabapentina por meio de um ECR, confrontando um grupo usando gabapentina *versus* placebo. Foram avaliadas as medidas da dor percebida e do consumo de analgésicos. No quarto estudo, os pacientes submetidos ao tratamento cirúrgico foram encaminhados para a reabilitação, utilizando um modelo de estudo igual ao realizado no segundo artigo. **Resultados:** 1) o alongamento e a IASTM são alternativas promissoras para reconstruir as características viscoelásticas e a integridade tensional do tecido conectivo subsinovial; 2) a combinação das terapias de alongamento e IASTM teve um efeito positivo sendo os resultados mantidos por seis meses; 3) A gabapentina pré-operatória foi efetiva na melhora da dor na mão operada, além de diminuir o consumo de analgésicos; 4) A combinação de terapias foi relevante na reabilitação pós-cirúrgica tanto da mão operada como na não operada em relação ao período com efeitos considerados grandes para a quase totalidade dos desfechos. A comparação de resposta entre a mão operada e a mão não operada teve um efeito positivo em ambas as mãos, demonstrando que a opção de operar a mão severa e tratar ambas as mãos com a combinação das terapias preconizadas, independentemente da sua gravidade, foi uma estratégia válida. **Conclusão:** Os métodos fisioterapêuticos utilizados são úteis na reabilitação da STC bilateral idiopática e o emprego combinado do alongamento e da IASTM mostrou ter um efeito aditivo no tratamento clínico. O uso de gabapentina preemptiva foi eficaz na redução da dor pós-operatória e a utilização da combinação alongamento/IASTM foi efetiva no tratamento pós-cirúrgico. A mão não operada obteve melhora expressiva,

independentemente da sua gravidade, o que demonstra a eficácia da estratégia utilizada para essa população.

Palavras-chave: Síndrome do Túnel do Carpo, Exercícios de Alongamento Muscular, Liberação Miofascial, Fisioterapia, Estudos Cross-Over.

GEORGETO, Sérgio Murilo. **Bilateral and Idiopathic Carpal Tunnel Syndrome: Clinical-Functional Characterization and the Efficacy of the Combination of Different Physiotherapy Techniques for Rehabilitation of Clinical and Surgical Patients.** 2022. 165 páginas. Tese (doutorado em Ciências da Reabilitação) - programa associado entre a Universidade Estadual de Londrina – UEL – e a Universidade Pitágoras Unopar [UNOPAR] – Universidade Pitágoras Unopar, Londrina, 2022.

ABSTRACT

Introduction: The present thesis carried out a study on idiopathic bilateral carpal tunnel syndrome (CTS), which is the most frequent compressive neuropathy in the adult world population. Despite its high prevalence, there are controversies in the literature regarding the best way to manage these cases. **Objectives:** The first study aimed to update the clinical-functional aspects of CTS and discussed some treatment options; the second study aimed to evaluate the combined use of stretching and myofascial mobilization with instruments (instrument-assisted soft tissue mobilization or IASTM) in the clinical treatment of mild and moderate bilateral idiopathic CTS; the third study analyzed the effect of gabapentin as a preemptive medication in the postoperative pain of idiopathic bilateral CTS; the fourth study verified the effect of the same combination of techniques used in the second article, in the post-surgical rehabilitation of CTS, analyzing the difference in response between the operated hand (OH) and the non-operated hand (NO). **Methods:** For the first study, an updated literature review was carried out on the intended theme. In the second study, a cross-over Randomized Clinical Trial (RCT) was performed with patients with mild and moderate idiopathic bilateral CTS, in order to evaluate the response to the therapeutic combination stretching/IASTM or IASTM/stretching during the six-month follow-up. For the third and fourth studies, individuals with bilateral idiopathic CTS with at least one hand presenting severe impairment were selected. In the third study, proof of the preventive effect of gabapentin was performed by a double-blind RCT, one group used the referred medication versus placebo. Measures of perceived pain and analgesic consumption were evaluated. In the fourth study, patients undergoing surgical treatment were referred into rehabilitation, using the same study design as that performed in the second article. **Results:** 1) rehabilitation methods such as stretching and IASTM are promising alternatives in reconstructing the viscoelastic characteristics and the tensile integrity of the subsynovial connective tissue; 2) the combination of stretching and IASTM therapies had a positive effect and the results were maintained for six months; 3) the use of preoperative gabapentin was effective in alleviating pain in the OH, in addition to reducing the consumption of analgesics; 4) The combination of therapies was relevant in the post-surgical rehabilitation of both OH and NO in relation to the period. The response comparison between OH and NO had a positive effect on both hands, demonstrating that the option of operating on the severe hand and treating both hands with the combination of the recommended therapies, regardless of their severity, was a valid strategy. **Conclusion:** The physiotherapeutic methods used are useful in the rehabilitation of idiopathic bilateral CTS and the combined use of stretching and IASTM has been shown to have an additive effect on clinical treatment; the use of preemptive gabapentin, in turn, proved to be efficient in reducing postoperative pain; the use of the stretching/IASTM combination was effective in postoperative treatment; finally, the unoperated hand had an expressive improvement, despite its severity, demonstrating that the strategy used was effective for this population.

Key words: Carpal Tunnel Syndrome, Muscle Stretching Exercises, Musculoskeletal Manipulations, Physiotherapies, Cross-Over Studies.

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LISTA DE ABREVIATURAS E SIGLAS

ACP - abdutor curto do polegar

ADM - amplitude de movimento

IASTM - instrument-assisted soft tissue mobilization

CA - cirurgia aberta

CC- centro de coordenação

CE - cirurgia endoscópica

CF- centro de fusão

cm - centímetro

CONSORT - *consolidated standards of reporting trials*

EAV- escala analógica visual

ENMG - eletroneuromiografia

IMC - índice de massa corpórea

MEC - matriz extra celular

MF- mobilização miofascial

mmHg - milímetro de mercúrio

mm - milímetro

m/s - Metros por segundo

mV - miliVolts

NM - nervo mediano

PEDro - *physiotherapy evidence database*

QTC - questionário do túnel do carpo

RM - ressonância magnética

SNAPs - (*sensory nerve action potentia*) potencial de ação sensorial do nervo

SF- sistema fascial

UFM - unidade miofascial

SMF - sequência miofascial

STC - síndrome do túnel do carpo

TCSS - tecido conectivo subsinovial

USG-P - ultrassonografia de punho

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1. INTRODUÇÃO

A síndrome do túnel do carpo (STC) é a neuropatia compressiva do nervo mediano (NM) mais comum na população, sendo consequente de qualquer condição anatomopatológica que cause uma redução da sua secção transversa ou uma expansão dos componentes do canal cárpico (1).

Sua prevalência estimada em uma população nos EUA foi de 5%, com uma incidência de 1 a 3 casos para 1000 habitantes (2). Já em uma população com STC no Rio Grande de Sul, Becker e colaboradores (2014) constataram que 53,35% dos participantes eram mulheres com predomínio na faixa etária entre 50 e 59 anos. Os casos bilaterais foram 80,8% do total, sendo 70,3% de comprometimentos moderado e grave, com maior concentração de casos severos na população acima de 80 anos (3).

A etiopatogenia da STC é multifatorial e tem como principais fatores constitucionais: a idade avançada, o sexo, o índice de massa corpórea elevado, a menopausa e a gravidez (4); e também as condições de trabalho, tais como o trabalho repetitivo ou o uso de instrumentos vibratórios (5). As comorbidades clínicas relevantes são o diabetes mellitus, o hipotireoidismo, a obesidade e a artrite reumatoide (6). Na impossibilidade de se determinar um agente causal, essa síndrome é denominada de idiopática (7).

O diagnóstico da STC pode ser feito por critérios clínicos ou eletroneuromiográficos. O quadro clínico se apresenta com mudanças sensoriais restritas à distribuição do nervo mediano (NM) na mão e os sinais de Tinel e Phalen, sendo fundamental a presença de um ou mais desses três achados fundamental para determinar o diagnóstico clínico (8). São descritos outros sintomas clínicos, tais como: as parestesias no território do NM, a fraqueza da musculatura na região tenar, as parestesias noturnas e as dores em membros superiores (5).

Adicionalmente, a eletroneuromiografia (ENMG) é utilizada tanto para o diagnóstico como para a quantificação da severidade de compressão do NM, a qual pode ter a graduação da severidade dividida em leve, moderada ou severa (9). A associação de critérios clínicos com exame ENMG aumenta de 58% para 73% a precisão diagnóstica (10).

O diagnóstico diferencial da STC é realizado com as radiculopatias cervicais, as plexopatias braquiais de tronco superior, a síndrome do desfiladeiro torácico, as

neuropatias proximais do NM e as polineuropatias. Algumas patologias corticais merecem atenção, pois podem mimetizar o quadro clínico de compressão do NM (11, 12).

O tratamento da STC pode ser feito por meio de procedimentos clínicos ou cirúrgicos. O tratamento clínico é indicado nos acometimentos leve e moderado, com várias terapias preconizadas na literatura, entre elas: o uso de fotobiomodulação (13, 14), a terapia com ultrassom terapêutico (15), os exercícios de alongamentos e a mobilização miofascial (MF), sem ou com instrumentos (IASTM) (16, 17). A terapia cirúrgica está indicada para os casos severos ou não responsivos a medidas clínicas (18), podendo ser associado ao pós-operatório a reabilitação fisioterápica (19).

As terapias de alongamento e a IASTM atuam sobre o tecido conectivo subsinovial (TCCS) que encontra-se alterado na STC (20). As repercussões sobre o TCCS não são restritas ao punho, ocorrendo ao longo de todo trajeto do membro superior e causando aderências e restrições à sua mobilidade que impactam diretamente na sua função (20).

A avaliação dos resultados das terapias utilizadas para no tratamento da STC podem ser feitas por medidas objetivas, como a força de preensão palmar e digital (21, 22), e subjetivas, tais como a avaliação da intensidade da dor, o questionário de Boston; e o questionário de qualidade de vida simplificado-SF12 (23-25). Os desfechos dessas medidas objetivas e subjetivas traduzem os resultados do tratamento utilizado tanto do ponto de vista do médico como do paciente (26).

2. OBJETIVOS

2.1 OBJETIVO GERAL

- Caracterizar aspectos clínicos e funcionais da STC bilateral idiopática e avaliar a utilização conjugada de dois procedimentos fisioterapêuticos (alongamento e mobilização miofascial com instrumentos) no tratamento clínico e na reabilitação pós-cirúrgica da STC bilateral idiopática.

2.2 OBJETIVOS ESPECÍFICOS

- Revisar os aspectos clínicos e funcionais relacionados à reabilitação da STC, com ênfase as terapias de alongamento e manipulação miofascial;
- Avaliar a combinação de duas técnicas fisioterapêuticas (alongamento e IASTM) na reabilitação de casos leves e moderados em pacientes com STC bilateral idiopática;
- Analisar o efeito da gabapentina preventiva para o controle da dor pós-operatória em pacientes com STC bilateral idiopática;
- Verificar o efeito de duas técnicas fisioterapêuticas combinadas (alongamento e IASTM) sobre a reabilitação cirúrgica e seguimento de seis meses de pacientes com STC bilateral idiopática.

3. REVISÃO DA LITERATURA - CONTEXTUALIZAÇÃO

3.1 DEFINIÇÃO E HISTÓRIA

A STC é decorrente da constrição do NM ao passar através do canal osteofibroso chamado de túnel do carpo (27). Este canal tem uma forma de arco, com as paredes laterais e o assoalho limitados pelos ossos do carpo, e o teto constituído pelo ligamento transversal do carpo (LTC) (28).

Sir James Paget em 1854 fez a descrição inicial do quadro clínico da STC, apresentando dois casos de compressão do NM decorrentes de uma fratura de rádio (29). Já o primeiro relato sobre o tratamento cirúrgico dessa síndrome foi em 1924 com Hebert Galloway (30), entretanto, o seu reconhecimento na área médica só ocorreu em 1950 em consequência dos trabalhos produzidos por Phalen (31).

3.2 ANATOMIA DO CARPO

O conhecimento das estruturas anatômicas que constituem a região do carpo é importante para compreender as diferentes questões envolvidas na STC. O túnel do carpo (TC) é composto pelo NM, pelos tendões dos flexores dos dedos (superficiais e profundos), pelo tendão do músculo flexor longo do polegar e pelas bursas cubital e radial, sendo limitado na face volar pelo LTC e na borda lateroinferior pelos ossos do carpo e seus ligamentos (32) (Figura 1).

Os movimentos do punho têm um efeito sobre as dimensões do TC, pois suas paredes ósseas não são rígidas. Os movimentos de flexão e extensão causam aumento da pressão dentro do túnel por diferentes mecanismos (33). O conhecimento desses conceitos é utilizado na terapia manual de mobilização de ossos do carpo para o tratamento da STC (34).

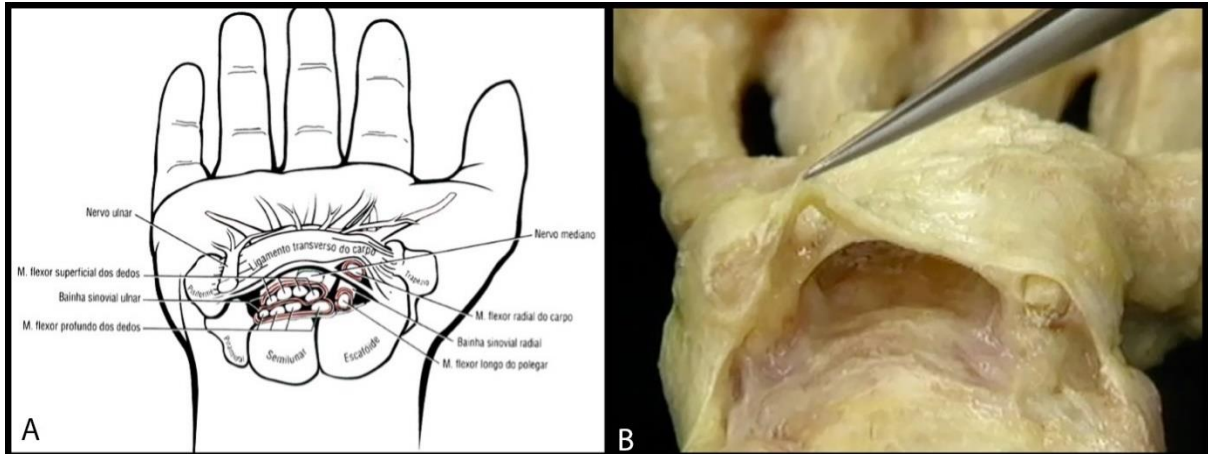


Figura 1: Representação anatômica do túnel do carpo. Fonte: Modificado da internet (A) <https://www.bibliomed.com.br/bibliomed/bmbooks/ortopedia>, acessado 11/21 e (B) Modificado de (35)

3.2.1 Ligamento Transverso do Carpo

Na última edição da Terminologia Anatômica foi proposta a mudança do termo ligamento transverso do carpo (LTC) para retináculo flexor pela *Federative Committee on Anatomical Terminology* (36). Entretanto, devido às suas características histológicas alguns autores discordam dessa variação de nomenclatura (37).

O LTC tem uma dupla função no punho, atuando tanto como estabilizador mecânico como um órgão sensorial, e seus elementos neurais são constituídos de terminações nervosas livres e dos corpúsculos de Pacini, que estão, também, amplamente presentes no tecido conjuntivo subsinovial (TCSS) circundante. Esses receptores, na presença de alterações patológicas do LTC e do TCSS, assumem a função de transmitir predominantemente informações algícas para às conexões neurais distais e proximais ao punho (38).

A espessura do LTC varia conforme as suas inserções radiais e ulnares. Nas porções ulnar proximal e radial distal, o LTC é mais fino e apresenta íntima relação com o NM, predispondo a compressão tanto por variações na espessura deste ligamento como por modificações na sua composição estrutural (39). A menor espessura do LTC na porção radial, associada à presença de fibras de colágeno na sua formação, possibilita que a técnica terapêutica mecânica do alongamento, seja utilizada no tratamento da STC (40). A representação das inserções do LTC está na Figura 2.

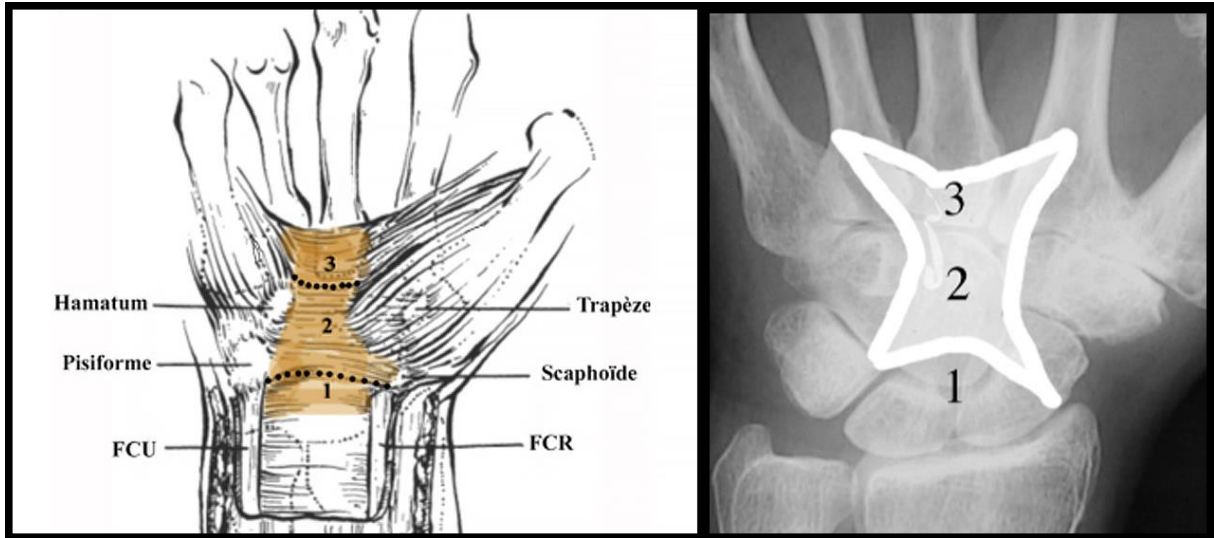


Figura 2: Representação anatômica do retináculo dos flexores (Ligamento transverso do carpo). Fonte: Modificado de (39).

3.2.2 Músculos Flexores dos Dedos

Os tendões dos músculos flexores superficiais e profundos dos dedos passam por um sistema de roldanas flexoras constituídas pelo LTC, pela aponeurose palmar e pelas polias digitais. Durante a movimentação dos dedos e da mão, na dependência da intensidade e da velocidade com que ocorrem, há uma excursão do tendão do flexor superficial dos dedos que podem causar injúrias tanto ao TCSS como ao NM. Assim, o abaulamento dos tendões dos flexores em direção à superfície volar do punho, comprime o NM e o TCSS contra o LTC, causando lesão dessas estruturas, a qual restringirá a sua livre excursão (41).

3.2.3 Nervo Mediano

O NM tem um posicionamento anterior em relação aos elementos que ocupam o túnel do carpo, sendo uma estrutura única na maioria das vezes, composta por fibras sensitivas, motoras e autonômicas. Sua origem está localizada na região da axilar, sendo proveniente da junção do fascículo lateral e medial. O primeiro é composto pelos segmentos espinhais da quinta e sexta raiz cervical e o segundo é formado pelos segmentos espinhais da sétima e oitava raiz cervical, adicionada a primeira raiz torácica (42).

Fibras sensitivas, motoras e autonômicas compõem o NM, o qual tem sua porção sensorial formada por uma trifurcação do tronco radial em nervos digitais

palmares e seus ramos sensoriais que inervam os três primeiros dedos na face palmar. Somente a face radial do quarto dedo é inervada por ramos digitais do mediano, sendo a sua face ulnar e o quinto dedo supridos pelo nervo ulnar (43).

Um ramo sensitivo que emerge cerca de 3 a 4 cm antes da margem proximal do canal do carpo, na sua porção anterolateral, passando superficialmente ao LTC. Esse ramo é responsável pela sensibilidade superficial proximal da eminência tenar, enquanto a sensibilidade da região hipotenar provém do braço transverso palmar, do ramo cutâneo palmar e do nervo de Henlé, pertencentes ao nervo ulnar (44).

A inervação motora do NM é feita pelo ramo recorrente motor, responsável por inervar o músculo abductor curto do polegar e os músculos lumbricais do segundo (primeiro lumbrical) e terceiro dedos (segundo lumbrical). Já a inervação dos músculos interósseos é feita pelo nervo ulnar (45).

A emergência do ramo recorrente motor do NM tem relações com o LTC, sendo extraligamentar em 46%, subligamentar em 31% e transligamentar em 23% dos casos (46). O conhecimento anatômico dessas variações é importante tanto para CA como CE a fim de evitar a lesão deste ramo motor (47, 48).

A face medial do NM é constituída por fibras autonômicas simpáticas que emergem do gânglio estrelado ou gânglio simpático cervical de Budge e são responsáveis pelas manifestações clínicas de disfunções autonômicas, tais como: dor em queimação contínua ou causalgia, sensações dolorosas a estímulos habituais ou alodínea e alterações tróficas por disfunção simpática (49, 50).

O NM apresenta um longo percurso desde a região cervical até a mão, tornando-se suscetível a pontos de constrição ao longo do seu trajeto. Esse quadro clínico é denominado de dupla compressão, podendo os sítios de constrição estarem localizados no nível do desfiladeiro torácico, no ligamento de Sthurthers, no músculo de Gantzer e no ponto em que o NM atravessar o músculo flexor superficial dos dedos na porção distal do antebraço (51).

Esses pontos de compressão podem simular a STC (52), deste modo o não reconhecimento da síndrome de dupla compressão do NM é responsável por insucesso no tratamento cirúrgico dessa síndrome (45).

3.2.4 Tecido Conectivo Subsinovial

O tecido conectivo subsinovial (TCSS) é formado por multicamadas de tecido frouxo fibroso interconectadas por fibras de colágeno e está localizado entre o NM e o tendão dos flexores (53). Esse tecido permite o deslizamento suave entre os tendões musculares do músculo flexor superficial dos dedos e o NM, além de fornecer proteção para que não ocorram impactos entre o NM e os tendões decorrentes do movimento do punho (54).

Na STC ocorre uma elevação crônica da pressão dentro do canal, que provoca um processo isquêmico, causando mudanças na composição do TCSS, tais como: alterações no tipo de fibras colágenas, aumento de atividade fibrótica e retenção líquida. Esses fatos causam um aumento na resistência ao deslizamento dos tendões, impedindo o livre movimento das estruturas circundadas pelo TCSS, como é o caso do NM (55).

O TCSS na STC tem alterações bioquímicas e estruturais específicas. Há um aumento da citocina profibrótica chamada de fator de crescimento transformador tecidual- beta (TGF- β), o qual promove a ativação dos fibroblastos, além de aumentar uma maior quantidade de colágeno do tipo III que por ser mais fraco em comparação a outros tipos de fibras colágenas, são predispostos a sucessivos ciclos de lesões no TCSS (56). A continuidade desse processo leva a uma fibrose não inflamatória associada com edema, aumento da densidade de fibroblastos e proliferação vascular e tem como resultado final uma restrição da movimentação entre os tendões e o NM (57).

O enrijecimento do TCSS irá impedir o deslocamento do NM para uma posição posterior ao tendão dos flexores superficial durante a flexão normal do punho, deixando-o exposto a injúrias pelo contato direto com a superfície dorsal do LTC (58) (Figura 3).

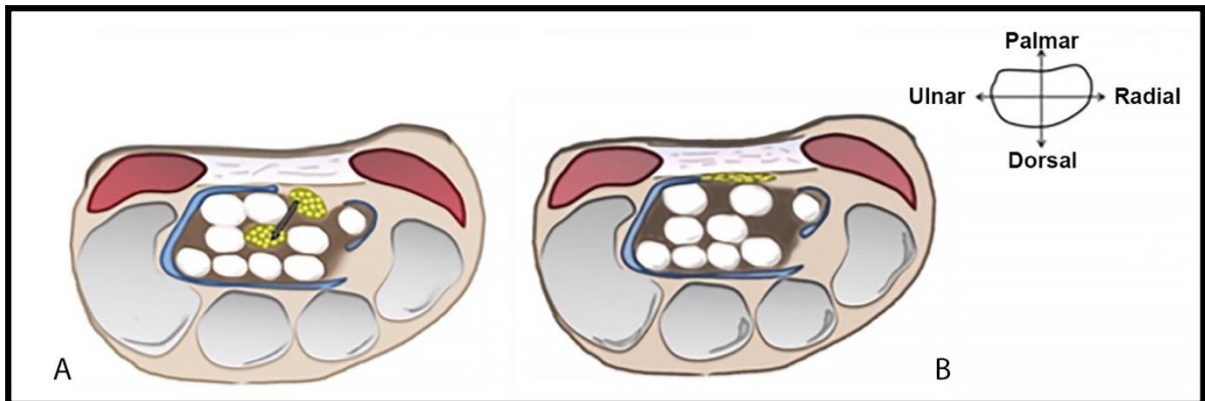


Figura 3: Representação da região do punho sem (a) e com (b) restrições do tecido conectivo subsinovial. Fonte: Modificado de (58)

Essas repercussões sobre o TCSS na STC não são restritas ao punho, ocorrendo ao longo de todo o trajeto do NM no membro superior e causando aderências e restrições a sua mobilidade que impactam diretamente na sua função (20). A Figura 4 demonstra a representação do NM no punho, em livros anatômicos tradicionais, sem a presença e com a presença de TCSS.

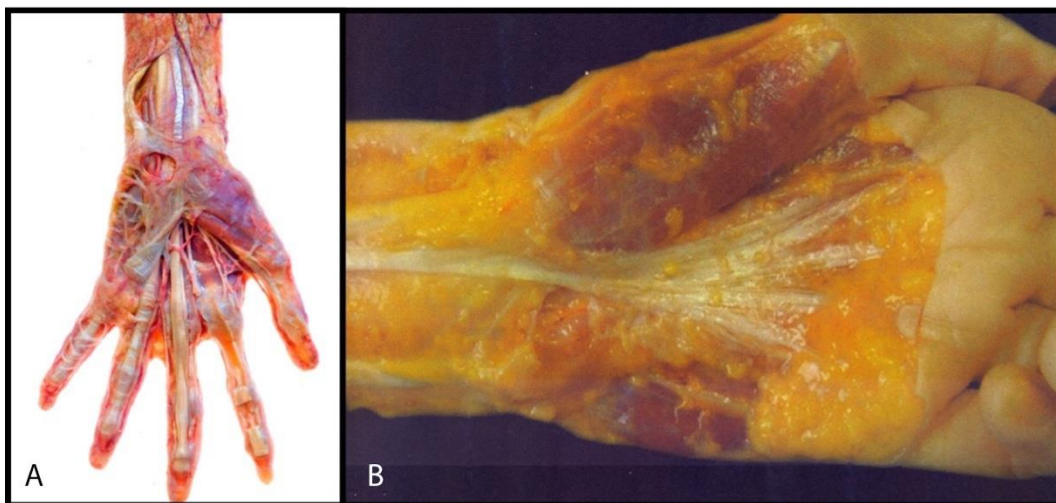


Figura 4: Nervo mediano no punho e na mão sem (a) e (b) com a presença do tecido conectivo subsinovial. Fonte: Modificados de (35)

O TCSS acompanha o NM ao longo de todo o seu trajeto em MMSS, regiões axilar, torácica e cervical, sendo estas relações demonstradas na Figura 5.



Figura 5: Relações do nervo mediano com o tecido conectivo subsinovial ao longo do membro superior, nas regiões do braço, axila, torácica e cervical (A) e ampliação das regiões axilar e torácica (B) Fonte: Modificados de (35)

3.3 FISIOPATOLOGIA DA STC

A STC é decorrente de várias situações que têm em comum uma desproporção entre o espaço e os elementos que formam o túnel cárpico. Este desequilíbrio pode ser decorrente dos seguintes fatores: o aumento do volume dos tendões ou do nervo, um estreitamento extrínseco do túnel ou um aumento do volume de estruturas que normalmente não compõem o canal, como é o caso do depósito de substâncias anômalas ou tumores (59, 60).

A conjunção de compressão e de tração sobre o NM provoca uma obstrução do retorno venoso e um edema local que dificulta a microcirculação intraneural (61). Essas alterações patológicas promovem um ciclo vicioso que acomete as bainhas de mielina, produzindo um bloqueio na condução neural (neuropraxia).

As associações entre a isquemia, a congestão venosa e as alterações metabólicas locais causam graus variados de lesão axonal por comprometeram o

transporte intra-axonal. As fibras mais vulneráveis são as amielínicas nociceptivas, sendo a sua lesão responsável pelas manifestações álgicas iniciais observadas na STC (62). Se o processo fisiopatológico não for interrompido, surgirá um processo inflamatório no TCSS que acarretará pontos de aderências ao longo do trajeto do NM. Associado a esses fatos, há um aumento da compressão e do estiramento sobre o NM (63), produzindo sintomas álgicos que podem ser irradiados até a região cervical (64).

O NM submetido a essa compressão intermitente decorrente dos movimentos repetitivos (65), leva a uma desmielinização na invaginação da bainha de mielina no nível da região paranodal aumentando a latência do potencial de ação. Essa alteração na condução nervosa pode ser detectada pela eletroneuromiografia (ENMG) (2).

O tempo de duração da compressão tem relação direta com as repercussões clínicas. Desse modo, as compressões intermitentes podem ser bem toleradas pelo NM, fazendo com que a sintomatologia seja branda, com períodos de remissão, por anos (66). Contudo, com o agravamento das repercussões fisiopatológicas sobre o NM os sintomas passarão a ser desencadeados por movimentos repetitivos do punho, surgindo sinais de irritação desse nervo (*Tinel e Dunken*) e as parestesias noturnas (67).

Os episódios de parestesias à noite estão relacionados a mecanismos hemodinâmicos, os quais estão associados à mudança da posição ereta para a deitada, que promove uma imediata redistribuição de sangue, retirando o fluxo dos membros inferiores e redirecionando-o para o tórax e membros superiores (68). O ingurgitamento venoso nos membros superiores produz um aumento gradual da pressão no túnel do carpo, que atinge o seu máximo de 3 a 6 horas após o indivíduo deitar-se. Isso causa a uma parestesia dolorosa nos braços, que desperta o indivíduo após um sono inicial, sendo necessário movimentá-los para obter um alívio dos sintomas (69).

Com a evolução da patologia, ocorrerá uma perda da barreira vascular entre o nervo e o vaso sanguíneo (*breakdown*), o que causa um acúmulo tanto de proteína como de células inflamatórias na porção intrafascicular do NM, gerando uma fibrose intraneural não inflamatória com perda axonal progressiva, resultando em uma repercussão clínica com parestesias persistentes e um déficit de força nas mãos (70). Esse decréscimo axonal causa uma hiperexcitabilidade neuronal do NM que provoca descargas ectópicas persistentes (70). Os estímulos neurais contínuos, por sua vez,

ativam os interneurônios comissurais localizados na medula espinhal, no tronco cerebral e no córtex cerebral, causando uma hipersensibilização do córtex sensitivo-motor que acarreta um ciclo inibitório no nível do sistema nervoso central (SNC) (71). Desse modo, a STC deve ser interpretada como uma neuropatia complexa que acomete tanto o SNC como o periférico (72).

3.4 EPIDEMIOLOGIA

A STC corresponde a 90% das neuropatias periféricas compressivas e acomete cerca de 10% da população mundial ao longo da vida, com cerca de três a quatro casos novos para cada 1000 habitantes por ano, (8). Ela também acomete três vezes mais mulheres do que homens, com uma prevalência na terceira e quarta década para as mulheres e na sexta até a oitava década para os homens, sendo bilateral em 60% dos casos (73).

Uma pesquisa realizada por Burton e colaboradores (2018) demonstrou um aumento da prevalência de STC nos últimos de vinte anos, tendo uma redução na faixa etária de acometimento em ambos os sexos (8). Em um estudo epidemiológico brasileiro com 3.108 pacientes com STC, Becker e colaboradores demonstraram que 53,3% eram mulheres e 28,1% eram homens, com idades variando de 20 a mais de 80 anos. O grupo acima de 80 anos continha 50% dos casos severos e o casos bilaterais constituíram 80,8% da amostra (3).

Os principais fatores constitucionais relacionados à STC são: a idade avançada, o sexo, o IMC, a menopausa e a gravidez (4); e, enquanto as comorbidades clínicas relevantes são: o *diabetes mellitus*, o hipotireoidismo, a obesidade e a artrite reumatoide (6).

Do mesmo modo, os estudos concluíram que existe uma associação significativa entre a STC e a exposição a trabalhos que exigem força manual, movimentos repetidos de punho e o uso de ferramentas vibratórias, assim como a prática de atividades físicas predisponentes, como o beisebol, o basquetebol, o fisiculturismo, o *motocross* e o ciclismo (74-76).

3.5 QUADRO CLÍNICO

A Academia Americana de Cirurgiões Ortopédicos definiu a STC como uma neuropatia de compressão sintomática do NM no nível do punho (77). Existem vários

sintomas e sinais que a caracterizam, no entanto há a presença de um ou mais, dos três achados descritos a seguir, que são fundamentais para determinar o seu diagnóstico clínico: as mudanças sensoriais restritas à distribuição do NM na mão; o desencadeamento de parestesias na distribuição do NM quando é feita uma percussão na crista distal do punho sobre o NM (sinal de Tinel) e a ocorrência de parestesias na distribuição do NM quando o paciente flexiona os punhos a 90° por 60 segundos (8), sendo este último achado conhecido como sinal de Phalen (78).

Outros sintomas e sinais são relatados na STC, tais como a dor e as parestesias localizadas na distribuição do nervo mediano. Essas queixas apresentam uma piora gradual na sua intensidade com o agravamento da doença deixando de ter um caráter intermitente e passando a perdurar o dia todo. Os movimentos repetitivos e a permanência prolongada dos membros superiores em uma mesma posição tendem a intensificar a dor e as parestesias (27).

Parestesias noturnas que despertam o indivíduo após um sono inicial são queixas frequentemente descritas, sendo necessário que o paciente chacoalhe os braços (*flick sign*) para obter o alívio desses sintomas. Esses episódios de despertar noturnos podem se repetir várias vezes, comprometendo a qualidade do sono e ocasionando transtornos do humor (79).

No exame físico são avaliados os sinais que refletem a disfunção do nervo mediano, como os sinais de Tinel e Phalen, e é feito o teste provocativo de Durkan (80). Já o comprometimento do músculo abductor curto do polegar (ACP) é evidenciado pela atrofia muscular na região tenar, que se associa a quedas frequentes de objetos das mãos (81). Entretanto, a sensibilidade e a especificidade dos testes de disfunção do NM variam conforme as séries analisadas por serem examinadores dependentes (82).

3.6 DIAGNÓSTICO DIFERENCIAL

A STC idiopática deve ser discriminada de outras condições que podem ocasionar um quadro clínico semelhante, tais como: os trabalhos que exigem manobras repetitivas com as mãos, gravidez, artrite reumatoide, hipotireoidismo, *diabetes mellitus* (83), traumas no punho, dor crônica de punho (84), presença de lesão expansiva no túnel, as amiloides, a sarcoidose, o mieloma múltiplo e os quadros leucêmicos (85).

Além das causas anteriores, devem ser excluídas as radiculopatias cervicais, especialmente no nível da sexta e sétima raiz; as plexopatias braquiais de tronco superior; a síndrome do desfiladeiro torácico; as neuropatias proximais do NM, como a síndrome do pronador redondo; e as polineuropatias. Algumas patologias do sistema nervoso central, como a esclerose múltipla e o infarto de pequenos vasos corticais, podem mimetizar o quadro clínico de compressão do NM (11).

Os processos inflamatórios sistêmicos, como as doenças do colágeno, as lesões traumáticas no NM ou no punho, os fenômenos vasculares como a síndrome de Raynaud e as lesões que ocupam espaços dentro do canal cárpico complementam a lista das doenças a serem diferenciadas da STC (86).

3.7 DIAGNÓSTICO POR IMAGEM

Os exames de imagens utilizados para o diagnóstico da STC são a ultrassonografia (USG) e a ressonância magnética (RM). Apesar de um estudo retrospectivo ter demonstrado que os exames de USG apresentaram sensibilidade e especificidade baixas, respectivamente 57,6% e 60,7%, eles se destacam pelo seu baixo custo (87). Na USG podem ser observados a espessura do LTC, o espessamento do NM e a presença de lesões extrínsecas comprometendo esse nervo dentro do túnel (88).

Dessas medidas citadas, a área de seção transversa do NM tem melhor valor preditivo entre os achados, podendo ser utilizada para correlacionar os valores anormais de área com graus de severidade. Porém, existe uma significativa discrepância entre a metodologia dos estudos e os locais de mensuração das áreas de seção transversa ao longo do túnel, o que torna difícil a comparação entre os resultados (89).

Em relação à RM, essa tem indicações limitadas em razão de seu alto custo, sendo reservada para a confirmação de lesões no interior do túnel (90) e nas avaliações de recidivas pós-cirúrgicas, apresentando uma sensibilidade de 96% e a especificidade de 38% (91).

3.8 ASPECTOS ELETRONEUROMIOGRÁFICOS

No estudo ENMG, é efetuado um estímulo elétrico no NM para analisar as latências e as velocidades de condução da resposta neuronal, as quais são

registradas tanto para o componente sensitivo quanto para o motor (92). Os objetivos desse exame são a confirmação da disfunção do nervo mediano no nível do canal do carpo, a quantificação neurofisiológica da severidade da doença e a definição das possíveis condições patofisiológicas resultantes da compressão (87).

A sensibilidade e a especificidade da ENMG para o diagnóstico de STC foram significativamente superiores quando comparadas aos sinais clínicos e à USG (93). Entretanto, a associação entre critérios clínicos e ENMG, aumenta de 58% para 73% a precisão diagnóstica (94).

A fim de assegurar a uniformidade dos achados na ENMG é importante que os exames sejam realizados no mesmo laboratório, na mesma máquina e com o mesmo eletrofisiologista, seguindo as normas técnicas preconizadas pela Associação Americana de Medicina Eletrodiagnóstica (95). Esses achados ENMG foram graduados em três níveis de severidade segundo Stevens (1997): i) grau leve- definido pelo prolongamento relativo ou absoluto do nervo mediano sensorial ou palmar, além disso, às vezes, a amplitude do potencial parece estar ligeiramente diminuída; ii) grau moderado- ambas as latências sensitivas e motoras são relativamente ou absolutamente prolongadas; iii) grau severo- ambas as latências motoras e sensoriais são prolongadas com um potencial sensorial ou palmar ausente ou baixa amplitude ou potencial motor ausente. O exame de agulha direcionada para o músculo ACP frequentemente revela fibrilações, redução de recrutamento e mudanças na unidade do potencial motor (9).

A ENMG estipular o grau de acometimento do NM. Sendo assim, o seu resultado auxilia na indicação da proposta terapêutica a ser empregada e colabora na avaliação dos resultados obtidos. Nos graus leve e moderado a indicação terapêutica são medidas clínicas (96); já nos graus severos o tratamento indicado é o cirúrgico (97).

A eletromiografia com agulha do músculo abductor curto do polegar (ACP), ao demonstrar a presença de descargas motoras autônomas, faz o diagnóstico diferencial com patologias que simulam a STC, mas que não apresentam esses achados, tais como as radiculares cervicais, as doenças do corno anterior da medula e as lesões nervosas corticais (2).

A predição do resultado de uma intervenção com base nos níveis de acometimento na ENMG tem tido resultados controversos na literatura. Há autores que correlacionam comprometimentos severos na ENMG com pior prognóstico

operatório (98). Contudo, existem relatos conflitantes na literatura, com autores demonstrando não haver associação entre o grau de severidade e a evolução pós-cirúrgica (99), porém outros pesquisadores afirmarem que os pacientes com comprometimentos severos apresentaram um melhor prognóstico (100, 101). Bland (2000) analisou o resultado de 7.410 cirurgias de STC, informando que os dados apresentados na literatura tentando associar a ENMG com os desfechos cirúrgicos eram contraditórios e podem ser explicados pelo fato de não existir uma relação linear entre essas variáveis (102).

Os valores de falso positivo e falso negativo são inconstantes na literatura, sendo os principais motivos para sua ocorrência: a falta de padronização dos parâmetros técnicos, a ausência de uma metodologia adequada para determinar os valores de corte das variáveis ENMG na população referenciada como normal e a inexistência de um teste padrão ouro para o diagnóstico da STC (103). Apesar disso, a ENMG continua a ser um método importante na identificação e quantificação da compressão do NM no túnel do carpo (104).

3.9 HISTÓRIA NATURAL DA STC

A STC idiopática pode ter uma melhora clínica sem nenhuma intervenção em 21% dos casos após 10 a 15 meses de seguimento. Um estudo observacional, por exemplo, feito com 257 indivíduos contendo STC idiopática e seguidos por 5 anos demonstrou a resolução dos sintomas no período de 6 meses em 34% dos casos (105). Assim, qualquer tratamento proposto terá que apresentar um resultado superior ao da história natural da doença (106).

Na presença de STC bilateral, a cirurgia de uma das mãos e o acompanhamento da mão contralateral demonstram resultados conflitantes na literatura, os quais serão descritos a seguir. De acordo com Agrawal e Southern (2010), a evolução da mão não operada nos casos com STC bilaterais apresentou uma melhora espontânea de 37% dos casos (107). Unno e colaboradores relataram que houve melhora na mão não operada em 94% de 65 casos, sendo detectada a partir do segundo dia de pós-operatório e persistindo 6 meses após (108). Contudo, há relato na literatura de que a mão não operada com carpos bilateral idiopático permaneceu inalterada após 6 meses de seguimento (109).

Assim sendo, há necessidade de futuras investigações em casos de STC bilaterais com indicação cirúrgica a fim de esclarecer as razões da melhora na mão contralateral que não foi operada em decorrência do ato cirúrgico da mão oposta (110).

3.10 TRATAMENTOS

Os tratamentos para STC idiopática podem ser realizados por meio de medidas clínicas ou cirúrgicas, sendo a sua indicação baseada na severidade da doença. Nos graus leve e moderado o tratamento é clínico, enquanto nos graus severos é indicada a cirurgia (81).

3.10.1 Tratamentos Clínico

O tratamento clínico é indicado nos casos em que os sintomas dolorosos interferem na atividade diária do paciente e quando os achados ENMG demonstram um comprometimento leve ou moderado da função do NM .(111)

As recomendações de modificações das atividades diárias, como evitar movimentos repetitivos, fazer uso de equipamentos ergonômicos, realizar intervalos regulares de descanso entre as atividades e as mudanças de função não apresentaram evidências clínicas na literatura (7).

As terapias clínicas que apresentaram um desfecho superior às da história natural da doença são as talas de punho, a cinta de mão e a injeção local de esteroides (112). De Angelis e colaboradores (2009) relataram que o uso da tala obteve melhora em 37% dos casos, entretanto não foi observada diferença entre o uso de tala de punho e a cinta de mão (113).

No entanto, a comprovação do benefício da tala permanece controversa na literatura, com autores revelando que existe melhora com o uso restrito ao período noturno (114), enquanto outros pesquisadores não evidenciaram vantagem na utilização da tala tanto em período diuturno como em uso exclusivamente noturno (115).

A mesma controvérsia ocorre em relação à angulação da tala com o punho, não havendo diferença se está em posição neutra ou a 20° de extensão em relação ao punho (116). Do mesmo modo, não foi demonstrada na literatura uma melhora da

STC com a utilização de talas por longo prazo, de modo que a progressão da doença pode ocorrer mesmo durante o uso (117).

A injeção de corticosteroides no punho, por sua vez, apresenta uma melhora imediata dos sintomas em 70% dos indivíduos (118). Todavia, em uma revisão sistemática, Marshall e colaboradores (2007) relataram que esse benefício não se manteve além de um mês (119).

A STC também pode ser tratada com medicamentos via oral, tais como esteroides (120), vitamina B6 (piridoxina) (121), antidepressivos (122) e gabapentinoides (123), contudo os resultados são conflitantes na literatura (124).

No tratamento das STC leves e moderadas, existem medidas terapêuticas clínicas que podem ser utilizadas, tais como: as modificações das atividades diárias, o uso da fotobioestimulação de baixa intensidade (14), a terapia com ultrassonografia (15), os exercícios de alongamento (125) e a manipulação miofascial (126).

Porém, devido à quantidade limitada de pesquisas e à baixa qualidade das evidências que demonstram os benefícios dos diferentes tipos de reabilitação no tratamento clínico da STC, há a necessidade de novos estudos (61).

3.10.2 Exercícios de Alongamento

A restauração da amplitude de movimento (ADM) de uma lesão é um dos principais objetivos de qualquer programa de reabilitação. A utilização de programas de alongamento efetivo em determinados músculos, altera a extensibilidade das unidades neuromusculotendíneas de determinadas articulações. Assim, os exercícios que alongam essas unidades e suas fáscias, com o tempo, aumentam a ADM possível na articulação (127, 128), auxiliando no controle da dor (129).

Durante muitos anos, a eficácia do alongamento na melhora da ADM tem sido atribuída, em termos teóricos, aos fenômenos neurofisiológicos que envolvem o reflexo de estiramento. Contudo, um estudo que revisa de modo extensivo a literatura existente sugere que as melhoras na ADM resultantes do alongamento possam ser explicadas por processos que vão além do reflexo de estiramento. Os autores indicam que há alterações na habilidade do músculo em tolerar o alongamento, associadas a mudanças nas propriedades viscoelásticas do músculo alongado (130).

Pacientes com STC, também, apresentaram uma diminuição da pressão dentro do túnel quando foram submetidos a exercícios para as mãos (131). Schmid e

colaboradores (2012) avaliaram a diminuição do edema no NM por RM em indivíduos que realizaram os exercícios fisioterápicos de alongamento em casa, durante uma semana, com dez repetições por dia da sequência proposta, após um treinamento prévio supervisionado. Os autores mostraram uma redução de edema no NM após uma semana de fisioterapia e melhora dos sintomas medida pelo questionário de Boston (132).

Os exercícios de alongamento promovem um aumento do fluxo circulatório para tecidos desidratados, que reduz o edema intercelular e reidrata os ligamentos e os tendões (Imai et al., 2015). O estiramento e a compressão das fibras musculares influenciam tanto os proprioceptores como os nociceptores, neutralizando os padrões disfuncionais ao nível da medula espinhal e córtex cerebral, decorrentes das cadeias miofasciais alteradas. Além disso, o alongamento promove um estiramento da região de interesse até o final da sua amplitude de movimento, que produz uma distensão das células do tecido conjuntivo, propiciando uma remodelação da matriz extracelular (133).

Contudo, existe uma carência de modelos topográficos e histológicos que expliquem as interações entre o alongamento e as suas repercussões funcionais que ocorrem nos tecidos adjacentes, tais como: os tendões, os nervos, os ligamentos e a fáscia (Solomonow, 2009).

A comparação dos resultados da terapia com exercícios de alongamento em artigos clínicos apresenta limitações devido à falta de padronização, decorrente de protocolos diferentes que variam quanto à intensidade, à duração, à frequência dos movimentos e ao tempo que deveria ser desprendido com o alongamento terapêutico, a fim de provocar os efeitos fisiológicos desejados (134, 135).

A sequência de alongamentos utilizados está no Apêndice C.

3.10.3 Mobilização Miofascial

A mobilização miofascial (MF) é uma técnica fisioterápica que pode ser utilizada no tratamento da STC, contudo, a fim de discutir este método, é necessário definir os conceitos de fáscia e de sistema fascial.

A fáscia é formada por camadas de tecido conjuntivo, que estão dispostas abaixo da pele e englobam os músculos e os órgãos internos. Já o sistema fascial abrange um conglomerado de funções inter-relacionadas, como as forças de

transmissão, as funções sensoriais e as regulações referentes à restauração tecidual (136).

O sistema fascial, por sua vez, forma uma rede de tecidos interdependentes que se interconectam e interagem de forma complexa, colaborando para a execução dos movimentos (137). Esse sistema pode ser afetado por patologias que acometem o tecido conectivo, causando alterações nociceptivas e proprioceptivas, disfunções vasculares e linfáticas, bem como limitações dos movimentos (138).

A fim de interpretar as inter-relações tridimensionais do sistema fascial, Stecco e colaboradores (2017) dividiram o corpo em quatorze segmentos: a cabeça, o pescoço, o tórax, a região lombar, a pélvis, a escápula, os ombros, o cotovelo, o antebraço, as mãos, o quadril, o joelho, o tornozelo e o pé. Segundo a interpretação dos autores, em cada uma das partes relacionadas há seis unidades miofasciais, que são compostas por músculos mono ou biarticulares e a sua fáscia correspondente.

A fáscia que apresenta uma distribuição espacial nos três planos ortogonais, portanto sua mobilidade deve se avaliada em seis direções diferentes, devendo os movimentos serem examinados no sentido anterior, posterior, lateral e medial, bem como, nas rotações interna ou externa (139). Cada uma das seis unidades miofasciais tem uma localização específica na fáscia profunda chamada de centro de coordenação, para onde convergem as forças vetoriais dos músculos envolvidos em um movimento (140).

Myers (1996) descreveu um modelo de distribuição espacial dos músculos, articulações, tendões e tecido fascial chamado de cadeias miofasciais ou trilhos anatômicos. O autor determinou que um trilho anatômico é uma estrutura construída por unidades de tecidos conectivos, em continuidade com os ossos, os tendões e fibras miofasciais, apresentando como condição essencial a continuidade dessas unidades de tecido conectivos, não podendo essas cadeias transporem uma articulação. Deste modo, as seguintes linhas anatômicas foram descritas por Myers: a posterior superficial, a frontal superficial e profunda, a lateral e as dos braços, que são divididas em anterior e posterior (141).

Stecco e colaboradores (2009) propuseram que existe uma inter-relação anatômica nos membros superiores entre os seus conceitos de unidades miofasciais e as definições de trilhos anatômicos feitas por Myers (1996) (142). Somando-se a esses conceitos Day e colaboradores (2009) propuseram que a regiões peitoral e

dorsal apresentam íntima relação anatômica e funcional com o membro superior (140).

Os mucopolissacarídeos ou glicosaminoglicanos são os elementos viscoelásticos da fáscia que permitem aos trilhos anatômicos deslizarem quase sem atrito entre si, conferindo ao sistema uma integridade estrutural resultante da interação entre as forças de tensão e compressão, ou seja, uma “tensegriedade” (143).

A mobilização miofascial (MF) se trata de procedimentos fisioterapêuticos direcionados para o tecido miofascial, que podem ser realizados somente com as mãos ou terem o auxílio de instrumentos. A MF manual foi derivada do conceito de massagem transversa profunda por fricção de Cyriax (144), sendo aperfeiçoada pelo acréscimo de princípios biomecânicos que foram feitos por dois fisioterapeutas nórdicos, criando o conceito de *Kaltenborn-Evjenth*® (145). A MF manual faz uma fricção sobre os pontos de restrição que podem existir na cadeia miofascial, sendo este estímulo biomecânico propagado por meio de forças vetoriais nos três planos dimensionais pelos tecidos fasciais (137).

A MF assistida por instrumento recebe o nome de *Instrument-assisted soft tissue mobilization (IASTM)* e tem como objetivo auxiliar a MF manual e facilitar os processos de recuperação tecidual, fazendo com que a energia mecânica desprendida seja mais eficiente com o auxílio instrumental (146).

Kurt Ekman foi o pioneiro na associação da MF manual aos ganchos (*crochets*), desenvolvendo a técnica denominada de “*crochetagem mioaponeurótica*” ou “*diafibrólise percutânea*”, que possibilita alcançar pontos de manipulação inacessíveis ao uso das mãos (147). A utilização de dispositivos para MF aprimora a sensibilidade do terapeuta para identificar pontos profundos de restrição da fáscia, permitindo o trabalho em diferentes ângulos de restrição e fazendo com que a energia mecânica desprendida se torne mais eficiente com o auxílio do instrumento (IASTM) (17).

A *IASTM* é fundamentada em uma abordagem centrípeta, isto é, inicia-se a terapia de fora para dentro dos tecidos, sendo a técnica composta de três fases sucessivas: a palpação digital, a palpação instrumental e a diafibrólise. A fase palpatória digital consiste em seguir as cadeias musculares e as fáscias acometidas, delimitando com a mão palpatória as áreas a serem tratadas. Na fase palpatória instrumental, a mão contralateral segura o gancho colocando o dedo indicador sobre a espátula, posicionado o *crochet* perpendicular às fibras tissulares de interesse (148).

Neste processo, a abertura do gancho escolhida deve permitir o acoplamento justo com a massa tecidual que se pretende aplicar a manipulação. Ao preceder os movimentos da mão instrumental, a mão palpatória segura o tecido por meio de uma pinça digital feita entre o polegar com o segundo dedo enquanto o terceiro dedo cria um efeito de onda ao tracionar a área de interesse.

Na fase de fibrólise, a mão instrumental faz uma tração complementar a que foi realizada pela mão palpatória, que alonga as fibras tissulares, rompendo as aderências miofasciais, restaurando a mobilidade tecidual, sem que isso cause dor. Em áreas com inserções ligamentares ou nas junções de tendões com o perióstio, pode-se associar uma raspagem dessas estruturas com o auxílio da parte dorsal do gancho (149).

A energia mecânica produzida pela fricção do gancho nos planos miofasciais induz a transformação e a proliferação de fibroblastos, promovendo tanto um aumento da síntese de colágeno como a remodelação dos tipos de fibras do colágeno e restaurando o formato do colágeno multimicrovacuolar de absorção dinâmica (150, 151), o que promove alterações estruturais na fáscia e no sistema fascial, local e a distância, recompondo a integridade estrutural dos tecidos fasciais comprometidos (152, 153).

Esse método tem se desenvolvido ao longo do tempo por meio do aprimoramento do material utilizado para confecção dos ganchos, da ampliação de suas indicações terapêuticas e da sua associação com outros procedimentos fisioterápicos (149), permitindo constatar que a MF com uso de *crochets* é um procedimento eficaz em inúmeras patologias (154), inclusive na STC (126).

Os tipos de ganchos ou *crochets* e a técnica de MF estão demonstradas na Figura 6, bem como as sequências de MF realizadas nas regiões dorsal e torácica, bem como, em ombro, braço e antebraço nas faces anterior, lateral e posterior, nos decúbitos ventral, lateral e dorsal estão no Apêndice D.

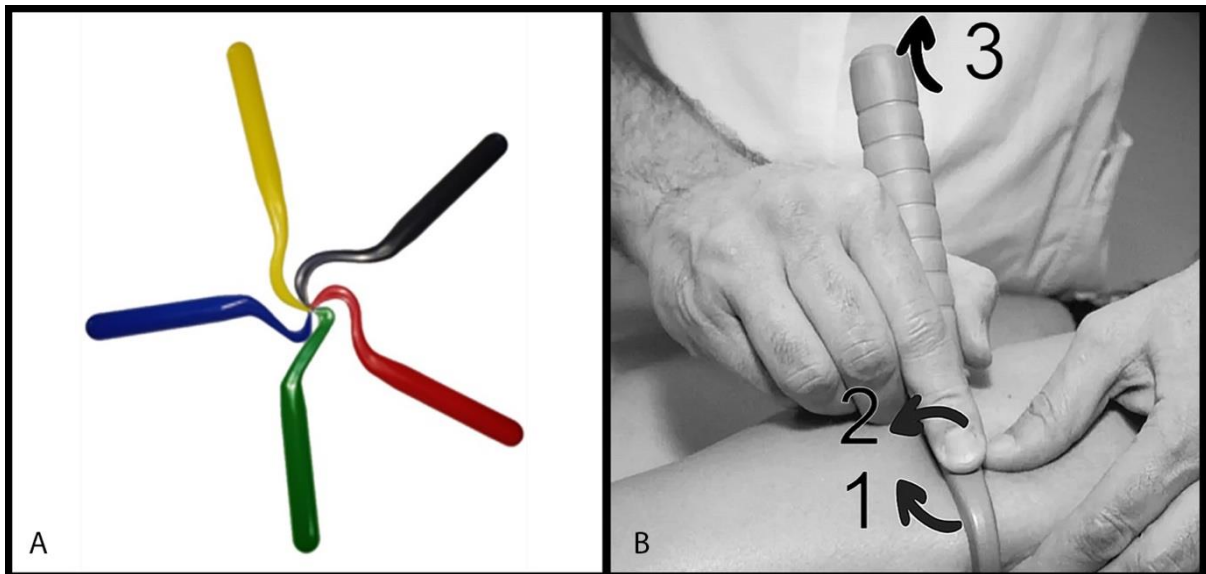


Figura 6: Tipos de ganchos ou crochets (a) e a sequência dos passos para realizar a mobilização miofascial com ganchos (b) Fonte: (a) acessado em 11/21: <https://www.facebook.com/pg/miofascial/posts> (b) Modificado de (149)

3.10.4 Tratamento Cirúrgico

Os casos de STC com compressão severa na ENMG tem indicação cirúrgica. O tratamento cirúrgico deve ser considerado, também, se as terapêuticas clínicas não forem eficazes no controle da doença em longo prazo e se houver piora tanto do quadro clínico como dos parâmetros eletroneuromiográficos (155).

A piora clínica pode se manifestar por meio da progressão do déficit motor, da presença de déficit sensorial contínuo ou da instalação de atrofia na musculatura tênar (81). Existem dois procedimentos cirúrgicos consagrados na literatura para essa finalidade: a cirurgia aberta (CA) e a cirurgia por via endoscópica (CE).

A CA tem algumas variações descritas na literatura com a finalidade de minimizar a agressão cirúrgica, como é o caso do acesso palmar que foi idealizado por Tubina (1990) e introduzida no Brasil pelo trabalho de Galbiatti e colaboradores (1991) (156, 157).

As considerações sobre a anatomia cutânea palmar sensitiva e a representação da abertura do retináculo dos flexores estão na Figura 7.

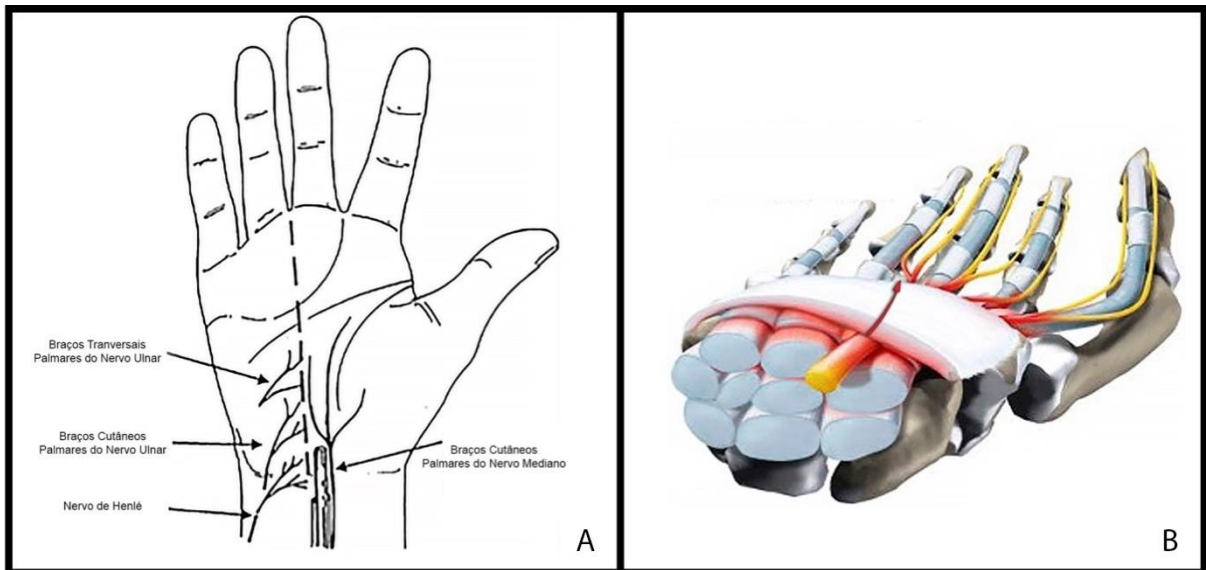


Figura 7: Anatomia cutânea palmar sensitiva (a) e representação esquemática da liberação do retináculo dos flexores. Fonte: (a) Modificado de (158) e (b) <https://www.hepsaglik.net/karpal-tunel-sendromu/> - acessado em 11/21

Na figura 8 é observado o nervo mediano após a abertura do retináculo dos flexores por CA.

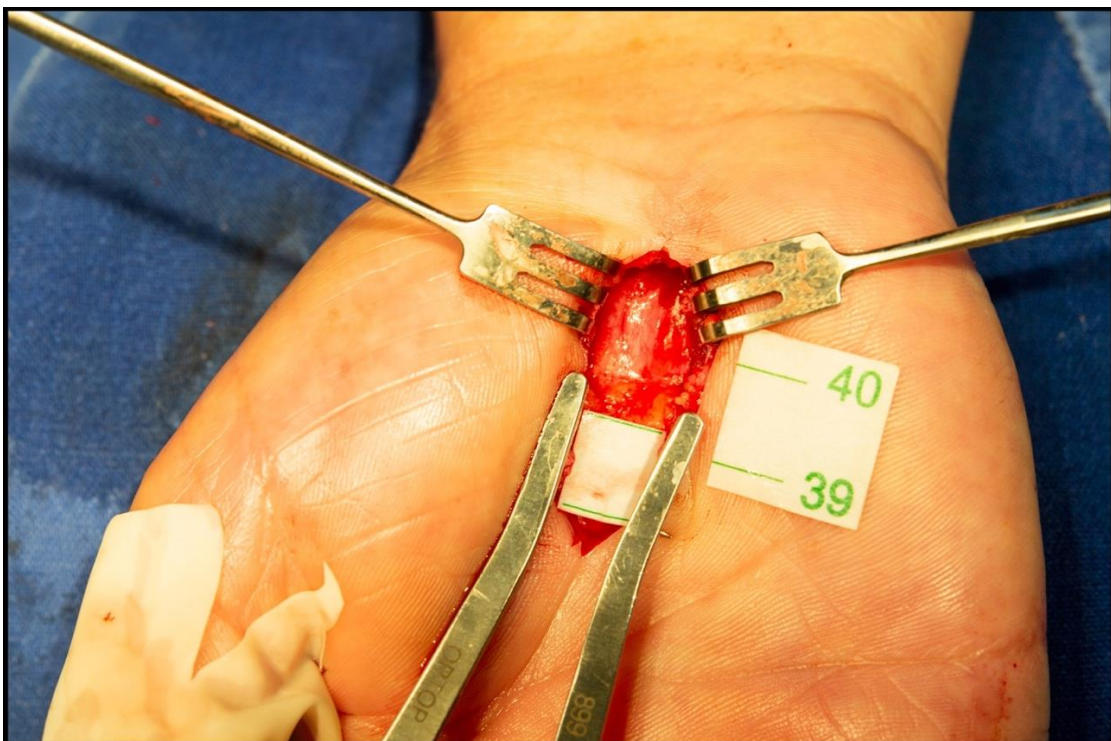


Figura 8: Visualização do nervo mediano após a abertura do retináculo dos flexores em CA. Fonte: O autor

Acessos palmares diminutos ou minimamente invasivos foram descritos por Bromley (1994) e por Huang e Zager (2004), (159, 160). Scholten e colaboradores

(2005) realizaram uma revisão de 60 estudos randomizados comparando a CA com várias outras técnicas, incluindo a CE. Os autores concluíram não haver superioridade entre a CA e as outras propostas (161).

Do mesmo modo, comparando a CA com a CE em 128 pacientes com um seguimento de cinco anos, Atroshi e colaboradores (2009) não encontraram diferença entre as técnicas (162). Por outro lado, ao analisar especificamente CA *versus* CE com acesso minimamente invasivo, Wong e colaboradores (2003) demonstraram a superioridade da CA em uma série de 30 pacientes operados e acompanhados por um ano (163).

Thoma e colaboradores (2004) realizaram uma meta-análise com 13 estudos randomizados comparando a CA e CE. Eles observaram que não havia superioridade entre as técnicas e que a decisão sobre qual das técnicas deveria ser utilizada é uma decisão que deve ser compartilhada entre o cirurgião e o paciente (164).

A fim de comparar os resultados do tratamento clínico com a terapêutica cirúrgica, Bland (2007) fez uma revisão de 209 estudos não randomizados, entre 2000 e 2006, com 32.936 intervenções cirúrgicas utilizando a CA. O autor concluiu que 75% dos casos operados com CA tiveram a resolução dos seus problemas ou permaneceram com sintomas leves, 17% tiveram melhora moderada e 8% reportaram piora dos sintomas.

Portanto, pensar que a melhora clínica se deve à queda da pressão no interior do túnel decorrente da liberação cirúrgica do LTC pode não ser uma realidade, pois isso não ocorreu em 25% dos casos operados (118). Matsuura e colaboradores (2016) propuseram que a não melhora após o tratamento cirúrgico na STC poderia ser decorrente de alterações no tecido conectivo subsinovial (TCSS) que comprometeriam o deslizamento normal entre o NM e os tendões dos flexores, causando lesões repetidas do NM pelo deslocamento dos tendões. Entretanto, são necessários novos estudos para compreender as repercussões que ocorrem no movimento quando se tem um TCSS estressado e tensionado (20).

Além disso, existem variáveis que são indicadoras de maus resultados pós-operatórios, tais como: a presença de polineuropatia associada ao *diabetes mellitus*, a idade avançada, o uso abusivo de álcool, o tabagismo, a presença de compressões do NM em mais de um local (*double crush syndrome*), a avaliação ENMG pré-operatória normal (165) e o gênero masculino (3).

Os achados físicos que predizem um pior resultado cirúrgico foram a atrofia do músculo ACP, os sintomas presentes bilateralmente e a presença do sinal de Phalen (166). A compensação trabalhista foi uma causa de retorno tardio ao trabalho, entretanto não houve relação com mau prognóstico (167).

O custo do tratamento cirúrgico nos Estados Unidos, por exemplo, foi superior a 2 bilhões de dólares (168). Já, no Brasil o custo com o tratamento operatório da STC entre 2008 e 2016 foi próximo a 30 milhões de reais (169). Sendo assim, devido à sua alta prevalência e incidência essa síndrome apresenta um elevado custo financeiro e social.

3.10.4.1 Manejo da Dor no Tratamento Cirúrgico

Várias técnicas anestésicas podem ser adotadas para realizar o procedimento cirúrgico na STC, tendo a anestesia local com lidocaína a vantagem de manter o indivíduo totalmente desperto durante o procedimento.

A associação da lidocaína com epinefrina na proporção de 1:100.000 visa diminuir o sangramento intraoperatório, evitando o uso de torniquete. Esse procedimento é conhecido como WALANT, sigla derivada da sua denominação na língua inglesa (*Wide Awake Local Anesthetic No Tourniquet*) (170).

A adição de bicarbonato de sódio a 8% na proporção de 1:10 à mistura anestésica anterior tem a finalidade de reduzir a acidez da lidocaína e, com isso, diminuir a dor durante a infiltração (171). O desconforto oriundo da injeção do anestésico pode ser amenizado com a utilização de uma única punção através da qual toda a infiltração anestésica é realizada. Esta técnica é descrita como *Hole-in-on* (172).

Por sua vez, a utilização de opioides como a codeína para controle da dor pós-operatória é uma estratégia que tem aumentado atualmente. Contudo, o seu emprego abusivo e indevido, apresenta um eventual potencial negativo por poder induzir à dependência (173). A fim de prevenir o uso exagerado de opioide, tem-se optado pela utilização da analgesia preventiva no controle da dor pós-cirúrgica (174). Essa analgesia é iniciada antes de o estímulo doloroso ser gerado e previne ou diminui a dor subsequente, permitindo uma menor necessidade de analgésico no pós-operatório (175).

Um dos medicamentos recentemente incluídos para analgesia preemptiva é a gabapentina que foi desenvolvida inicialmente para o tratamento da epilepsia, mas

passou a ser utilizada para o tratamento da dor (176). A gabapentina tem ação no sistema nervoso central e periférico e sua administração pode ser iniciada até 24 horas antes da cirurgia (177). Embora o seu mecanismo de ação não seja completamente compreendido, acredita-se que a gabapentina se ligue às duas subunidades dos canais de cálcio dependentes de voltagem neural, diminuindo a liberação de glutamato, norepinefrina e substância P, um neuropeptídeo que atua como neuromodulador (178).

A gabapentina ao reduzir a hiperexcitabilidade do neurônio no corno posterior da medula espinhal, que foi induzida pelo dano tecidual originário do procedimento cirúrgico, reduz a dor pós-operatória por um mecanismo de dessensibilização central (179). Devido a esse mecanismo preventivo, a gabapentina pode ser uma ferramenta útil para o controle da dor pós-cirúrgica, auxiliando na reabilitação do indivíduo (180).

3.11 INSTRUMENTOS DE AVALIAÇÃO DE RESULTADO DE TRATAMENTO

Vários instrumentos são propostos para avaliar os resultados de uma terapia específica para STC, podendo ser empregadas medidas objetivas e subjetivas. As avaliações objetivas são a ENMG, os exames de imagem como a USG de punho, a dinamometria palmar e digital, a avaliação de sensibilidade com monofilamentos de Semmes-Weinstein e a discriminação de dois pontos (22, 95, 181-184).

A dinamometria palmar avalia a força de preensão, que é utilizada como parâmetro de melhora tanto na área científica como na prática clínica das terapias utilizadas para a reabilitação da mão (185). Ademais, a preensão é entendida como indicador geral de força e potência musculares (186).

Existem dois tipos de preensão descritos na literatura: a força manual e a força de precisão. A primeira consiste em flexionar os dedos sobre a região palmar, enquanto a segunda está relacionada à força exercida entre o dedo polegar e o indicador. As mensurações dessas forças são feitas por dinamômetros que quantificam a pressão aplicada nesse sistema que é baseado em células de carga (187).

Os dinamômetros são divididos nos tipos isocinético e isométrico, sendo este último tradicionalmente utilizado nas medidas de força de preensão manual (FPM) e nas medidas de força digital, tais como: a pinça polpa-a-polpa (digital) e a pinça lateral (pinça em chave) (22).

A FPM traduz a força isométrica máxima ou *power grip* como a pressão resultante da ação de todos os dedos da mão, sendo a mais referenciada na literatura (21, 187, 188). A preensão digital polpa-a-polpa (pinça digital) é realizada entre as polpas digitais do polegar e do indicador, sendo empregada para pegar objetos pequeno. Essa é a medida mais sensível para avaliar a musculatura adutora do polegar, portanto a sua mensuração é relevante na avaliação de indivíduos com STC (21, 22).

As medidas objetivas de força de preensão palmar (pinça palmar) e força de preensão digital (pinça digital tipo ponta) estão demonstradas na Figura 9.



Figura 9: Preensão palmar (pinça palmar) (a,b,c) e força de preensão digital (d,e) (pinça digital tipo ponta). Fonte: O autor

Além dos instrumentos objetivos, é importante conhecer a percepção do paciente com relação aos resultados, ampliando dessa forma uma avaliação com medidas subjetivas (189), as quais podem ser divididas em testes físicos e instrumentos de resultados de saúde.

Entre os achados de exame físico estão os testes de Phalen e Durkan e o sinal de Tinel (190). A fim de medir o nível de dor percebida pelo paciente pode ser usada a escala visual analógica (EVA) (191), sendo os escores de saúde avaliados pelo questionário de Boston para STC e pelo questionário de qualidade de vida na sua forma simplificada, o SF-12 (24, 192-195).

A dor deve ser mensurada por ser uma experiência sensorial e emocional desagradável para o indivíduo, tendo um impacto negativo tanto na recuperação como na experiência global do tratamento (196). A EVA mede a dor aguda ou crônica por

meio de uma escala que vai de zero a dez, sendo que o valor zero é referente a ausência de dor e o dez é referente à pior dor estimada pelo indivíduo (23).

O questionário de Boston é um instrumento específico para STC que foi proposto por Levine e colaboradores (1993). Esse questionário reflete o impacto funcional da STC na vida do indivíduo, sendo constituído por dois escores. O primeiro é o da severidade dos sintomas que se refere aos sintomas da doença num período típico de 24 horas, durante as duas últimas semanas. Ele é composto por 11 questões com 5 alternativas sendo que a sua variação é de 11 a 55. O segundo escore é o da severidade funcional que é composta por 8 perguntas com 5 alternativas que refletem a dificuldade para realizar tarefas diárias, sendo que sua amplitude de graduação varia entre 8 e 40. Quanto maior o valor inicial para qualquer um dos escores pior é o quadro clínico e a melhora com a terapia é avaliada com a redução dos valores nas duas métricas (197). O questionário permite a padronização, a unificação e a reprodutibilidade das medidas a que se propõe e apresenta uma versão de Campos e colaboradores (2003) validada para o português (24).

Com base nos itens do SF-36, foi desenvolvido um questionário genérico de qualidade de vida, o SF-12, que é mais rápido e objetivo na sua aplicação, não demandando tanto tempo nem sofrendo influências das condições individuais anteriormente citadas (195). O SF-12 traz informações do escore qualidade de vida, quanto ao nível do estado cognitivo e das condições físicas, bem como as subescalas de dor corporal que são úteis para dores musculoesqueléticas, e tem sido utilizado para avaliar a eficácia do tratamento proposto (198). Camelier (2004) validou a versão do SF-12 para a língua portuguesa (25).

Diante do exposto, a interpretação dos resultados obtidos com medidas objetivas e subjetivas traduz os resultados dos tratamentos propostos para STC tanto do ponto de vista do médico como do paciente, pois ambos tendem a ter prioridades diferentes. Os médicos privilegiam os resultados positivos demonstrados pelos incrementos dos desfechos objetivos, enquanto os pacientes priorizam a melhora dos sintomas e a volta às atividades (26).

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5. PRODUTO 1 – CAPÍTULO DE LIVRO - ASPECTOS CLÍNICOS E FUNCIONAIS ENVOLVIDOS NA REABILITAÇÃO DE INDIVÍDUOS COM SÍNDROME DO TÚNEL DO CARPO.

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RESUMO

A síndrome do túnel do carpo (STC) é considerada a neuropatia compressiva mais comum dos membros superiores na população adulta e, devido a sua alta prevalência e incidência, tem um elevado custo social e financeiro. A STC é decorrente da constrição do nervo mediano no interior do túnel do carpo. Essa síndrome se apresenta bilateralmente na maioria dos casos e sua etiopatogenia é multifatorial. Ela pode ser classificada por critérios clínicos e eletroneuromiográficos em graus leve, moderado ou severo. Nos casos leves e moderados, são indicadas medidas terapêuticas clínicas como injeção de corticosteroides, medicação via oral e tratamento fisioterapêutico; já nos casos severos, a indicação é cirúrgica, com acesso aberto ou por endoscopia, sendo a fisioterapia recomendada também no pós-operatório a fim de auxiliar a recuperação dos pacientes. Na STC há um comprometimento do tecido conjuntivo subsinovial (TCSS), tanto ao nível do punho como ao longo do trajeto do nervo mediano no membro superior. Desta forma, métodos fisioterapêuticos direcionados para o TCSS, como é o caso do alongamento ou da manipulação miofascial, podem ser úteis para esses pacientes. Apesar da alta prevalência da STC, há uma escassez na literatura no que se refere ao melhor tratamento para reabilitação combinado ao tratamento clínico ou cirúrgico da STC. Diante do exposto, o presente capítulo tem como objetivo revisar os aspectos clínicos e funcionais relacionados à reabilitação da STC, com ênfase nas terapias de alongamento e manipulação miofascial.

PALAVRAS-CHAVE: Síndrome do túnel do carpo; Nervo mediano; Reabilitação; Alongamento; Manipulação miofascial.

ABSTRACT

Carpal tunnel syndrome (CTS) is considered the most common compressive neuropathy of the upper limbs in the adult population and, due to its high prevalence and incidence, it has a high social and financial cost. CTS is due to the constriction of the median nerve inside the carpal tunnel. This syndrome is presented bilaterally in most cases and its etiopathogenesis is multifactorial. It can be classified by clinical and electroneuromyography criteria in mild, moderate or severe status. In mild and moderate cases, clinical therapeutic measures are indicated, such as corticosteroid injection, oral medication and physical therapy treatment; On the other hand, in severe cases, there is surgical recommendation, with open access or by endoscopy and physiotherapy is also recommended in the postoperative period to assist patients' recovery. In CTS, there is a compromise of the subsynovial connective tissue (TCSS), both at the wrist as well as along the pathway of the median nerve in the upper limb. Thus, physiotherapeutic methods such as stretching or myofascial manipulation directed to the TCSS can be useful for these patients. Despite the high prevalence of CTS, there is a lack of evidence regarding the best treatment for rehabilitation combined to clinical and surgical treatment of the CTS. Therefore, this chapter aims to review the clinical and functional aspects related to CTS rehabilitation, with an emphasis on stretching and myofascial manipulation therapies.

KEY-WORDS: Carpal Tunnel Syndrome; Median nerve; Rehabilitation; Stretching; Myofascial manipulation.

1 INTRODUÇÃO

A síndrome do túnel do carpo (STC) é a neuropatia compressiva do nervo mediano (NM) mais comum na população, sendo consequente de qualquer condição anatomopatológica que cause uma redução da sua secção transversa ou uma expansão dos componentes do canal cárpico (1).

O valor estimado para a população geral nos EUA é de 5 % de prevalência, com incidência de 1 a 3 casos para 1000 habitantes (2). Em uma população com STC no Rio Grande de Sul, Becker e colaboradores (2014) constataram que 53,35% dos participantes eram mulheres, com predomínio na faixa etária entre 50 e 59 anos. Já os casos bilaterais foram 80,8% do total, 70,3% tinham comprometimentos moderado e grave, com a maior concentração de casos severos na população acima de 80 anos (3).

A etiopatogenia da STC é multifatorial, sendo as condições predisponentes para o seu surgimento as atividades físicas de impacto, os trabalhos manuais extenuantes ou repetitivos, os fatores constitucionais e as comorbidades clínicas (4). Ao mesmo tempo, o gênero, a idade e o tamanho do túnel do carpo são os fatores predisponentes mais importantes descritos na literatura (5). Contudo, na impossibilidade de se determinar um agente causal, essa síndrome passa a ser denominada de idiopática, a qual representa a maioria dos casos (6).

A STC pode ser diagnosticada por critérios clínicos ou eletromiográficos (ENMG), de modo que a associação desses dois parâmetros aumenta a precisão de 58% para 73% dos casos (7). O grau de severidade dessa síndrome também pode ser inferido pelos sintomas e sinais (3) ou pelo exame de ENMG (8). Stevens (9) propôs uma classificação da gravidade baseada na ENMG, dividindo o acometimento em casos leve, moderado e severo.

O tratamento recomendado para os achados ENMG leve e moderado são medidas clínicas, tais como o uso de fotobiomodulação (9, 10), a terapia com ultrassom terapêutico (11), os exercícios de alongamento (12) e a manipulação miofascial (MF) (13). Já o tratamento cirúrgico é indicado no acometimento de casos severos (14).

Os dois procedimentos operatórios principais são a cirurgia aberta (CA) e a cirurgia endoscópica (CE). Na presença de STC idiopática bilateral severa existe a opção de operar as duas mãos simultaneamente ou então operar uma delas e

avaliar a evolução da outra (15). No pós-operatório é recomendado também o tratamento fisioterapêutico, com a finalidade de auxiliar na recuperação tanto da mão operada como da não operada (16).

Entretanto, apesar da alta prevalência da STC, há uma escassez na literatura no que se refere aos possíveis métodos fisioterapêuticos para uma reabilitação eficaz combinado ao tratamento clínico ou cirúrgico desses pacientes.

2 DEFINIÇÃO, ETIOPATOLOGIA, FISIOPATOLOGIA E EPIDEMIOLOGIA DA STC

Por definição, a STC é decorrente da constrição do NM ao passar através do canal osteofibroso, chamado de túnel do carpo (17), o qual está localizado ao nível do punho. Várias situações têm em comum uma desproporção entre o espaço e os elementos que formam o túnel cárpico, podendo esse desequilíbrio ser decorrente do aumento do volume dos tendões ou do NM, de um estreitamento extrínseco do túnel ou do aumento do volume de estruturas que normalmente não compõem o canal, como é o caso do depósito de substâncias anômalas ou tumores (18, 19).

A fisiopatologia decorre dos efeitos compressivos, tendo uma relação direta com o tempo de duração da compressão, sendo os períodos inferiores a 4 horas bem tolerados pelo NM, não comprometendo fibras amielínicas nem causando degeneração axonal. Assim, nessa fase da doença não haverá quadro algíco constante ou atrofia da musculatura da região tenar, podendo permanecer uma sintomatologia intermitente por anos (20).

Contudo, o NM previamente submetido a uma compressão intermitente ficará mais sensível à isquemia, levando à evolução da doença, com sintomas desencadeados por movimentos repetitivos do punho, sinais de irritação do NM e parestesias noturnas (21), que são relacionados a mecanismos hemodinâmicos, associados à mudança da posição ereta para a deitada, promovendo assim uma imediata redistribuição de sangue, retirando o fluxo dos membros inferiores e redirecionando-o para o tórax e membros superiores (22)

O ingurgitamento venoso nos membros superiores produz um aumento gradual da pressão no túnel do carpo, que atinge o seu máximo de 3 a 6 horas após

o indivíduo se deitar, o que causa uma parestesia dolorosa em seus braços, despertando-o após um sono inicial e conduzindo-o a movimentar os braços para obter um alívio dos sintomas (23). A sucessão desses episódios acarreta uma perda da barreira vascular entre o nervo e o vaso sanguíneo (*breakdown*), o que provoca um acúmulo tanto de proteína como de células inflamatórias na porção intrafascicular do NM, gerando no nervo uma fibrose intraneural não inflamatória, com perda axonal progressiva, que poderá causar parestesias persistentes e déficit de força nas mãos (24).

Quadro semelhante foi descrito por Kim e colaboradores (2010) na lesão isquêmica seguida de reperfusão, que ocorre quando há um estresse oxidativo focal (25). Nessa etapa fisiopatológica, existe uma hiperexcitabilidade neuronal do NM que provoca descargas ectópicas persistentes (24). Esses estímulos contínuos em indivíduos com STC bilateral ativam os interneurônios comissurais localizados na medula espinhal, no tronco cerebral e no córtex cerebral. A hipersensibilização deste último gera um ciclo inibitório que compromete as vias sensitivas, causando uma repercussão tanto no sistema nervoso periférico como no central (26).

A STC corresponde a 90% das neuropatias periféricas compressivas, acometendo cerca de 10% da população mundial ao longo da vida, com aproximadamente três a quatro casos novos para cada 1000 habitantes por ano, tendo apresentado um aumento gradual na última década (27). A síndrome atinge três vezes mais mulheres do que homens, com uma prevalência na terceira e quarta década para mulheres e na sexta até a oitava década para os homens.

Além disso, a STC se apresenta bilateralmente em 60% dos casos (28), sendo o quadro bilateral quatro vezes mais frequente em mulheres na faixa etária de 45 a 65 anos e com índice de massa corpórea acima de 29 (29). Conforme o estudo de Claire e colaboradores (2018), tem ocorrido um aumento da prevalência de STC ao longo de um período de vinte anos, além da redução da razão entre o sexo feminino e masculino, que era de 2,74 em 1993 para 1,93 em 2013, e um aumento da idade média de acometimento, que para as mulheres foi de 49 e 53 anos e para os homens foi de 54 e 59 anos (27).

Assim, devido à sua alta prevalência e incidência, a STC apresenta, além da importância do ponto de vista patológico, um elevado custo social (30). Os Estados Unidos, por exemplo, tem um gasto superior a dois bilhões de dólares somente com

tratamento cirúrgico (31). No Brasil, o custo com o tratamento operatório da STC entre 2008 e 2016 foi próximo a trinta milhões de reais (32).

3 QUADRO CLÍNICO E HISTÓRIA NATURAL DA STC

A Academia Americana de Cirurgiões Ortopédicos definiu a STC como uma neuropatia de compressão sintomática do NM ao nível do punho (33). Embora sejam descritos vários sintomas e sinais que a caracterizam, a presença de um ou mais, dos três achados a seguir confirmam o diagnóstico da síndrome. São eles: as mudanças sensoriais restritas à distribuição do NM na mão; o desencadeamento de parestesias na distribuição do NM, quando é feita uma percussão na crista distal do punho sobre o NM (sinal de Tinel); e a ocorrência de parestesias na distribuição do NM, quando o paciente flexiona os punhos a 90° por 60 segundos (34). Este último achado é conhecido como sinal de Phalen (35).

Os principais fatores que predispõem a STC são divididos em constitucionais, tais como a idade avançada, o gênero, o índice de massa corporal, a menopausa e a gravidez (36), e em comorbidades clínicas, como o *diabetes mellitus*, o hipotireoidismo, a obesidade e a artrite reumatoide (37). Do mesmo modo, estudos concluíram que existe uma associação significativa entre a STC e a exposição a trabalhos que exigem força manual, movimentos repetidos de punho, uso de ferramentas vibratórias, assim como a prática de algumas atividades esportivas como o beisebol, o basquetebol, o fisiculturismo, o *motocross* e o ciclismo (38-40).

A história natural demonstra que a STC idiopática pode ter uma melhora clínica sem nenhuma intervenção em 21% dos casos, após 10 a 15 meses de seguimento (41). Um estudo observacional com 257 indivíduos com STC idiopática seguidos por 5 anos demonstrou a resolução dos sintomas no período de 6 meses em 34% dos casos (42).

Ao avaliarem 65 STC bilaterais onde os participantes tiveram uma mão operada e outra não, Unno e colaboradores (2015) relataram que houve melhora na mão não operada em 94% dos casos, sendo esse resultado positivo detectado a partir do segundo dia pós-operatório e persistindo seis meses após a cirurgia (43). Resultados semelhantes foram relatados por Agrawal e Southern (2010) em carpos bilaterais, descrevendo uma melhora da mão não operada em 37% dos casos (44).

As razões da melhora na mão não operada ainda não são bem compreendidas e há necessidade de futuras investigações a fim de esclarecer a indicação ou não do tratamento cirúrgico simultâneo em carpos bilaterais (45). Desse modo, qualquer tratamento proposto para STC deverá apresentar um resultado superior ao da história natural da doença (41).

4 TRATAMENTO

Os tratamentos para STC idiopática podem ser realizados por medidas clínicas ou cirúrgicas, sendo a sua indicação baseada na severidade da doença. Nos graus leves e moderados o tratamento é clínico, enquanto nos graus severos é indicada a cirurgia, podendo ser complementada com terapias de reabilitação pós-operatórias (46).

4.1 TRATAMENTO CLÍNICO

O tratamento clínico é indicado nos casos em que os sintomas dolorosos interferem na atividade diária do paciente e quando os achados ENMG demonstram um comprometimento leve ou moderado da função do NM. As terapias clínicas que apresentaram um desfecho superior ao da história natural da doença são as talas de punho, a cinta de mão, a injeção local de esteroides e o uso de tala mão-punho, que tem sido recomendado há vários anos no tratamento da STC (47).

De Angelis e colaboradores (2009) relataram que o uso da tala obteve melhora em 37% dos casos, entretanto não foi observada diferença entre o uso de tala de punho e a cinta de mão (48). O tempo que o indivíduo deve usar a tala para obter os benefícios permanece controverso na literatura, com autores revelando que existe melhora com o uso restrito ao período noturno (49), enquanto outros pesquisadores não evidenciaram vantagem com o uso da tala tanto em período diuturno como em uso exclusivamente noturno (50).

A mesma controvérsia ocorre em relação à angulação da tala com o punho, não havendo diferença se está em posição neutra ou a 20° de extensão em relação ao punho (51). Do mesmo modo, não foi demonstrada na literatura uma melhora

da STC com a utilização de talas em longo prazo, de modo que a progressão da doença possa ocorrer mesmo durante o uso (52).

A injeção de corticosteroides no punho apresenta uma melhora imediata dos sintomas em 70% dos indivíduos (53). Todavia, em uma revisão sistemática, Marshall e colaboradores (2007) relataram que esse benefício não se manteve além de um mês (54). A STC pode ser tratada também com medicamentos via oral, tais como esteroides (55), vitamina B6 (piridoxina) (56), antidepressivos (57) e gabapentinóides (58), contudo os resultados são conflitantes na literatura (59).

Outras medidas são utilizadas para o tratamento clínico da STC, como terapia única ou como associação. Além das modificações das atividades diárias (60), o tratamento fisioterapêutico é recomendado, podendo incluir o uso de laserterapia de baixa intensidade (10), terapia com ultrassonografia (11), exercícios de alongamento (12) e manipulação miofascial (MF) (61). Porém, devido à quantidade limitada de pesquisas e à baixa qualidade das evidências sobre os benefícios dos diferentes métodos, há a necessidade de estudos mais robustos sobre o tema (62).

4.2 TRATAMENTO CIRÚRGICO

Os casos de STC com compressão severa, observada na ENMG, têm indicação cirúrgica. Além disso, se as terapêuticas clínicas não forem eficazes no controle da doença em longo prazo e se houver piora do quadro clínico e dos parâmetros eletroneuromiográficos, o tratamento cirúrgico deve ser considerado (63).

A piora clínica manifesta-se por meio da progressão do déficit motor, da presença de déficit sensorial contínuo e da instalação de atrofia na musculatura tenar (46). Para tratar a situação, existem dois procedimentos cirúrgicos consagrados na literatura para essa finalidade: a cirurgia aberta (CA) e a cirurgia por via endoscópica (CE). Thoma e colaboradores (2004) realizaram uma metanálise com 13 estudos randomizados comparando CA e CE e observaram que não havia superioridade entre as técnicas e que a decisão sobre qual delas utilizar cabe à preferência do cirurgião e do paciente (64).

A fim de comparar os resultados do tratamento clínico aos da terapêutica cirúrgica, Bland (2007) fez uma revisão de 209 estudos não randomizados, entre 2000 e 2006, com 32.936 intervenções cirúrgicas utilizando a CA. O autor concluiu que 75% dos casos tiveram a resolução dos seus problemas ou permaneceram com sintomas leves, 17% referiram melhora moderada e 8% reportaram piora dos sintomas. Portanto, pensar que a melhora clínica se deve à queda da pressão no interior do túnel decorrente da liberação cirúrgica do LTC pode não ser uma realidade, pois isso não ocorreu em 25% dos casos operados (53).

Matsura e colaboradores (2016) propuseram que a não melhora poderia ser decorrente de alterações no tecido conectivo subsinovial (TCSS), que no seu estado normal permite o deslizamento suave entre os tendões e o NM, além de fornecer proteção para este último contra os impactos decorrentes dos movimentos dos tendões (65). Porém, são necessários novos estudos para compreender as repercussões que ocorrem no movimento quando o TCSS se encontra estressado e tensionado.

5 ESTRATÉGIAS DE FISIOTERAPIA DIRECIONADAS PARA A REABILITAÇÃO DE INDIVÍDUOS COM STC

A utilização de métodos e recursos fisioterapêuticos direcionados para o TCSS são úteis na reabilitação clínica e pós-cirúrgica de indivíduos com STC (66). Dentre eles, o alongamento e a manipulação miofascial têm apresentado potencial relevante como estratégias de reabilitação desses pacientes (67, 68).

5.1 EXERCÍCIOS DE ALONGAMENTO

A restauração da amplitude de movimento (ADM) após uma lesão é um dos principais objetivos de qualquer programa de reabilitação. A utilização de programas de alongamento efetivo em determinados músculos altera a extensibilidade das unidades neuromusculotendíneas de determinadas articulações. Assim, os exercícios que alongam essas unidades e suas fáscias, com o tempo, aumentam a ADM possível na articulação (69, 70), auxiliando também no controle da dor (71).

No passado, a eficácia do alongamento na melhora da ADM foi atribuída, em termos teóricos, aos fenômenos neurofisiológicos que envolviam o reflexo de estiramento. Contudo, um estudo que revisa de modo extensivo a literatura existente sugere que as melhoras na ADM resultantes do alongamento possam ser explicadas por processos que vão além do reflexo de estiramento. O autor indica que há alterações na habilidade de o músculo tolerar o alongamento, associadas a mudanças nas propriedades viscoelásticas do músculo alongado (72).

Pacientes com STC apresentaram uma diminuição da pressão dentro do túnel quando foram submetidos a exercícios para as mãos (73). Schmid e colaboradores (2012) relataram diminuição do edema no NM, registrada pela ressonância magnética, e melhora clínica avaliada pelo questionário de Boston em indivíduos que realizaram os exercícios de alongamento em casa, durante uma semana, com dez repetições por dia da sequência proposta, após um treinamento prévio supervisionado (74).

Os exercícios de alongamento promovem um aumento do fluxo circulatório para tecidos desidratados, que reduz o edema intercelular e reidrata os ligamentos e os tendões (75). O estiramento e a compressão das fibras musculares influenciam tanto os proprioceptores como os nociceptores, neutralizando os padrões disfuncionais ao nível da medula espinhal e córtex cerebral, decorrentes das cadeias miofasciais alteradas. Além disso, o alongamento promove uma distensão da região de interesse até o final da sua amplitude de movimento, que produz uma distensão das células do tecido conjuntivo, propiciando uma remodelação da matrix extracelular (76).

Contudo, existe uma carência de modelos topográficos e histológicos que expliquem as interações entre o alongamento e as repercussões funcionais que ocorrem nos tecidos adjacentes, tais como tendões, nervos, ligamentos e fáscia (77). A comparação dos resultados da terapia com exercícios de alongamento em artigos clínicos apresenta limitações devido à falta de padronização, decorrente de protocolos diferentes que variam quanto à intensidade, à duração, à frequência dos movimentos e ao tempo que deveria ser despendido com o alongamento terapêutico, a fim de provocar os efeitos fisiológicos desejados (78, 79).

6 MOBILIZAÇÃO MIOFASCIAL (MF)

A MF é uma técnica fisioterápica que pode ser utilizada no tratamento da STC, contudo, a fim de discutir esse método, é necessário definir os conceitos de fáscia e de sistema fascial (80).

A fáscia é formada por camadas de tecido conjuntivo, que estão dispostas abaixo da pele e englobam os músculos e os órgãos internos. Já o sistema fascial abrange um conglomerado de funções inter-relacionadas, como as forças de transmissão, as funções sensoriais e as regulações referentes à restauração tecidual (81). Esse sistema forma uma rede de tecidos interdependentes que se interconectam e interagem de forma complexa, colaborando para a execução dos movimentos (82). Além disso, ele pode ser afetado por patologias que acometem o tecido conectivo, causando alterações nociceptivas e proprioceptivas, disfunções vasculares e linfáticas, bem como limitações dos movimentos (83).

A fim de interpretar essas inter-relações tridimensionais do sistema fascial, Stecco e colaboradores (81) dividiram o corpo em quatorze segmentos: cabeça, pescoço, tórax, lombar, pélvis, escápula, ombros, cotovelos, antebraços, mãos, quadril, joelhos, tornozelo e pés. Segundo a interpretação dos autores, em cada uma das partes relacionadas há seis unidades miofasciais, que são compostas por músculos mono ou biarticulares e a sua fáscia correspondente.

A fáscia apresenta uma distribuição espacial nos três planos ortogonais, portanto sua mobilidade deve se avaliada em seis direções diferentes, sendo examinados os movimentos no sentido anterior, posterior, lateral e medial, bem como as rotações interna ou externa (84). Cada uma das seis unidades miofasciais tem uma localização específica na fáscia profunda que é chamada de centro de coordenação, com pontos específicos de convergência das forças vetoriais dos músculos envolvidos em um movimento (85).

Outra interpretação dessa distribuição espacial da fáscia foi feita por Myers (1996), que descreveu um modelo de distribuição espacial dos músculos, articulações, tendões e tecido fascial, criando o conceito de cadeias miofasciais ou trilhos anatômicos. O trilho anatômico é construído por unidades de tecidos conectivos ou miofasciais, em continuidade com o osso, tendões e outras fibras fasciais, tendo como condição essencial a continuidade das fibras e a não transposição de uma articulação (86).

Desse modo, o autor relatou as seguintes linhas anatômicas: posterior superficial, frontal superficial, lateral, frontal profunda e dos braços, que é dividida

em anterior e posterior. Os mucopolissacarídeos ou glicosaminoglicanos que constituem os elementos viscoelástico da fáscia permitem que esses trilhos deslizem quase sem atrito em um ambiente gerado entre a tensão e o equilíbrio dessas linhas, conferindo ao sistema uma tensegriedade, ou seja, uma integridade estrutural resultante da interação entre as forças de tensão e compressão (87).

Os procedimentos fisioterapêuticos direcionados para o tecido miofascial, ou seja, a manipulação fascial (MF), podem ser realizados somente com as mãos ou acrescer o auxílio de instrumentos ao trabalho manual. A MF manual foi derivada do conceito de massagem transversa profunda por fricção de Cyriax (88), sendo aperfeiçoada pela adição de princípios biomecânicos que foram feitos por dois fisioterapeutas nórdicos, criando o conceito *Kaltenborn-Evjenth*® (89).

A MF manual faz uma fricção sobre um ou mais pontos de restrição que podem existir na cadeia miofascial, sendo esse estímulo biomecânico propagado por meio de forças vetoriais nos três planos dimensionais pelos tecidos fasciais (82). A MF assistida por instrumento recebe o nome de *Instrument-Assisted Soft Tissue Mobilization* e tem como objetivo facilitar os processos de recuperação tecidual, fazendo com que a energia mecânica desprendida seja mais eficiente com o auxílio instrumental.

Kurt Ekman foi o pioneiro na associação MF manual com ganchos (*crochet*), desenvolvendo a técnica “*Crochetagem Mioaponeurótica*” ou “*Diafibrólise Percutânea*”, tendo por finalidade alcançar pontos de manipulação inacessíveis ao uso das mãos (90). O uso de dispositivos para MF aprimora a sensibilidade do terapeuta para identificar pontos profundos de restrição da fáscia, permitindo o trabalho em diferentes ângulos de restrição (91).

O tratamento se baseia em uma abordagem centrípeta, iniciando de fora para dentro dos tecidos, sendo a técnica composta por três fases sucessivas: palpação digital, palpação instrumental e diafibrólise. A fase palpatória digital consiste em seguir as cadeias musculares e as fáscias acometidas, delimitando com a mão palpatória as áreas a serem tratadas.

Na fase palpatória instrumental, por sua vez, a outra mão segura o gancho colocando o dedo indicador na espátula, posicionando o conjunto perpendicular às fibras tissulares de interesse. A abertura do gancho corresponde ao acoplamento justo com a massa tecidual que se pretende aplicar a manipulação por meio do *crochet*. Precedendo os movimentos da mão instrumental, a mão palpatória, segura

o tecido por meio de uma pinça digital entre o polegar com o segundo e o terceiro dedo, a fim de criar um efeito de onda ao tracionar a área de interesse (92).

Já na fase de fibrólise, a mão instrumental faz uma tração complementar que alonga as fibras tissulares, rompendo as aderências miofasciais e promovendo a restauração da mobilidade tecidual, sem que isso cause dor. Pode-se associar, em áreas com inserções ligamentares ou de tendões no periósteo, uma raspagem dessas estruturas com o auxílio do gancho associado à manipulação manual (93).

A energia mecânica produzida pela fricção do gancho nos planos miofasciais induz à transformação e proliferação de fibroblastos, promovendo tanto um aumento da síntese de colágeno como a remodelação dos tipos de colágeno, restaurando o sistema de colágeno multimicrovacuolar de absorção dinâmica (65, 75), que promove alterações estruturais na fáscia e no sistema fascial, tanto local como a distância, produzindo a recomposição da integridade estrutural dos tecidos fasciais comprometidos (94, 95).

Esse método tem tido aprimoramentos ao longo do tempo em relação ao tipo de gancho, ao material utilizado para sua confecção, às indicações terapêuticas e à sua associação com outros procedimentos fisioterapêuticos (96), permitindo que a MF com uso de *crochets* seja um procedimento eficaz em inúmeras patologias (97, 98), inclusive na STC (68).

7 CONCLUSÃO

A STC é uma patologia complexa, com uma interpretação atual que excede a noção anterior de uma neuropatia compressiva focal do NM. Em razão de sua alta prevalência e incidência, essa patologia tem um elevado custo social e financeiro.

Na STC há um envolvimento do TCSS local ao nível do carpo e ao longo do NM. Desta forma, métodos de reabilitação como o alongamento e a manipulação miofascial são uma alternativa para reconstruir as características viscoelásticas e a integridade tensional desse tecido conectivo, quer seja ao nível do carpo, quer seja a distância, recuperando a funcionalidade do sistema fascial.

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6. PRODUTO 2 – ARTIGO 1 - BILATERAL AND IDIOPATHIC CARPAL TUNNEL SYNDROME: CLINICAL – FUNCTIONAL FEATURES AND EFFECT OF THE TWO COMBINED PHYSIOTHERAPEUTIC TREATMENT METHODS IN MILD AND MODERATE CASES.

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ABSTRACT

Introduction: Carpal tunnel syndrome (CTS) is the most common compressive neuropathy in the adult population worldwide and is mostly bilateral. The stretching and myofascial mobilization with instrument (IASTM) has been recommended for the treatment of mild and moderate cases, yet evidence of its combined results is limited. **Objective:** To evaluate the effect of two sequences of physical therapy treatments in patients with mild and moderate idiopathic bilateral CTS, both during the therapy period and at a six-month follow-up period of outpatients. **Method:** A 2x4 randomized controlled cross-over study with 30 participants using both objective (handgrip and digital pinch) and subjective (Visual Analog Scale (VAS), Boston questionnaire and SF-12) outcome variables. Participants were selected at random using blinded and sealed envelopes by an unrelated research staff member into two groups: starting with stretching followed by IASTM or starting with IASTM followed by stretching. Before starting therapy, patients were assessed (baseline). Both stretching and IASTM were performed in two sessions per week over a period of four weeks, according to standardized protocols. After the one-week interval (wash-out 1), outcome measures were collected at time 1. Next, participants who initially performed stretching were referred to IASTM and vice-versa, following the same patterns as before. Assessment at time 2 occurred after a second interval period (wash-out 2), and outpatient reevaluations were done three and six months after time 2. **Results:** Data analysis by ANOVA Cross-Over allowed evaluating the results regarding the components: used sequence, treatment, loading and period. For significant results in the ANOVA Cross-Over, the effect size was calculated. The sequences used did not show significant differences for any outcome. Treatment was statistically significant ($p < 0.01$) for pain in both hands, and the effect size was large ($d > 0.80$) for both pain and digital pinch, bilaterally. The data also pointed to a better performance of the IASTM in these variables. There was a significant difference ($p < 0.01$) for all outcomes regarding the period, with large effect sizes ($d > 0.80$), with the exception of SF-12 physical, which was intermediate ($d = 0.67$). **Conclusion:** Combined association of stretching and IASTM proved to be both supplementary and effective with robust results both during the course of the applied therapies and at the six-month follow-up period in patients with idiopathic bilateral CTS with mild and moderate impairment.

Key words: Carpal tunnel syndrome; Muscle stretching exercises; Myofascial mobilization; Connective/soft tissue techniques; Physiotherapy; Cross-Over Studies.

1 INTRODUCTION

Carpal tunnel syndrome (CTS) may be defined as a symptomatic compression neuropathy of the median nerve (MN) at the wrist level (1), making it the most common compressive syndrome of the upper limbs. Its incidence is 3 to 4 new cases per 1000 population/year, affecting women predominantly in the age range of 45 to 65 years old, and being bilateral in 65% of cases (2).

CTS etiopathogenesis is multifactorial: advanced age, gender, high body mass index, menopause and pregnancy are the main constitutional factors (3). Relevant clinical comorbidities, on the other hand, are *diabetes mellitus*, hypothyroidism, obesity, and rheumatoid arthritis (4). When a causative agent cannot be found, this syndrome is referred to as idiopathic (5).

The diagnosis of CTS can be made by clinical or electroneuromyography criteria. The clinical condition presents sensorial changes restricted to the distribution of the NM on the hand and Tinel and Phalen's signs. The presence of one or more of these three findings is fundamental to determine the clinical diagnosis, according to the proposal of Claire and colleagues (2018) (6). Additionally, electroneuromyography (ENMG) is used for both diagnosing and quantifying the severity of NM compression, and severity levels can be divided into mild, moderate, or severe (7).

Clinical treatment may be considered in cases of mild and moderate CTS due to the possibility of cure (8), as well as avoiding the risks of a surgical procedure (9). The indicated therapies are those that have a superior outcome over the natural history of the disease: cases of wrist splints, hand brace, and local steroid injection (10).

Currently, other methods are being used in clinical therapies for CTS, such as photobiostimulation use (11, 12), ultrasound therapy (13), stretching exercises and myofascial mobilization (14), these methods are being used alone or in association with others (15). Borgi and colleagues (2013) suggest that manual therapies are more promising for the non-surgical treatment of CTS (16), as stretching exercises and myofascial mobilization have an additive effect on functional rehabilitation (17).

Page and colleagues (2012) in a Cochrane meta-analysis, with emphasis on mobilization exercises and interventions for the treatment of CTS highlight that

there is a limited amount and low-quality evidence of benefit for various types of exercises and mobilization interventions for CTS (18).

There is also some controversy in literature regarding the outcomes of clinical treatments (19), especially when the sample contains patients with bilateral CTS. Page and colleagues (2013) when analyzing the allocation methods and statistical analyses of randomized controlled trials (RCTs) of patients with bilateral CTS undergoing clinical treatments found that the reported evidence of the effects of therapies was weak, and improved study design and statistical analyses were needed in order to provide reliable evidence for clinical practice (18, 19).

In this context, the present study aims to analyze the effect combined of stretching and myofascial mobilization with instrument (IASTM) in the clinical rehabilitation of patients with idiopathic bilateral mild and moderate CTS degrees.

2 METHODS

This is a prospective, randomized, double-blind, 2x4 cross-sample study. All participants were recruited by the Neurosurgery team of the Irmandade da Santa Casa de Londrina, in the carpal tunnel outpatient clinic, during the period between February 2017 and January 2018. The study was approved by the ethics committee of the Irmandade da Santa Casa de Londrina under number 3.276.439, registered at ClinicalTrials.gov (NCT04347746), and the Informed Consent Form was signed by all participants.

The inclusion criteria for participants were to be 18 years of age or over, have idiopathic bilateral CTS, present one or more of the clinical criteria defined by Claire and colleagues (2018) (6), present normal results on laboratory tests to exclude associated pathology (CBC, renal function glucose curve, rheumatic profile, and thyroid profile), have ENMG criteria indicating mild or moderate impairment in the different hand combinations according to Stevens' criteria (1997) (7), and have no upper limb limitations or skin lesions that would prevent them from performing the suggested therapies.

Patients with a history of psychiatric disorders or mental retardment, pregnant women, who had received previous treatment with steroid infiltration for CTS or who were symptomatic for a period of less than six months were

excluded. All ENMG were performed in the same laboratory, on the same machine (Dantec Ketpoint, Natus®, Pleasanton, USA) and by the same specialist electrophysiologist, following the service reference values, based on the Stevens classification (1997) and the technical standards recommended by the American Association for Electrodiagnostic Medicine (20).

Patients who met the inclusion criteria were referred to the rehabilitation sector of the Pitágoras/Unopar University, where they were randomly allocated into two groups using the random function of the Excel® program, in a 1:1 ratio. Opaque envelopes were used according to random sequence, which were numbered and closed. Inside each envelope was the task of starting with the static active stretching technique (S or Streaching) or with the myofascial mobilization technique (M or IASTM), and randomization was done by a member not involved in the research. After choosing the envelopes and defining the sequence to be followed, all participants were evaluated at time zero (T0).

2.1 STUDY PROTOCOL

The selected participants from both group S/M (stretching followed by myofascial mobilization) and group M/S (myofascial mobilization followed by stretching) received the same treatment on both sides. Static active stretching was performed on six muscle groups located in the cervical region, shoulder, arm, forearm, wrist, and fingers, totalizing 20 exercise sequences, in the standing position. A stretching series was performed for each exercise sequence, lasting 40 seconds and with a one-minute rest interval between each muscle group. The stretching was performed aiming for the greatest possible amplitude to the point of discomfort, but not to the point of pain, remaining in the position for 40 seconds. The supervised stretching was done twice a week for four weeks, with a total time per session of approximately 45 minutes.

Myofascial mobilization was performed exposing the target region, without the use of any cosmetics on the skin. The protocol consisted in mobilizing the myofascial tissue of the thoracic and dorsal regions, shoulder muscles, arm and forearm muscles, in the anterior and posterior face, in the dorsal, ventral and

lateral decubitus, bilaterally, with a total time per session of approximately 45 minutes.

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A superficial scraping was added, using the convex part of the crochets, on the insertions of the major pectoral muscles at the sternum and the trapezius at the occipital, bilaterally.

After a one-week rest period (wash-out 1), the participants were re-evaluated with the outcome instruments (time T1). Subsequently, the participants who had started with stretching began to receiving IASTM and vice versa, following the same schedule described above. At the end of the fourth week, after a one-week rest period (wash-out 2), the participants were reassessed (time T2), and there were no complications during the use of both therapies. Then, patients were referred for outpatient follow-up, and new re-evaluations were performed at three months (time T3) and 6 months (time T4) after T2. Throughout the treatment period there were no recommendations for the use of orthoses, pain medication, or restrictions on hand use.

All professionals involved in the research were blinded as to the outcome of the randomization, collection of the results at the different times, and data analysis.

2.2 ASSESSMENT INSTRUMENTS

The outcome analysis were assessed by the following instruments:

a) In the maximal force assessment in isometric contraction, the Hydraulic Hand Dynamometer (Jamar ® Patterson Medical, Warrenville, IL, USA) for palmar grip and Hydraulic Pinch Gauge (Jamar ® Patterson Medical, Warrenville, IL, USA) for digital pinch were used. The technical standards for the acquisition of the two measurements followed the instrument manual of each device (21, 22)

and the result used, both for the palmar grip and the digital pinch, was the better of three successive measurements, with verbal command and 30 seconds rest between measurements. The same dynamometers were used for all reevaluations during the study.

b) In assessing perceived pain, the Visual Analog Scale (VAS) adapted with the Wong-Baker face scale (23) was used. The assessment of pain intensity was based on the present moment, with a value of 0 on the scale equivalent to no pain and a value of 10 referring to the worst possible pain. Improvement was evaluated by the reduction of pain intensity values.

c) The functional impact was evaluated by the Boston Carpal Tunnel Questionnaire (BCTQ) scores, by score of Boston Sensitive or scale symptom severity scale (SSS) and score of Boston Function or state scale functional (FSS). The SSS is composed of 11 questions, with scores ranging from 11 to 55; and the FSS is composed of 8 questions, and its range is between 8 and 40. The higher the initial value for any of the score, the worse the clinical condition, and the improvement with therapy is evaluated with the reduction of the values in the two metrics (24, 25). These two scores were used separately to assess the outcome.

d) Life quality in the physical and mental aspects was evaluated using the SF-12 (12-Item Short Form Health Survey) questionnaire (26), considering the subjects' perception of their health in the last 4 weeks. The physical (Physical Component Summary) and mental (Mental Component Summary) scores varied on a scale from 0 to 100, associating higher values in each of the two aspects to a better level of quality of life (27, 28).

2.3 STATISTICAL ANALYSIS

The sample estimate for a Cross-Over Study, with statistical power of 80%, pondering the hypothesis of occurrence of loading, typical of these study designs, should be estimated at 12 participants per group according to Mills and colleagues (2009) and Chow and Wang (2001) (29, 30).

The Statistical Package for Social Sciences version 25.0 and the Stata program version 15.0 were used, and a 5% significance level was set for the

applied tests. The ANOVA Cross-Over models were estimated by Ordinary Least Squared (OLS), using the Stata v.15 pkcross routine.

The zero period observations served as baseline, that is, the ANOVA Cross-Over models were developed from the difference results of the T0 period (baseline), that is: $T1 = T1' - T0$, ..., $T4 = T4' - T0$, as indicated by Tudor, Koch and Catillier (2000) (31).

In addition to the ANOVA Cross-Over, the differences between treatments were also evaluated only in the first period in order to completely exclude the effects of loading. From the differences in the outcomes at baseline and the first period between the groups (IASTM *versus* S), the Mann-Whitney (z) test was performed. This same test was used to compare the profile scalar variables between the sequences in the sample description, and in this section the Fisher's Exact Test was used for the categorical variables. Between repeated measures the Wilcoxon (z) Test was also used.

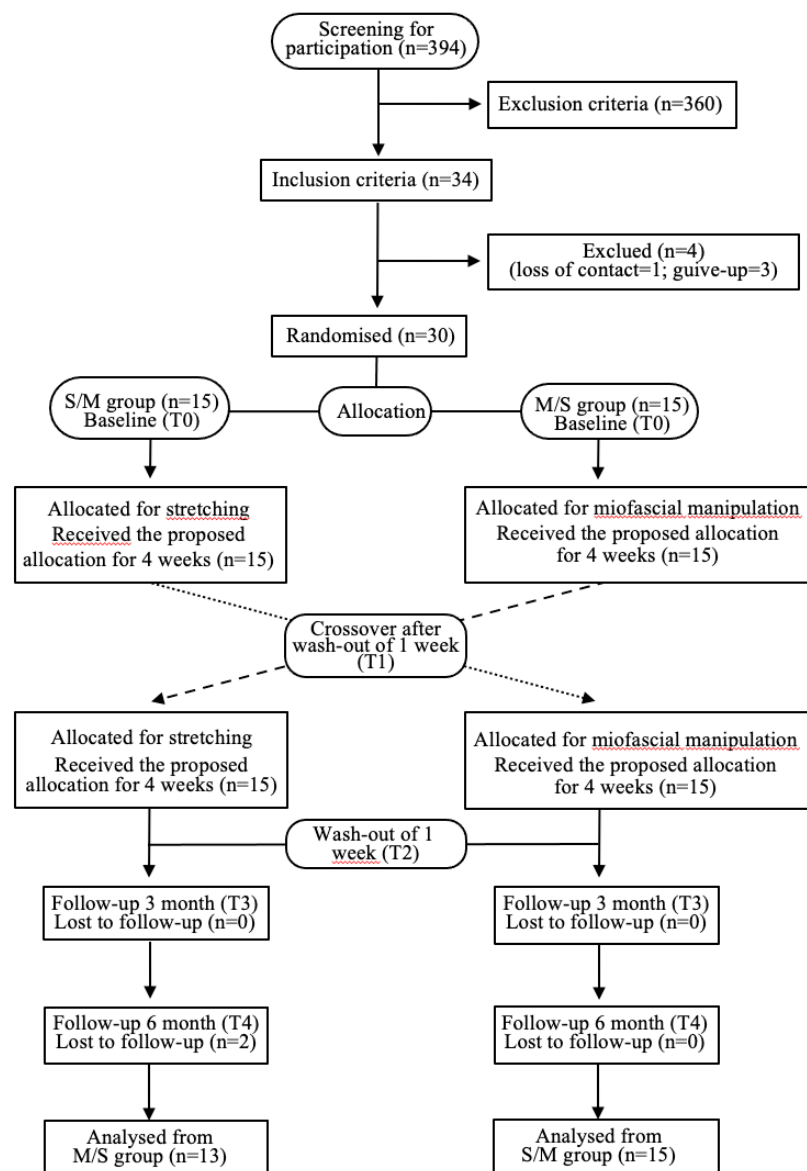
After having checked the statistical significance of the outcome variables, the effect size was calculated by Cohen's d in the G*Power 3.1.9.7 program (32, 33). The classification of the effect size was based on the criteria established by Cohen (1988) (34).

3 RESULTS

3.1 SAMPLE PROFILE

The study followed the CONSORT guidelines. A total of 394 patients were initially recruited, but only 34 participants met the eligibility criteria, and four of these were excluded from the study for various reasons. Thirty participants were randomized, with two losses in the M/S group due to change of status, not completing the final assessment (T4), resulting in 118 observations (Figure 1).

Figure 1: Sample allocation flowchart



The main features of the sample were: women (90.0%), housewives (31.0%), overweight or obese (50.0%), moderate involvement on the ENMG scale in both hands (65%), mean duration of symptoms was 4 years (± 2.95) in the right hand and 3.5 years (± 3.37) in the left hand. In general, the sample was homogeneous regarding its sociodemographic aspects, regardless of the sequence (S/M or M/S) in which the participant was randomized, as shown in Table 1.

Table 1: Sample profile by treatment sequence.

Variable	Category	Treatment sequence [n (%)]			Test	
		S/M [n= 15]	M/S [n= 15]	Total [n= 30]	χ^2/z	p-value
Sex	Female	14 (93.3)	13 (86.7)	27 (90.0)	0.370 [‡]	1.00
Ethnicity	White	7 (77.8)	11 (84.6)	18 (81.8)	0.167 [‡]	1.00
Marital status	Married	11 (78.6)	13 (92.9)	24 (85.7)	1.167	0.29
Occupation	Housewife	4 (26.7)	5 (35.7)	9 (31.0)	0.277	0.70
Education	High school	8 (57.1)	12 (85.7)	20 (71.4)	2.800 [‡]	0.20
Family income	Up to 1.000 BRL	8 (57.1)	8 (57.1)	16 (57.1)	0.000	1.00
BMI	Overweight/Obesity	8 (53.3)	7 (46.7)	15 (50.0)	0.133	1.00
Dominant hand	Right	14 (93.3)	13 (86.7)	27 (90.0)	0.370	1.00
Moderate CTS	Right hand	9 (60.0)	11 (73.3)	20 (66.7)	0.600	0.70
	Left hand	9 (60.0)	10 (66.7)	19 (63.3)	0.144	1.00
Symptom time (mean years \pm SD)	Right hand	4.27 \pm 3.43	3.75 \pm 2.42	4.02 \pm 2.95	-0.044	0.98
	Left hand	3.96 \pm 4.11	3.93 \pm 2.46	4.45 \pm 3.37	-0.042	0.97
Age (mean years \pm SD)	Years	51.73 \pm 11.61	52.33 \pm 13.37	52.03 \pm 12.31	-0.021	0.98

SD=Standard Deviation; S=Stretching; M=Myofascial Mobilization; BRL=Brazilian Real; BMI=Body Mass Index; CTS=Carpal Tunnel Syndrome. χ^2/z =Fisher's exact test (χ^2) and the Mann-Whitney test (z) [for age and symptom time]. The categories indicated in the table are the most frequent. [‡]Indicates that even with the reclassifications, an expected count of less than five was obtained in two cells.

3.2 ANOVA CROSS-OVER

The values shown in Table 2 and 3 indicate the results of the ANOVA Cross-Over as recommended by Li and colleagues (2015) (35). The difference between the periods, i.e., the difference for the baseline period (T0) and for the objective variables can be seen in Table 2 and for the subjective variables in Table 3. Overall, it was observed that the difference value increases over time, although the difference value between the sequences is nevertheless small.

Table 2: Objectives outcomes (difference to baseline in Kgf) from a double treatment, four-period cross-over trial

Outcome	Treatment sequence S/M (n=60) M/S (n=58)	Treatment period Δ [mean (\pm SD)]				Effect F (p)			
		T1-T0 (n=30)	T2-T0 (n=30)	T3-T0 (n=30)	T4-T0 (n=28)	Sequence	Treatment	Carryover	Period
Hand grip strength (right hand)	S/M	3.1 (\pm 2.1)	9.7 (\pm 5.0)	11.6 (\pm 5.2)	12.8 (\pm 4.7)	0.55 (p=0.47)	26.23 (p<0.00)	6.89 (p=0.01)	46.35 (p<0.00)
	M/S	5.0 (\pm 3.4)	7.0 (\pm 3.4)	9.2 (\pm 4.2)	10.6 (\pm 4.6)				
Hand grip strength (left hand)	S/M	2.3 (\pm 2.2)	7.8 (\pm 5.6)	10.6 (\pm 5.1)	11.7 (\pm 4.5)	0.06 (p=0.80)	24.58 (p<0.00)	18.30 (p<0.00)	41.11 (p<0.00)
	M/S	4.9 (\pm 4.3)	6.6 (\pm 4.6)	8.1 (\pm 4.7)	9.0 (\pm 4.2)				
Tip pinch gauge (right hand)	S/M	0.3 (\pm 0.4)	1.2 (\pm 0.5)	1.4 (\pm 0.6)	1.8 (\pm 0.9)	0.41 (p=0.53)	11.47 (p<0.00)	9.24 (p<0.00)	35.16 (p<0.00)
	M/S	0.8 (\pm 0.6)	1.2 (\pm 0.5)	1.3 (\pm 0.5)	1.5 (\pm 0.4)				
Tip pinch gauge (left hand)	S/M	0.4 (\pm 0.4)	1.2 (\pm 0.6)	1.3 (\pm 0.7)	1.5 (\pm 0.7)	0.10 (p=0.76)	20.26 (p<0.00)	16.04 (p<0.00)	53.27 (p<0.00)
	M/S	0.7 (\pm 0.4)	1.2 (\pm 0.5)	1.2 (\pm 0.5)	1.2 (\pm 0.3)				

T=Period; SD=Standard Deviation; S=Stretching; M=Myofascial Mobilization with instruments or *IASTM*. Effect F (p) refers to F test (p-value) of ti effects estimated from ANOVA Cross-Over.

Table 3: Subjective outcomes (difference to baseline) from a double treatment, four-period cross-over trial.

Outcome	Treatment sequence S/M (n=60) M/S (n=58)	Treatment period Δ [mean (\pm SD)]				Effect F (p)			
		T1-T0 (n=30)	T2-T0 (n=30)	T3-T0 (n=30)	T4-T0 (n=28)	Sequence	Treatment	Carryover	Period
VAS (right hand)	S/M	-2.3 (0.8)	-4.4 (1.2)	-5.1 (1.1)	-5.5 (1.1)	0.11	16.54	3.33	64.48
	M/S	-3.1 (1.2)	-4.1 (1.4)	-5.1 (1.0)	-5.5 (1.0)	(p=0.74)	(p<0.00)	(p=0.07)	(p<0.00)
VAS (left hand)	S/M	-2.3 (0.8)	-4.3 (1.1)	-4.9 (1.1)	-4.8 (1.0)	0.46	18.25	3.25	52.74
	M/S	-3.3 (1.0)	-4.1 (1.3)	-4.7 (0.8)	-4.9 (1.1)	(p=0.50)	(p<0.00)	(p=0.07)	(p<0.00)
BCTQ (sensitive)	S/M	-8.1 (3.5)	-13.6 (5.6)	-16.4 (6.2)	-17.3 (5.2)	2.17	3.55	0.56	57.90
	M/S	-11.6 (3.4)	-15.1 (2.8)	-18.7 (4.3)	-19.0 (3.6)	(p=0.15)	(p=0.06)	(p=0.45)	(p<0.00)
BCTQ (function)	S/M	-7.2 (4.4)	-11.3 (4.1)	-12.6 (5.0)	-13.1 (4.5)	0.29	1.50	0.05	16.67
	M/S	-7.4 (3.6)	-9.6 (3.2)	-12.3 (3.4)	-12.5 (3.3)	(p=0.59)	(p=0.22)	(p=0.82)	(p<0.00)
SF-12 (physical)	S/M	0.5 (5.0)	2.5 (4.7)	4.3 (5.6)	3.5 (4.6)	0.53	0.00	2.11	6.03
	M/S	1.7 (5.5)	4.9 (4.5)	3.7 (4.5)	4.5 (6.5)	(p=0.47)	(p=0.97)	(p=0.15)	(p<0.00)
SF-12 (mental)	S/M	7.0 (8.9)	12.9 (7.6)	15.9 (8.5)	18.2 (8.9)	0.64	0.02	0.06	37.77
	M/S	4.8 (6.9)	10.2 (7.8)	13.8 (7.6)	16.1 (8.5)	(p=0.43)	(p=0.89)	(p=0.81)	(p<0.00)

T = Period; SD = Standard Deviation; S = Stretching; M = Myofascial Mobilization with instruments or *IASTM*; VAS = Visual Analogue Scale; BCTQ = Boston Carpal Tunnel Questionnaire; SF-12 = 12-Item Short Form Health Survey. Effect F (p) refers to F test (p-value) of the effects estimated from ANOVA Cross-Over.

This perception was supported by the ANOVA Cross-Over, since the period effect was significant ($p < 0.01$) for all the outcomes (both objective and subjective) and the sequence effect was not significant ($p > 0.05$) for any of the outcomes.

The treatment effect was statistically significant ($p < 0.01$) for all objective outcomes, however there was the presence of loading, also significant in these cases ($p < 0.01$). The separability measure of treatment and loading (Cramer's 1-V) indicates that only 48.63% of the variability can be individualized, i.e., there is approximately 51% shared variance between treatment and loading. In this respect, conclusions for the treatment effect on objective outcomes should be evaluated with some caution.

For the subjective outcomes, the treatment results for VAS for both the right and left hand were significant, with no effect of loading. The BCTQ and SF-12 showed no treatment or loading effect ($p > 0.05$). Although these results direct to differences between stretching and IASTM in the reduction of perceived pain, this difference should be cautiously considered, once the non-significance of loading was marginal ($p = 0.07$).

3.3 EFFECT SIZE

From the previous models, mainly for the purpose of controlling the loading effect, expected in the present study, the analyses progressed to evaluate the treatment effect without the presence of loading. To this end, the effect sizes between the treatments (stretching and myofascial mobilization) were calculated only in the first period (T1). Thus, based on the differences in the outcomes at baseline, we performed the Mann-Whitney test (z) to assess their significance and Cohen's d was calculated, as shown in Table 5.

The effect sizes in the Mann-Whitney test for digital forceps and VAS were considered large. The statistical analyses directed toward supporting the better performance of IASTM versus stretching for pain reduction (VAS) and digital pinch, including large effect sizes.

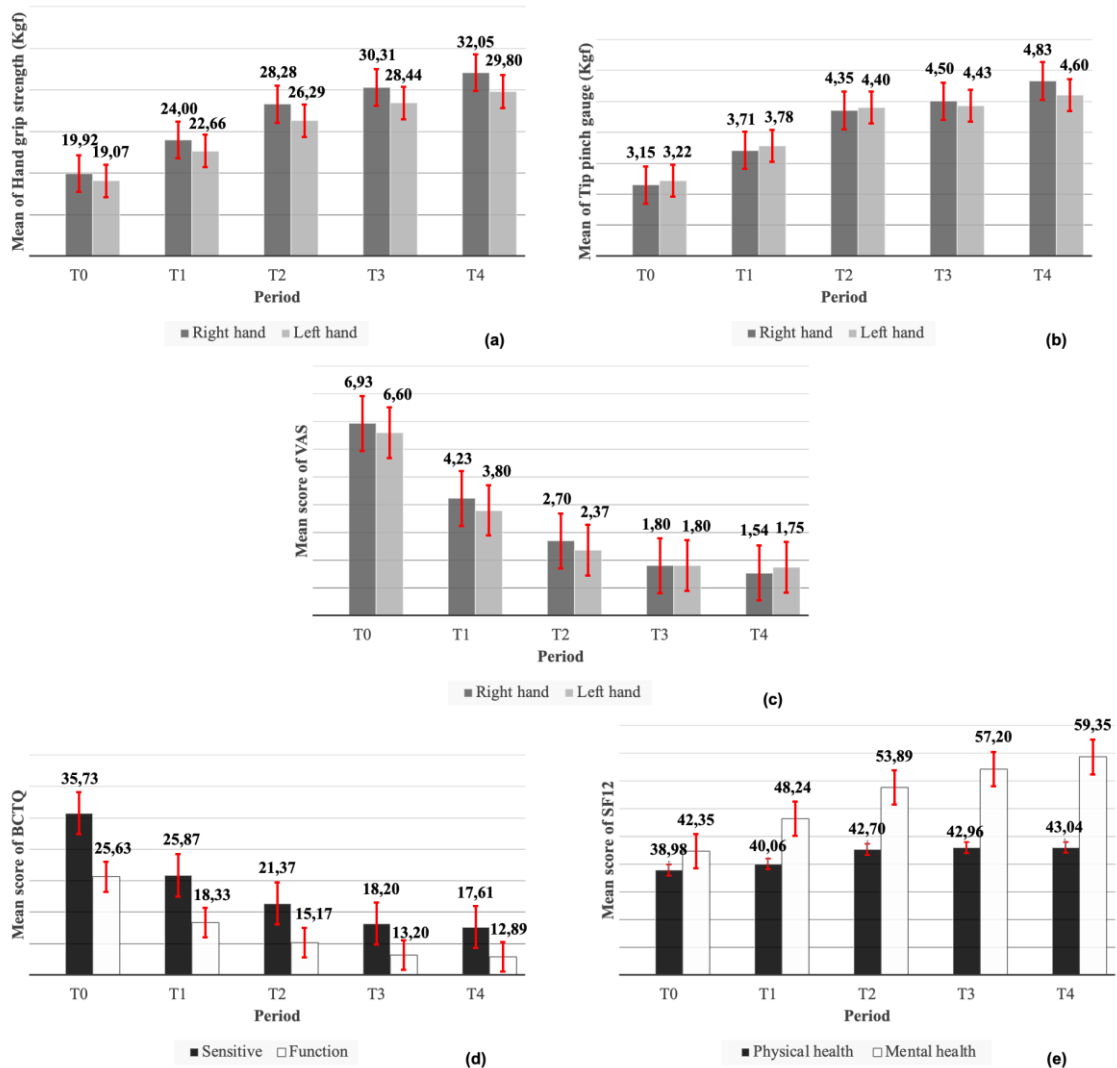
Table 5: Effect size by treatment and period

Outcome	Measure	Effect size [<i>d</i> de Cohen (IC95%)]	
		Treatment (T1-T0)	Period (T4 / T0)
Hand grip strength (Kgf)	Right hand	–	3.03 (2.27; 3.78)
	Left hand	–	2.95 (2.20; 3.71)
Tip pinch gauge (Kgf)	Right hand	-1.00 (-2.07; 0.07)	3.81 (2.93; 4.69)
	Left hand	-0.92 (-1.99; 0.14)	3.83 (2.95; 4.72)
VAS	Right hand	0.86 (-0.20; 1.91)	-4.36 (-5.32; -3.40)
	Left hand	1.00 (-0.07; 2.08)	-3.66 (-4.51; -2.80)
BCTQ	Sensitive	–	-3.59 (-4.43; -2.74)
	Function	–	-2.78 (-3.51; -2.05)
SF-12	Physical	–	0.67 (0.13; 1.21)
	Mental	–	1.71 (1.10; 2.32)

VAS = Visual Analogue Scale; BCTQ= Boston Carpal Tunnel Questionnaire; SF-12 = 12-Item Short Form Health Survey. The cell values show that the respective bivariate tests (Mann-Whitney for treatment and Wilcoxon for period) were significant at the 5% level. For treatment we considered the difference between the baseline of the endpoint and the first period (T1-T0) between the groups (M-S). To evaluate the period effect, we considered the endpoint value at baseline and the endpoint value at the fourth period as paired samples (T0 | T4).

Additionally, Table 5 also presents the effect sizes for the period. In this calculation, only the outcome values at baseline and the fourth period were considered. The effect sizes for the period were considered to be large for all outcomes, except for the effect of the SF-12 physical score, which was intermediate, with those values being better visualized in the graphs of Figure 2. Effectively, the outcomes progressed significantly during the physiotherapy sequences, showing strong effect sizes throughout the follow-up period.

Figure 2: Outcomes means by period



Note: VAS = Visual Analogue Scale. The figure illustrates the mean differences between the periods for digital pinch (a), palmar grip (b), VAS (c), BCTQ (d) and SF-12 (e). According to ANOVA Cross-Over models and Wilcoxon tests considering the basal period and fourth period as paired samples, all outcomes evolved positively at the end of physical therapy. When comparing only the results of T0 and T4, the differences were highly significant, with major effect sizes, as shown in Table 5.

4 DISCUSSION

The object of research, i.e., the effect of two shared physiotherapy techniques, was analyzed by objective and subjective metrics, both when performing the therapies and at the six-month follow-up period.

Data analysis by ANOVA Cross-Over allowed the results to be evaluated in terms of the sequence applied (S/M or M/S), the treatment, the carryover, i.e., the

transfer of effect between treatments, and the follow-up period. The results showed a positive response for the two proposed sequences.

The outcome variables VAS and the digital pinch were statistically significant for both hands, without carryover, having a major treatment effect, with data pointing to a better performance of the IASTM. Considering the period, all evaluations evolved positively, and effects considered to be positive for almost all outcomes. The increase in the strength of the digital pinch, in part, translates to an improvement in the function of the abductor pollicis brevis muscle (36) and 2-point or more-point decrease in VAS pain represents a clinically significant improvement in chronic pain therapies proposed for clinical trials (37).

In the cross-over design, given that the individual him/herself is the referent, there is a reduction in the results variability when compared to intergroup confrontation studies (31). Data analysis using ANOVA Cross-Over managed the information repetition consequent to bilaterality, producing reliable results without overestimated values (38).

In the present study, stretching and IASTM had a complementary effect, this fact being explained, in part, by the properties of each therapy. Stretching alters the extensibility of neuromusculotendinous units, which influenced proprioceptors and nociceptors to correct dysfunctional patterns in both the spinal cord and cerebral cortex (39), thereby aiding in pain control (40). Stretching also provided increased circulatory flow to the dehydrated tissues, reducing intercellular edema (41).

In turn, myofascial mobilization generates a mechanical energy, which promotes a cellular stimulation causing structural changes in the fascia and fascial system, locally and at a distance, providing the restoration of structural integrity (42, 43). The association of instruments, such as crochet, to fascial mobilization performed solely with the hands allows the therapist to improve their sensitivity by identifying and mobilizing the deep points of restriction (44).

Baysal and colleagues (2006) used stretching associated with another physiotherapeutic procedure for the treatment of CTS. In this study, patients were divided into three groups: splint and stretching, splint and ultrasound therapy, and the association of these three therapies. The results showed that the combination of the three therapies achieved better performance (45).

Myofascial mobilization was compared to laser therapy by Pratelli and colleagues (2014) in a sample consisting of 70 patients with unilateral mild and

moderate CTS. The authors have shown a superior result of myofascial mobilization for all outcome variables during the three-month follow-up (46).

The association between myofascial mobilization and stretching was used by Crane and colleagues (2018) in the treatment of axillary network syndrome and thoracic rotation dysfunction. The authors reported improvement in shoulder motion range and decreased pain with this association (47). These results support Bailey et al and colleagues (2017) studies on shoulder motion range deficits. By associating myofascial mobilization and stretching, the authors obtained decreased stiffness and increased amplitude when compared to the stretching technique alone (48). In healthy individuals, the association between myofascial mobilization and stretching was also superior to the use of stretching alone, in the evaluation of shoulder movement range, according to the studies by Hussey and colleagues (2018) and Jurdado-Garcia and colleagues (2021) (49, 50).

Despite the high incidence of bilateral CTS, studies having in their samples exclusively participants containing bilateral carpus are scarce in the literature (51), which makes it difficult to compare the results of stretching and myofascial mobilization therapies. Currently, for example, there is some controversy in the outcome interpretation, especially when using stretching, as protocols vary in terms of technique, intensity, duration, and frequency of movements (52, 53).

Although myofascial mobilization presenting some experimental studies that prove its mechanism of action and its effect (54), there is still a lack of clinical studies proving its results, especially in CTS.

A limitation of the present study is the absence of a control group to evaluate the natural improvement of symptomatology. However, this fact was not imperative, as the average symptomatology time among the participants was extensive, which makes spontaneous improvement unlikely when it comes to idiopathic bilateral CTS (55). In addition, it was impossible to provide the same treatment to a control group after the end of the project, which caused ethical restrictions.

Therefore, there is a need for further studies containing exclusively idiopathic bilateral CTS samples, with appropriate statistical analyses in view of the data repetition caused by bilaterality (38, 56). There is a need to establish a consensus on the therapeutic options available for the clinical treatment of CTS in order to allow easier comparison between studies (57). There is also a lack of studies that report a

long-term follow-up, i.e. equal to or greater than six months, in order to assess the maintenance of the effect of the applied therapies (58).

Instrument-based myofascial mobilization was developed with the purpose of supplementing the effects of associated therapies, and is not intended to replace existing treatments (17). In this regard, the sequences used showed a positive effect both during their use and at six-month follow-up. Although the treatment methods employed in the current study have been used in other existing studies, their combined use has never been performed for CTS. Thus, the absence of scientific evidence in the literature makes it difficult to compare the results in similar samples, and additional studies are needed to confirm the reports.

5 CONCLUSION

Based on the results presented in this article, it can be concluded that the sequences used did not statistically impact any of the outcomes, as well as the types of treatments were statistically significant for some specific outcomes, such as VAS and digital pressure strength in both hands. However, the combination of stretching with myofascial mobilization over the period showed robust results for most outcome variables. Therefore, the physical therapy strategy used proved to be effective during the six-month follow-up period in patients with bilateral CTS with mild and moderate impairment.

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**7. PRODUTO 3 – ARTIGO 2 - PREOPERATIVE USE OF GABAPENTIN FOR PAIN
REDUCTION IN OPEN SURGERIES UNDER LOCAL ANESTHESIA FOR
IDIOPATHIC BILATERAL CARPAL TUNNEL SYNDROME.**

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ABSTRACT

This article aims to evaluate the preoperative use of gabapentin in the control of intra- and postoperative pain in patients with idiopathic bilateral carpal tunnel syndrome (CTS). A prospective, randomised, double-blind study involving 45 subjects with severe CTS, 23 receiving treatment (gabapentin 600 mg) and 22 receiving placebo (control), who underwent an open surgical approach in one hand under local anaesthesia. Information related to the patients' profile, safety of the surgical procedure, history of pain, adverse effects, numbness, and medications used were collected during the 14 days of the procedure and evaluated by Generalised Estimated Equations and Generalised Linear Mixed Models. The treatment and control groups were homogeneous regarding the patients' profile and surgical procedure data. The patients who used gabapentin 600 mg had a better evaluation during surgery ($d = 0.655$), anaesthesia ($d = 0.854$), and on the first night of sleep ($d = 1.323$), and they reported a higher degree of satisfaction with the surgery after 14 days ($d = 1.091$). The treatment group reported decreased pain in the operated hand in a 24-hour period ($r = 0.34$, 95% CI: 0.223–0.457) and in the 14-day follow-up period ($r = 0.412$, 95% CI: 0.217–0.608). These results were not impacted by the medications used and remained consistent over time. The use of a single dose of gabapentin 600 mg in the preoperative period proved to be safe and effective in reducing postoperative pain, and the improvement was noticed by the patient.

KEYWORDS: Carpal Tunnel Syndrome; Preoperative Period; Adjuvants, Anesthesia; Gabapentin.

RESUMO

Esse artigo tem por objetivo avaliar o uso pré-operatório da gabapentina no controle da dor intra e pós-operatória em indivíduos com síndrome do túnel do carpo (STC) bilateral idiopática. Foi realizado um estudo prospectivo, randomizado e duplo cego com 45 indivíduos, 23 que receberam tratamento (gabapentina 600 mg) e 22 que receberam placebo (controle), os quais se submeteram a uma abordagem cirúrgica aberta em uma das mãos, sob anestesia local, com grau severo de STC. Informações relacionadas ao perfil dos indivíduos, segurança do procedimento cirúrgico, histórico de dor, efeitos adversos, dormência e medicamentos utilizados foram coletadas ao longo do procedimento, durante 14 dias, para serem avaliadas por modelos Generalized Estimated Equations (GEE) e Generalized Linear Mixed Models (GLMM). Os grupos de tratamento e de controle mostraram-se homogêneos em termos de perfil e no que concerne aos dados do procedimento cirúrgico. Os pacientes que utilizaram gabapentina 600 mg atribuíram uma melhor avaliação intraoperatória ($d = 0,655$) durante a anestesia ($d = 0,854$) e na primeira noite de sono ($d = 1,323$) e maior grau de satisfação com a cirurgia após 14 dias ($d = 1,091$). O grupo de tratamento percebeu uma melhora na dor da mão operada no período de 24 horas ($r = 0,34$; IC95%: 0,223-0,457) e no período do seguimento de 14 dias ($r = 0,412$; IC95%: 0,217-0,608). Esses resultados não foram impactados pelos medicamentos utilizados e se mantiveram consistentes ao longo do tempo. O uso de gabapentina 600 mg em dose única no pré-operatório mostrou-se seguro e eficaz na redução da dor no pós-operatório, com melhora percebida pelo paciente.

PALAVRAS-CHAVE: Síndrome do Túnel do Carpo; Período Pré-Operatório; Adjuvantes Anestésicos; Gabapentina.

RESUMEN

Este artículo tiene como objetivo evaluar el uso preoperatorio de gabapentina para controlar el dolor intra y postoperatorio en individuos con síndrome de túnel carpiano (STC) bilateral idiopático. Se llevó a cabo un estudio prospectivo, aleatorizado y doble ciego con 45 individuos, 23 que recibieron tratamiento (gabapentina 600 mg) y 22 que recibieron placebo (control), que se sometieron a un abordaje quirúrgico en una mano, con anestesia local, con grado grave de STC. A lo largo del procedimiento se recopiló información relacionada con el perfil de las personas, la seguridad del procedimiento quirúrgico, la historia del dolor, los efectos adversos, el entumecimiento y los medicamentos utilizados durante todo el procedimiento, durante 14 días, para ser evaluados mediante modelos Generalized Estimated Equations (GEE) y Generalized Linear Mixed Models (GLMM). Los grupos de tratamiento y control eran homogéneos en términos de perfil y en términos de datos de procedimientos quirúrgicos. Los pacientes que utilizaron gabapentina 600 mg atribuyeron una mejor evaluación intraoperatoria ($d = 0,655$) durante la anestesia ($d = 0,854$) y en la primera noche de sueño ($d = 1,323$) y mayor grado de satisfacción con la cirugía después de 14 días ($d = 1,091$). El grupo de tratamiento notó una mejora en el dolor de la mano operada en 24 horas ($r = 0,34$; CI95%: 0,223-0,457) y en el período de seguimiento de 14 días ($r = 0,412$; IC95%: 0,217-0,608). Estos resultados no se vieron afectados por los medicamentos utilizados y se mantuvieron consistentes con el tiempo. El uso de gabapentina 600 mg en dosis única en el período preoperatorio demostró ser seguro y eficaz en la reducción del dolor postoperatorio, con una mejoría percibida por el paciente.

PALABRAS CLAVE: Síndrome del Túnel Carpiano; Período Preoperatorio; Adjuvantes Anestésicos; Gabapentina.

1 INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common compressive neuropathy of the upper limbs. It has a higher incidence in women aged 45-65 years, tending to be bilateral in 65% of cases (1). In the USA, due to its high prevalence, the surgical treatment of CTS has an annual cost of more than USD 2 billion (2). Brazil spent approximately BRL 30 million between 2008 and 2016 on CTS surgeries under the Unified Health System (Sistema Único de Saúde - SUS) (3).

The surgical treatment of this neuropathy is indicated when severe involvement of the median nerve is observed during clinical evaluation or electroneuromyography (ENMG) (4). Open surgery (OS) or endoscopic surgery (ES) can be used (5); several studies have indicated no statistical difference between the outcomes of OS and ES.

OS with the palmar approach was idealised by Tubina (1990) and introduced in Brazil by Galbiatti et al. (1991) (6, 7). It can be performed using several anesthetic techniques, but local anesthesia with lidocaine allows the patient to keep fully awake during the procedure, which is known as WALANT (Wide Awake Local Anesthesia No Tourniquet) (8).

The combination of lidocaine and epinephrine is aimed at decreasing intraoperative bleeding and avoiding the use of a tourniquet. Sodium bicarbonate 8% can be added to decrease discomfort resulting from the anaesthetic injection (9), and an anesthetic block can be performed through a single orifice, a technique called hole-in-one (10).

As local anaesthesia cannot maintain postoperative analgesia, postoperative surgical pain management becomes an important (11). Pain intensity can be measured subjectively using the visual analogue scale (VAS), a numerical scale from zero to ten where zero represents the absence of pain and ten represents the worst pain estimated by the patient (12). Opioids are mainly chosen as the option to control postoperative pain. However, their excessive use has a negative potential for patients and the community, as they can cause addiction and other side-effects (13).

In this sense, acute postoperative pain prevention can be optimised with the use of preventive analgesia, which attenuates the process by blocking pain stimulus before tissue manipulation (14). Gabapentin is promising for this purpose, as it has a multimodal effect and acts on both central and peripheral nervous systems. It can be administered for up to twenty-four hours before surgery (15).

A systematic review with meta-analysis showed that the preoperative use of gabapentin was effective in reducing opioid use after abdominal, spinal, and thyroid surgeries (16). However, there are no reports in the literature on the use of gabapentin as a preoperative analgesic strategy for OS under local anesthesia for CTS (17).

Therefore, the aim of this study was to evaluate the effectiveness and safety of preventive gabapentin for controlling the intra- and postoperative pain in patients with idiopathic bilateral CTS.

2 METHODOLOGY

The study was approved by the ethics committee of the Irmandade da Santa Casa de Londrina under number 3,276,439; it was registered at ClinicalTrials.gov (NCT04347746), and all participants signed an Informed Consent Form (ICF). It is a study of the type prospective, randomized, and double-blind.

All participants were treated by the neurosurgery team of the Irmandade da Santa Casa de Londrina at the carpal tunnel outpatient clinic from 2018 to 2019. The inclusion criteria were an age of 18 or more years, idiopathic bilateral CTS, American Society of Anesthesiology (ASA) physical status I or II (18), and severe impairment in at least one hand using the ENMG criteria according to Stevens (1997) (19).

All ENMG tests were performed in the same laboratory with the same machine (Dantec Ketpoint, Natus®, Pleasanton, USA) by the same specialist electrophysiologist, following the relevant reference values and the technical standards recommended by the American Association of Electrodiagnostic Medicine (20).

The exclusion criteria were history of allergy to the drugs used in this study, drug usage, psychiatric disorders or mental retardation, pregnancy, CTS treatment within the previous three months, or duration of symptoms of less than six months.

The sample size was calculated according to the recommendations of Hjerstad et al. (2011), who determined that a 30% reduction in the initial VAS score was clinically relevant (21). Considering the expected effect size, a beta of > 95%, an alpha level of 5%, and an estimated standard deviation in the population of 2.44 (22), the calculated sample size was 18 patients per group.

The participants were randomized into two groups using the random function of the Excel® software. The first participant used gabapentin 600 mg, and the second (control) received a placebo. Subsequently, opaque envelopes, described as “control”

or “use of gabapentin” according to the random sequence, were numbered and sealed. All the participants involved in the research were blinded to the randomization, as well as the recruitment, hospital care, outpatient follow-up, and data collection and analysis.

The participants chose an envelope on admission and, depending on the result, received either a 600 mg gabapentin tablet or a placebo tablet similar to the drug used. The patients' vital signs were assessed. The level of pain was also assessed in both hands using VAS during the preoperative period, the surgical procedure, and within the subsequent 24 hours.

The hand with severe involvement on ENMG, according to the criteria by Stevens (1997), was operated on. However, when the patient presented bilateral severe involvement, the most symptomatic hand was selected for surgery.

OS with a palmar incision and local anesthesia with 1% lidocaine solution, adrenaline 1:100,000, and sodium bicarbonate 8% at a 1:10 ratio was used, following the guidelines described in WALANT (8). The hole-in-one technique was used for anesthetic infiltration (10). All participants were operated on with the same technique by the same neurosurgeon.

At the end of the surgery, a simple dressing was made, and the patient was instructed to keep the operated hand elevated to avoid postoperative oedema. Prophylactic antibiotic therapy and wrist-hand splints were not used during the postoperative period.

Vital signs and VAS were reevaluated on admission and repeated six, 12, and 24 hours after surgery. Paracetamol 500 mg or codeine 30 mg were used for postoperative analgesia. Paracetamol was used if the VAS score for pain was 4-7, and it was readministered if necessary at doses of up to 4 grams/day. If the VAS score for pain was equal to or greater than eight, codeine was administered at doses of up to 120 mg/day.

On discharge, the participants were encouraged to use the operated hand, and the analgesics were prescribed to be used in case of pain, according to the criteria established on admission.

The patients were asked to complete a pain diary for fourteen days, noting the level of pain in each hand based on the VAS and, when necessary, the medication used and its quantity. On the fourteenth day, data on the pain diary, side effects of the medications used, the degree of satisfaction with the surgery, and reports of night numbness in the hands compared with the preoperative period were collected.

The profile of the sample was descriptively analysed using frequencies, means, and standard deviation with the Fisher's exact test (χ^2) and the t-test for potential differences between groups (control/used gabapentin).

The same tests were used to analyse the differences in the safety of the surgical procedure in the groups after the use of gabapentin. For the t-test, the normality and homogeneity of the data were evaluated before using the Shapiro Wilk (W) and Levene's (F) tests, respectively. In general, the lack of normality and homogeneity caused no major problems; however, as a precaution, the t-test was used with a bootstrap ($n = 1,000$), corrected, and accelerated for bias. Nonparametric tests (Mann-Whitney U) were used only for ordinal variables, such as Likert-type scales.

Regarding the clinical data, the mean arterial pressure, heart rate, and O_2 saturation were used to assess the safety of the surgical procedure. The VAS scores (main outcome) were collected more than once during hospitalization.

Statistical Package for Social Sciences (SPSS) version 25.0 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) was used for the statistical analysis.

The Generalized Estimating Equations (GEE) and the estimations of the Generalized Linear Mixed Models (GLMM) [Wald (χ^2)] used the patient as the subject and time as a repeated measure. These models were based on maximum likelihood with a robust covariance matrix. The advantages of these models, compared with classic repeated sample models such as ANOVA and MANOVA, are that the probability distribution of the outcome variable can be chosen, random effects can be included, and different patterns of correlations within subjects can be evaluated.

After assessing the statistical significance of the outcome variables, the size of the treatment effect was also calculated using Cohen's d statistics and odds ratios based on the post hoc procedure in the G*Power 3.1.9.7 software (Heinrich Heine, Universität Düsseldorf). Standardized coefficients were used for the parameters provided by the GEE/GLMM models. Effect size classifications were based on the recommendations of Cohen (2013) and Hattie (2012), and a p-value of < 0.05 was considered significant for all purposes (23, 24).

3 RESULTS AND DISCUSSION

3.1 SAMPLE RECRUITMENT

The study followed the CONSORT recommendations. A total of 49 participants met the eligibility criteria, and four were excluded for various reasons. A total of 45 patients were randomised; 23 were included in the “gabapentin group” and 22 were included in the “control group”. There was no loss during the 14-day follow-up, as shown in Figure 1.

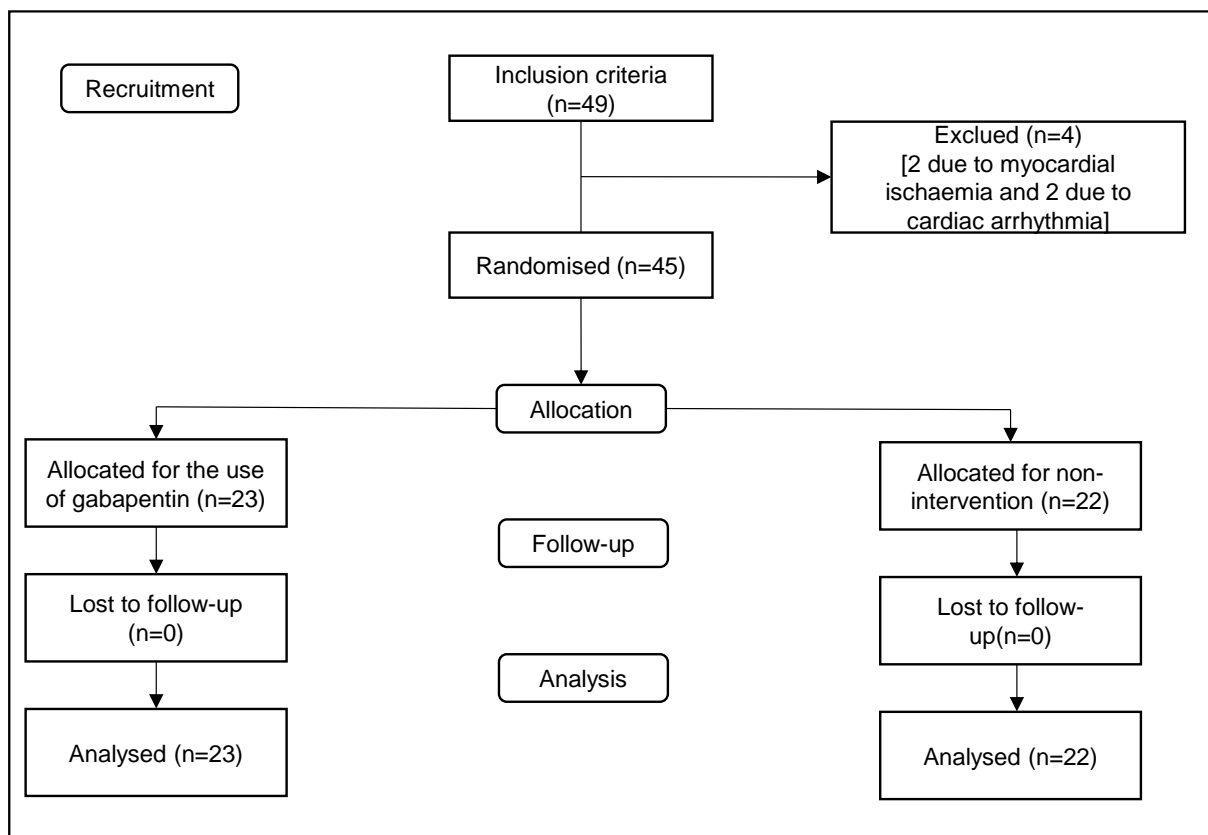


Figure 1. Recruitment and allocation flowchart.

3.2 SAMPLE PROFILE

In general, the sociodemographic and clinical profiles of the sample were homogeneous, as shown in Table 1. The operated hands of all the patients had severe CTS according to Steven’s classification. Statistically ($\chi^2 = 1.10$; $p = 0.38$), the hypothesis that the non-operated hands were different in the treatment group could not be rejected.

Table 1. Sample profile by treatment group.

Variable	Category	Use of gabapentin 600 mg						Test	
		No (n=22)		Yes (n=23)		Total (n=45)			
Sex	Female	0	0.9%	2	5.7%	2	3.3%	.407*	.608
Ethnicity	White	4	7.8%	4	3.7%	8	5.7%	.084*	.000
Marital status	Married	6	6.2%	6	2.7%	2	4.4%	.068	.000
Occupation	Housewife		3.3%		9.1%	6	6.4%	.159	.761
Education	High school	2	7.1%	2	7.1%	4	7.1%	.000	.000
Family income	Between BRL 1,000 and 3,000	2	0.0%		5.0%	1	2.5%	.921	.523
BMI Classification	Overweight	8	1.8%	0	7.0%	8	4.4%	.226*	.699
Dominant hand	Right	0	0.9%	1	1.3%	1	1.1%	.002*	.000
Operated hand	Right	3	9.1%	7	3.9%	0	6.7%	.112	.353
Stevens classification (Non-operated hand)	Light		3.6%		6.1%		0.0%		
	Moderate	0	5.5%		7.4%	4	1.1%	.097	.376
	Severe		0.9%	3	6.5%	2	8.9%		
Age (years)	Mean (\pm SD)	2.41	12.01)	1.09	8.67)	1.73	10.34)	.425	.673

χ^2 (t) = refers to the *Chi* Square or Fisher's exact test or the t- test in the case of age. The observations were reclassified between the most frequent (and adjacent) and less frequent (other) categories for the Fisher's exact test. The categories indicated in the table are the most frequent. For the CTS classification variable, the frequency of all categories is presented. * indicates that even with the reclassifications, an expected count of less than five was obtained in two cells. Therefore, the Fisher Exact Test was performed instead of *Chi* Square.

3.3 SAFETY OF THE SURGICAL PROCEDURE

The mean duration of the surgical procedure was 54.33 minutes (\pm 10.58), and there was no difference between the groups ($t = -1.50$; $p = 0.15$). The same applied to the duration of anaesthesia and the amount of anaesthetic injected. The mean duration of anaesthesia was 5.53 hours (\pm 0.63), with no evidence of a difference between the groups ($t = -1.83$; $p = 0.09$). For the quantity of anaesthetic injected, there was also no difference between the groups ($t = 0.08$; $p = 0.94$), and the general mean was 18.69 ml (\pm 3.10).

Figures 2 to 4 show the mean arterial pressure, heart rate, O₂ saturation, and adverse reactions after the use of 5% lidocaine throughout the preoperative period to up to 24 hours after surgery. The illustrations show similar patterns of the groups.

The mean arterial pressure was higher after two hours (Figure 2) in the control group; this can be attributed to the relatively higher number of hypertensive patients [n = 14 (63.60%)] than patients who used gabapentin [n = 7 (30.40%)] ($\chi^2 = 4.98$; p = 0.03). The GEE model of repeated measures for the mean arterial pressure, using the groups as a fixed effect, showed no evidence that the mean arterial pressure was different in the treatment group (Wald (χ^2) = 0.11; p = 0.75).

This result were the same if hypertensive patients were used as controls [Wald (χ^2) = 0.14; p = 0.70]. The gamma distribution, with a link log function and unstructured covariance matrix, was used to adjust these models, considering that the correlations showed no apparent pattern. These decisions were guided by the Quasi Information Criterion (QIC) and Quasi Information Criterion Corrected (QICC).

The similar patterns shown in Figures 3 and 4 for heart rate and O₂ saturation were confirmed by the estimated GEE model, with the use of gabapentin as a fixed effect and time as a repeated measure. For heart rate, the Wald Test (χ^2) result for treatment effect was 0.65 (p = 0.80), and that of O₂ saturation was 0.05 (p = 0.83). The same GHG model used for the mean arterial pressure was used for heart rate and O₂ saturation (gamma distribution with link log function and unstructured covariance matrix).

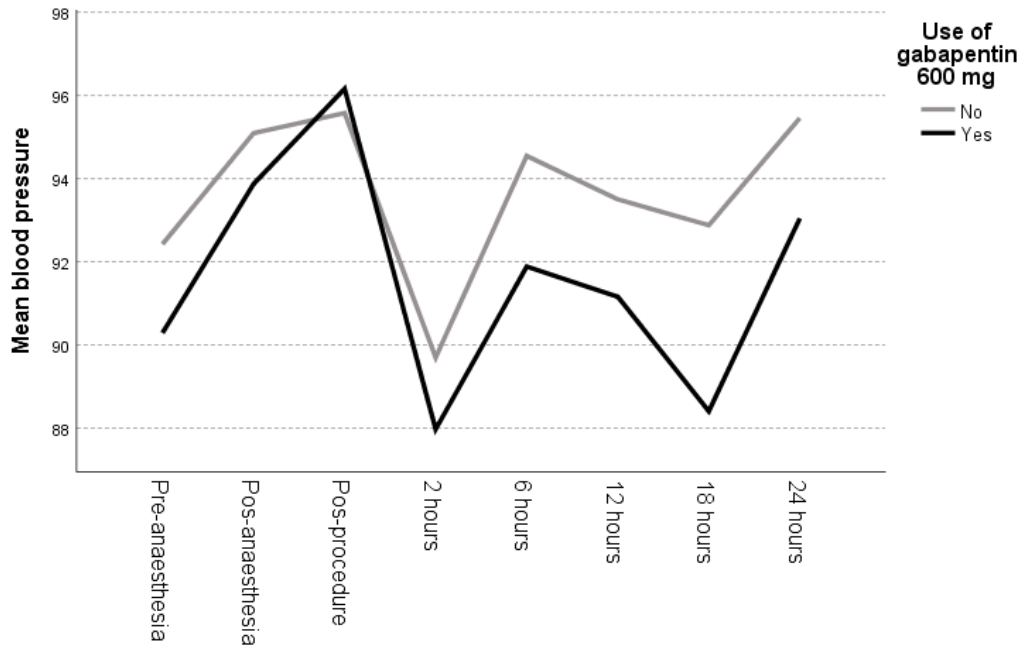


Figure 2. Mean arterial pressure during the procedure and after up to 24 hours.

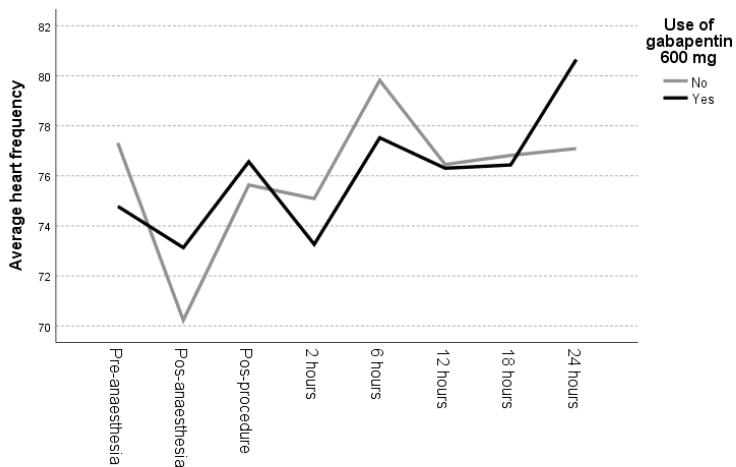


Figure 3. Mean heart rate during the procedure and after up to 24 hours.

There were no cases of unconsciousness, seizure, or arrhythmia as adverse reactions from the use of 5% lidocaine in any of the groups. The adverse reactions with the use of 5% lidocaine (Figure 5) were statistically equal in the treatment groups. Fisher's exact test was performed for all confrontations, and it showed no differences in the presence/absence of adverse reactions between groups.

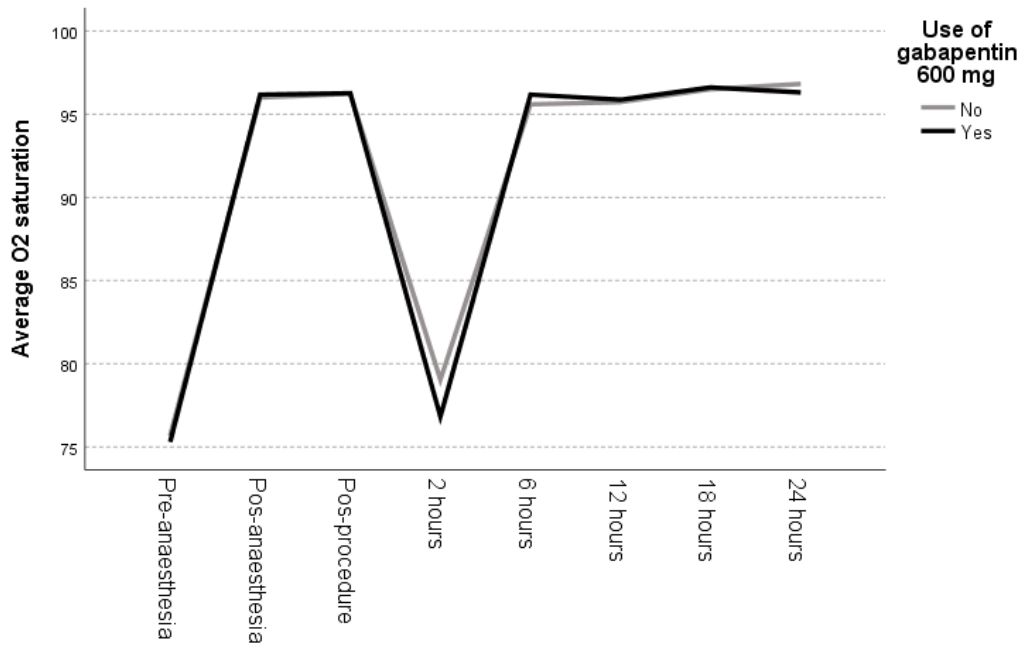


Figure 4. Mean O₂ saturation during the procedure and after up to 24 hours.

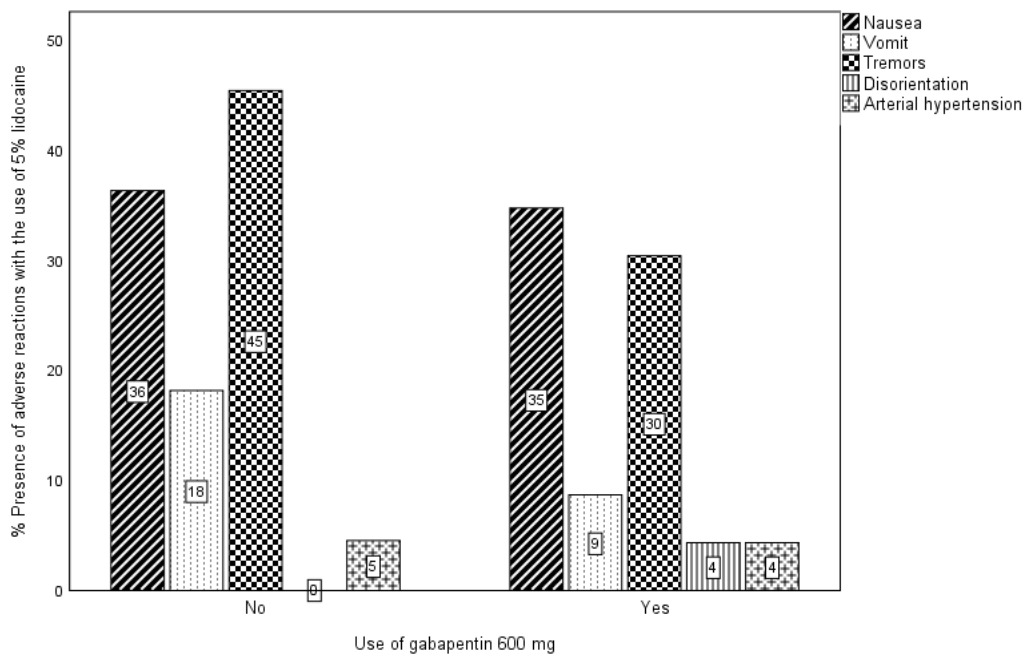


Figure 5. Adverse reactions with the use of 5% lidocaine.

3.4 GABAPENTIN EFFECTS

The adverse effects observed in the 23 participants using gabapentin were drowsiness and dizziness in four patients (17.39%), tinnitus in two patients (8.69%), and a metallic taste in one patient (4.34%). The Likert-type scale from 0 to 4 was used

at the end of the 24 hours in the gabapentin and control groups to evaluate comfort during anaesthesia and the surgical procedure, the first night of sleep, and the degree of satisfaction with the surgical procedure after 24 hours and 14 days (Figure 6).

The ratings by the patients in the gabapentin group were higher for all the evaluations than those of the control group. These results were statistically significant ($p < 0.05$), and the Mann-Whitney U test was used for the comparison. The smallest effect was observed for comfort during surgery ($d = 0.66$), even so, it can be considered an intermediate effect (23). The other evaluations showed desired (24) and large effects ($d > 0.80$) (23) (25).

The effects of the subjective evaluation of the first night of sleep and satisfaction with the surgery were significant ($d = 1.32$ and $d = 1.09$, respectively), respectively, and the effect of comfort during anaesthesia was also significant ($d = 0.85$).

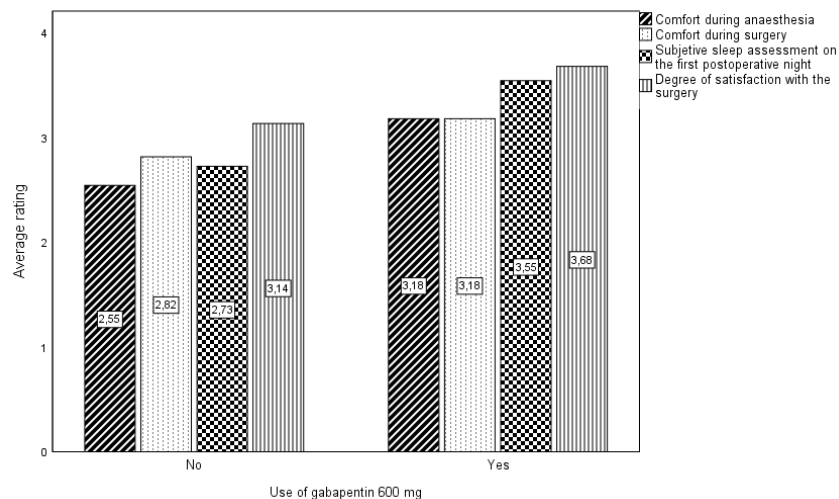


Figure 6. Evaluation of anaesthesia, surgery, and the first night of sleep.

Regarding the hand numbness, the comparison of the gabapentin and control groups using the Fisher's exact test (χ^2) showed no statistically significant differences ($p > 0.05$, figure 7). However, a decreased sensation of numbness in the non-operated hand was observed immediately after the surgery ($\chi^2 = 7.17$; $p = 0.01$), confirmed by the relevant power (0.81) and odds ratio (6.69).

The pain assessment using the VAS was divided into two stages. The first stage included a comparison of the pre- and postoperative pain immediately after surgery and after six, 12, and 24 hours in both hands (Figure 8). The second stage included the analysis of pain during 14 days, using information from the pain diary (Figure 9).

The participants were instructed to register their pain sensation for both hands to obtain results for the operated and non-operated hands.

During the first period, the mean VAS score for the non-operated hand was slightly lower in the gabapentin group than in the control group (Figure 8), but the estimated GEE model showed no statistically significant difference [Wald (χ^2) = 1.61; $p = 0.21$].

A normal function with an identity link was used to adjust the GEE model, using the follow-up/time (preoperative up to 24 hours of hospitalisation) as a repeated measure. The QIC and QICC indicated the normal function adjustment models and an AR-type covariance matrix as the most appropriate (1). The indication of a covariance matrix was expected due to the anticipated decrease in the VAS score over time, as shown in Figure 8.

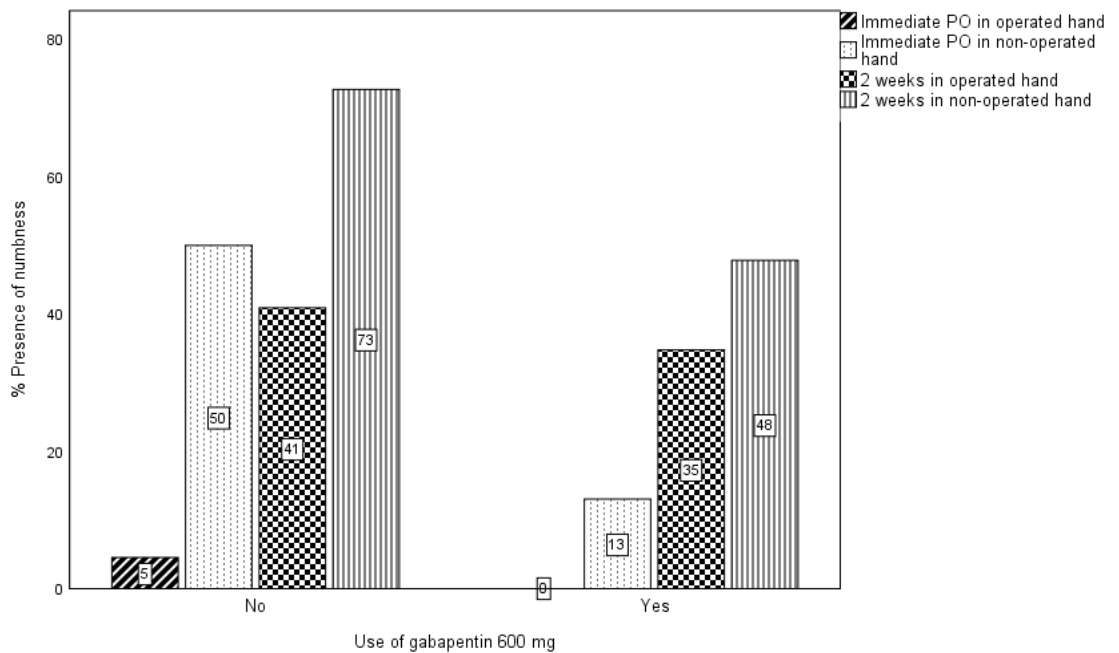


Figure 7. Numbness in the operated and non-operated hands immediately and two weeks after the surgery.

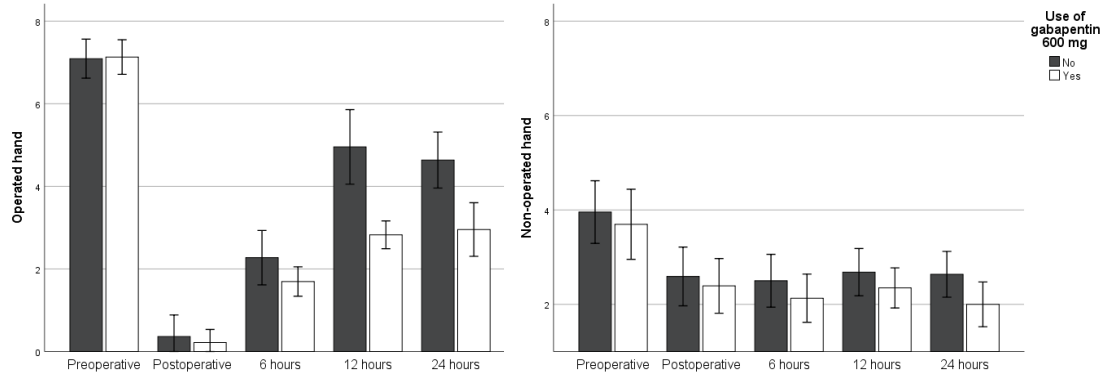


Figure 8. VAS during the procedure and after up to 24 hours.

The GEE model structure estimated for the non-operated hand was also the most consistent for explaining the VAS score of the operated hand during the first stage (Figure 8). However, the operated hand showed statistically significant results [Wald (χ^2) = 32.54; $p < 0.001$]. The mean VAS score was approximately 0.91 lower (CI 95%: 0.59-1.22) in the gabapentin group than in the control group. This result was mainly influenced by the significantly decreased pain 12 and 24 hours after surgery, as shown in Figure 8.

The information criteria also showed the same structure as the normal GEE model, with the identity function and the AR covariance matrix (1) for the second stage; the 14-day follow-up period for the operated and non-operated hands. The information shown in Figure 9 was statistically proven in the operated hand, with a mean VAS score higher in the control group than in the gabapentin group [Wald (χ^2) = 17.08; $p < 0.00$]. The mean score in the gabapentin group was 0.45 lower (CI95%: 0.25-0.69) than that in the control group.

The results did not favour the hypothesis of different pain perceptions in the groups over the 14-day follow-up for the non-operated hand [Wald (χ^2) = 2.58; $p = 0.11$]. The results presented above for the operated and non-operated hands are similar, considering the entire VAS collection period: five collections during the first stage and 14 collections during the second stage, totalling 19 periods.

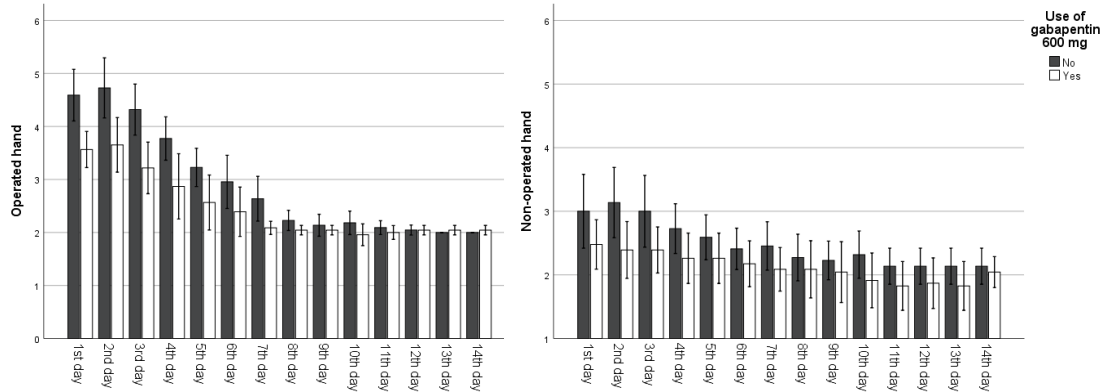


Figure 9. VAS over the 14-day follow-up period for the operated and non-operated hands in the treatment and control groups. There was no use of medication on day 14 by any of the groups.

Additionally, the GEE models for the operated hands were re-designed for stages 1 and 2, considering the VAS score. This showed the magnitude of the effect size, as the parameters of the estimated equation are the standardised coefficients. The size of the treatment effect for the operated hand model was 0.34 (CI 95%: 0.22-0.46) during the 24 hours and 0.41 (CI 95%: 0.22-0.61) during the 14-day follow-up. In both models, the effect sizes were within the desirable limits (24), and they can be considered as intermediate and large, respectively, according to the criterion previously described (23). Although there was no difference in the perceived pain in the non-operated hand in the groups, there was a decrease in perceived pain over the 14-day follow-up (Figure 10).

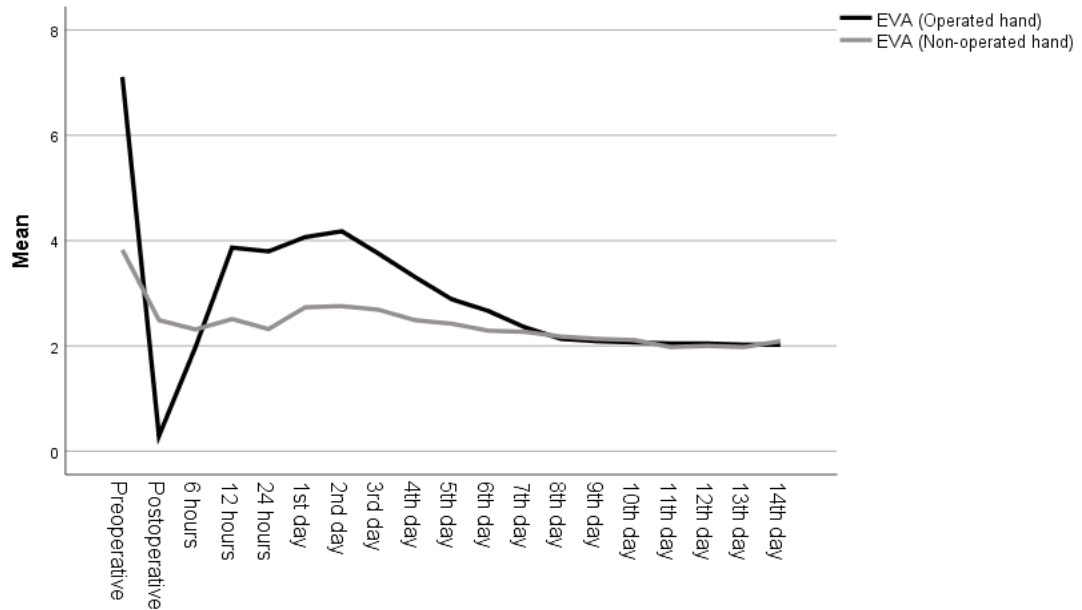


Figure 10. Effect of time on pain reduction in the operated and non-operated hands, regardless of gabapentin use.

An estimated GLMM model, with treatment, time, and VAS of the operated hand as fixed effects, showed a significant F-value (39.72, $p < 0.001$) for the effect time taken to reduce pain in the non-operated hand. There was a mean reduction of 0.05 in the VAS score (CI 95%: 0.07-0.04) over the 14 days or a 1.6% reduction over the period (CI95%: 2.30% - 0.90%). This effect size is desirable (24) and can be considered intermediate (23); the effect size of the estimated time using the same model but standardised variables was -0.27 (CI95%: -0.35 - -0.18).

The gabapentin group presented decreased perceived pain, which was demonstrated by the lower use of medications (codeine 30 mg and paracetamol 500 mg) over the 14-day follow-up, especially during the first week (Figure 11). The patients who reported using the medication used only one pill.

The patients who used gabapentin reported a lower use of extra medication, mainly codeine 30 mg [Wald (χ^2) = 42.62; $p < 0.001$]. To assess this hypothesis, a GEE model was used for analysis; the use of medication (paracetamol, codeine, and not used) was the dependent variable and treatment was the fixed effect. A multinomial function with an accumulated logistic link and an AR-type covariance matrix was considered (1) to adjust the GEE model, using follow-up/time (six hours to 14 days) as a repeated measure.

Patients using gabapentin are approximately 249% more likely to avoid using any medication (OR = 3.49; CI95%: 2.38-5.08). This value is substantially higher when

considering only 30 mg codeine; patients not using gabapentin were 430% more likely to use 30 mg codeine (OR = 5.29; CI95%: 3.50-8.00).

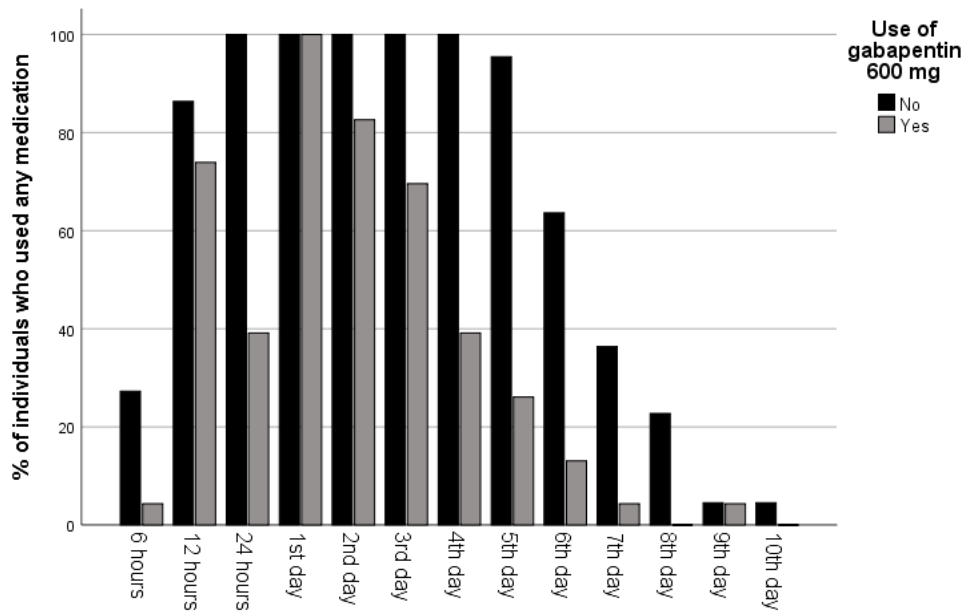


Figure 11. Patients who used at least one medication in the postoperative period and during ten days in the treatment and control groups.

4 DISCUSSION

Gabapentin has been used at a dose of 600 mg as a pre-emptive medication for medium-sized surgery (26). However, the ideal dose for minor orthopaedic procedures is controversial, with indications ranging from 300 mg to 1,200 mg (15).

The preoperative gabapentin dose of 600 mg was effective in reducing pain in the first 24 hours in the operated hand with severe CTS. These findings could not be explained by the use of local anaesthesia, as demonstrated by Chapman et al. (2017), who assessed postoperative pain in CTS OS. The authors compared local anaesthesia using the WALANT technique *versus* intravenous sedation with midazolam, reporting no significant difference between the two groups (27).

In the 14-day period, the operated hands in the gabapentin group maintained significant pain improvement compared to the control group, with a positive effect and an intermediate and significant magnitude according to the criteria by Page (2014) (28). However, these findings differ from the study by Sadatsune et al. (2016), who compared the effect of preventive gabapentin at a dosage of 600 mg to control

postoperative pain in CTS OS and found no significant difference in the two-week period compared with the placebo group (29).

There are differences between this present study and the reports by Sadatsune et al. (2016), making it difficult to compare the results. Initially, the sample used in the present study was composed exclusively of bilateral idiopathic CTS, which is different from what was described by the other authors, who included patients with CTS secondary to diabetes mellitus in their evaluation and presented a different surgical result from that of idiopathic CTS (30).

Another difference between the studies was related to the operated hands. In the present study, all hands undergoing surgical treatment presented severe CTS, unlike the sample described by Sadatsune et al. (2016), in which the operated hands presented mild and moderate CTS. These comprised 40% of the patients who used gabapentin and 50% of the placebo group, according to the criteria to compare EMNG scales proposed by Sonoo et al. (2018) (31). In addition, surgical results are different depending on the stage of this pathology (32). Therefore, the results of this study and the ones presented by Sadatsune et al. (2016) should be carefully compared.

The non-operated hand showed decrease pain both in the first 24-hour period and in the 14-day follow-up, regardless of the use of gabapentin. Unno et al. (2015) described an improvement in the non-operated hand with bilateral CTS, both in the immediate postoperative period and maintained for six months after surgery. Therefore, the described findings may be due to surgical therapy (33).

Codeine consumption was significantly lower in the gabapentin group both in the first 24-hour period and in the 14-day follow-up. This decrease is a positive factor, as it avoids abusive prescription (34), reducing the possibility of triggering drug addiction (35). In addition, better postoperative pain control is associated with a decrease in the onset of chronic pain (36).

The use of preoperative gabapentin proved to be safe, presenting no significant side effects during the surgical procedure. The patients' assessment of the surgical treatment was better in the gabapentin group, presenting a large or intermediate effect size for all analysed items (27). Therefore, the analysis of the results of a procedure should not only include the doctor's opinion but should also evaluate the procedure expectations from the patient's point of view (37).

The present study has limited applicability because it was conducted in a single medical centre, which restricts its external validity. However, the relevant findings in

the group that used preoperative gabapentin, such as decreased post-surgical pain, decreased use of opioids, absence of significant side effects, and better assessment of the procedure by the patient, suggest that the use of pre-emptive analgesia with gabapentin is a strategy that can be recommended in daily practice.

5 CONCLUSION

The results showed that preemptive gabapentin has the advantage of significantly reducing opioid use in the postoperative period. The use of a single dose of 600 mg of this drug in the preoperative period proved to be safe and effective in reducing postoperative pain, in addition to increasing the quality of the surgical procedure according to the participants' assessment.

CTS is the most common compressive neuropathy in the adult population, being in most cases bilateral. The use of local anesthesia for the surgical treatment of CTS is a frequent analgesic strategy. Despite the prevention of postoperative pain by optimizing analgesia with the use of gabapentin has not been demonstrated in the literature, further multicenter studies are necessary to consolidate these findings.

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8. PRODUTO 4 - ARTIGO 3 – BILATERAL IDIOPATHIC CARPAL TUNNEL SYNDROME: CLINICAL-FUNCTIONAL CHARACTERIZATION AND EFFICACY OF TWO COMBINED POSTOPERATIVE PHYSIOTHERAPEUTIC.

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ABSTRACT

Introduction: Carpal tunnel syndrome (CTS) is the most common compressive neuropathy in the adult population worldwide, and most cases are bilateral. In these cases, there is the possibility of operating on the more severe hand and following the course of the non-operated hand. The use of postoperative physiotherapy aims to improve surgical outcomes; however, due to the small number of studies and the low quality of the results, the subject remains controversial. **Objectives:** Evaluate the efficacy of combined association instrument myofascial mobilization (IASTM) and stretching in patients with idiopathic bilateral CTS operated on one hand and to analyze the response of the operated (OH) and non-operated (NH) hand according to the different therapeutic sequences. **Method:** Randomized controlled crossover study with 43 participants using the objective outcome variables palmar grip strength and digital pinch and the subjective variables pain, sensory and functional severity and quality of life. Patients were randomly assigned to two groups to start rehabilitation after surgery: stretching followed by instrument myofascial mobilization (IASTM) and starting with IASTM followed by stretching. After the one-week interval the participants who started with stretching were referred to IASTM and vice versa, following the same previous patterns. The outpatient reassessments took place at three to six months. The ANOVA Cross-Over, Mann-Whitney (z) test, the Fisher's Exact Test, the Wilcoxon (z) test and the Cohen's d test were used for statistical analysis. **Results:** The sequences were significant ($p < .01$) for pain on the NH, physical and mental SF-12, suggesting that starting with IASTM followed by stretching had a superior outcome for these outcomes. Treatment had a significant difference in the subjective SF-12 mental and VAS measures for OH ($p < .01$), the results of which suggested better stretching performance on these outcomes. Period was the most significant outcome for all variables ($p < .01$) both during therapies and at six-month follow-up. Both hands responded positively to the therapies regardless of the severity of the NH. Regarding differences in response to the combined therapies between OH and NH, there were differences for both OH and NH, with the greatest impact on OH for the palmar grip and VAS variables in period. The type of sequence was also meaningful with better response for VAS from NH. **Conclusion:** The combination of IASTM with stretching, used in the postoperative period of bilateral idiopathic CTS, proved to be additive, with significant results and large effect sizes for most of the outcomes assessed, both during the time of application of the therapies and in the six month follow-up for both hands, which may be an effective therapy for this population.

Keywords: Carpal tunnel syndrome; Musculoskeletal Manipulations; Rehabilitation; Muscle Stretching Exercises; Cross-Over study.

1 INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common median nerve compression neuropathy in the adult population worldwide, arising from any pathological condition that causes decreased cross-sectional area or expansion of the carpal tunnel components (1).

CTS is related to constitutional factors and comorbidities. The main constitutional factors are advanced age, gender, high body mass index, menopause, and pregnancy (2). Relevant clinical comorbidities are diabetes mellitus, hypothyroidism, obesity and rheumatoid arthritis (3). If a causative agent cannot be found, this syndrome is referred to as idiopathic (4).

Clinical treatment is encouraged in mild and moderate CTS (5). Surgical treatment is indicated in severe cases (6) the surgical approach can be done either by open surgery (OS) or endoscopic surgery (ES) (7). There are no statistical differences in postoperative outcomes between OS and ES procedures in literature (8-10). In the presence of bilateral CTS, it is possible to operate one hand (OH) and follow the unoperated hand (NH) (11).

Postoperative physiotherapy has been advocated in the literature for the rehabilitation process of the operated hand (12). However, despite the high prevalence of bilateral CTS, there are literature controversies on the use of postoperative therapies and their benefits (13), as well as a lack of common ground on the protocols to be established in postoperative rehabilitation (14).

Instrument myofascial mobilization (IASTM) and stretching are one of the methods used for rehabilitative physiotherapy (15, 16), however, their combined use has never been employed in the postoperative period of idiopathic bilateral CTS, as well as the practice of performing these therapies bilaterally on the entire upper limb, shoulder, cervical and thoracic region, on the anterior, lateral and posterior sides is unprecedented.

The present study aims to evaluate the efficacy of two combined therapies in patients with idiopathic bilateral CTS submitted to surgery on one hand. It also aimed to evaluate the response to combined therapies in operated (OH) and non-operated (NH) hands after unilateral surgical release in this type of sample.

2 METHODS

This is a prospective, randomized, double-blind, 2x4 cross-over sample study (cross-over 2x4). All participants were recruited by the Neurosurgery team of *Irmandade da Santa Casa de Londrina*, in the carpal tunnel outpatient's unit, from January 2018 to February 2019. The study was approved by the ethics committee of *Irmandade da Santa Casa de Londrina* under number 3.276.439, registered at ClinicalTrials.gov (NCT04347746), and the Informed Consent Form was signed by all participants.

Inclusion criteria for participants were: age of 18 years or older with idiopathic bilateral CTS, presenting one or more of the clinical criteria defined by Claire and colleagues (2018) (17), physical status I or II by the American Society of Anesthesia (ASA) (18), normal laboratory test results to exclude associated pathology (blood count, renal function, glycemic curve, rheumatic profile, and thyroid profile), having no upper limb limitations as well as skin lesions that could prevent them from performing the suggested therapies, and presenting, through the electroneuromyography (ENMG) exam, indicating severe impairment in one of the hands, according to Stevens' (1997) criteria (19).

Participants with a history of allergy to the drugs used in this treatment, drug users, people with psychiatric disorders or intellectual disability (MR), pregnant women, patients who had received previous treatment with infiltration of corticosteroids or who had symptoms for less than six months were excluded.

Patients who met the inclusion criteria were referred to the rehabilitation sector of the Pitágoras/Unopar University, where they were randomly assigned to two groups using the random function of the Excel® program, in a 1:1 ratio. In the sequence blind envelopes were used according to the random sequence, which were then numbered and closed. Inside each envelope there was the designation to start with the static active stretching technique or with the IASTM technique, and the randomization was done by a member not involved in the research. After the choice of envelopes and the definition of the sequence to be started, all participants were evaluated at time zero (T0).

All the ENMG were performed in the same laboratory, on the same equipment (Dantec Ketpoint, Natus®, Pleasanton, USA) and by the same specialist

electrophysiologist, following the reference values of the service, based on the Stevens classification (1997) (19) and the technical standards recommended by the American Association of Electrodiagnostic Medicine (20).

Patients underwent surgery on the hand that presented the most severe degree of involvement on ENMG, but this degree was bilaterally severe, the more symptomatic hand was selected. The surgical approach used was CA, with a palmar incision and local anesthesia with a 1% lidocaine solution, adrenaline 1:100,000 and 8% sodium bicarbonate in a 1:10 ratio, following the precepts described in WALANT (Lalonde 2019). Anesthetic infiltration followed the technique described as Hole-in-one (Lalonde 2010). All participants were operated on using the same technique by a single neurosurgeon, without the use of a splint or restriction for the use of the hand post-surgery.

After 30-day postoperative period participants were referred to rehabilitation process according to the randomized groups. Starting with stretching followed by IASTM (group S/M) or starting with the IASTM technique followed by stretching (group M/S).

2.1 STUDY PROTOCOL

The selected participants, both from group S/M and group M/S, received the same bilateral treatment in the upper limbs. Static active stretching was performed on six muscle groups located in the cervical region, shoulder, wrist, and fingers, totaling 20 exercise sequences, in the standing position. One stretching series was performed for each exercise sequence, lasting 40 seconds and with a 1-minute rest interval between each muscle group. Stretching was performed aiming for the greatest possible amplitude to the point of discomfort, but not to the point of pain, remaining in the position for 40 seconds. Supervised stretching was performed twice a week for four weeks, with a total time per session of approximately 45 minutes.

The IASTM was performed exposing the target region, without the presence of any cosmetics on the skin. The protocol consisted of mobilizing the chest and back muscles, as well as the shoulder, arm and forearm muscles, both on the anterior, lateral and posterior surfaces; in dorsal, ventral and lateral decubitus. In myofascial

mobilization, up to five types of instruments (crochets) were used, with appropriate conformation of opening and inclination for each muscle group, allowing the best coupling between the crochet and the portion of myofascial tissue to be mobilized. The IASTM technique had centripetal direction and was divided into three successive phases: digital palpation, instrumental palpation with crochets and mobilization.

At the end of mobilization with the crochets, a superficial scraping was added, using the convex part of the crochets, on the insertions of the major pectoral and trapezius muscles at the level of the sternum and occipital bone respectively, with a total time per session of approximately 45 minutes.

After a one-week rest (wash-out 1), participants were reassessed with the outcome instruments (T1). Following this, those who started with stretching moved on to receive IASTM and vice-versa, following the same schedule described above. At the end of the fourth week, after another week of rest (wash-out 2), the participants were reevaluated (T2) and there were no complications during the use of both therapies. Next, participants were referred for outpatient follow-up, and further re-evaluations were performed at 3 months (T3) and 6 months (T4) after T2. During the entire treatment period there were no recommendations for the use of orthoses, analgesic medications, or restrictions on the use of the hands.

The professionals involved in the research were blinded as to the randomization result, in the collection of the results at the different times and in the data analysis.

2.2 ASSESSMENT INSTRUMENTS

The outcome analyses were evaluated from objective and subjective variables, according to guidelines; i) the best of three successive measurements, with 30 seconds rest between measurements for maximum force in isometric contraction of the palmar grip and digital pinch, using Hydraulic Hand Dynamometer and Hydraulic Pinch Gauge, respectively (both from Jamar ® Patterson Medical, Warrenville, IL, USA) following its manual for measurement acquisition. Both instruments were new and calibrated, being kept for exclusive use during the project; ii) Visual Analog Scale (VAS) adapted with the Wong-Baker face scale (21), the evaluations of pain intensity were related to the current moment, where the value 0 on the scale was equivalent to the absence of pain

and the value 10 referred to the worst possible pain. Improvement was evaluated by the reduction of pain intensity values.; and iii) the impact of STC was evaluated by score of Boston Sensitive or scale symptom severity scale (SSS) and score of Boston Function or state scale functional (FSS), domains of the Boston Carpal Tunnel Questionnaire (Boston Carpal Tunnel Questionnaire-BCTQ), where the SSS is composed of 11 questions, with scores ranging from 11 to 55; and FSS is made up of 8 questions, with a range between 8 and 40. The higher the initial value for any of the pillars, the worse the clinical status, and improvements in therapy were evaluated with the reduction of values in both metrics (22) and scores of the Mental and Physical domains of the quality of life questionnaire SF-12 (12-Item Short Form Health Survey) (23), considering the perception of the individual in relation to his/her health, with scores in each of the domains varying on a scale from 0 to 100, with higher values associated to a better quality of life level (24).

2.3 STATISTICAL ANALYSIS

The sample size for a cross-over design, with statistical power of 80%, weighting the hypothesis of loading, typical of these study designs, was estimated at 12 participants per group (25).

Statistical Package for Social Sciences version 25.0 and Stata version 15.0 software were used, and a 5% significance level was set for the applied tests. The ANOVA Cross-Over models were estimated by Ordinary Least Squared (OLS), using the `pkcross` Stata v.15 routine.

The observations from period T0 served as baseline, that is, the ANOVA Cross-Over models were developed from the difference results of interval T0 ($T1=T1'-T0$, ..., $T4=T4'-T0$), as indicated by Tudor, Koch and Catillier (26).

In addition to the ANOVA Cross-Over, the differences between treatments were also evaluated only in the first period to completely exclude the effects of loading. From the differences in outcomes at T0 and T1 between the groups (S/M and M/S), the Mann-Whitney (z) test was used.

This same test was used to compare the scalar variables of the profile between the sequences in the sample description, and in this section the Fisher's Exact Test

was used for the categorical variables. To compare the results between the operated and non-operated hand and between the T0 and T4 periods, i.e. paired samples, the Wilcoxon (z) test was used.

After determining the statistical significance of the outcome variables, the effect size was calculated by Cohen's d, with classification based on established criteria (Cohen 1988). For instruments a) and b), the procedures were developed in the context of the operated hand (OH), non-operated hand (NH), and the difference between OH - NH.

3 RESULTS

3.1 RECRUITMENT AND SAMPLE PROFILE

The study followed the CONSORT guidelines for its completion. After recruiting 252 patients with bilateral CTS, 45 participants met the eligibility criteria, of which 2 were excluded from the study for various reasons and 2 participants lost follow-up before joining physiotherapy treatment. Forty-three participants were randomized, however 1 participant from the M/S group and 2 from the S/M group did not complete all the evaluation phases. Therefore, 19 in the S/M group and 21 in the M/S group remained for final analysis (T4). The allocation flowchart is show in Figure 1.

Figure 1: Sample allocation flowchart.

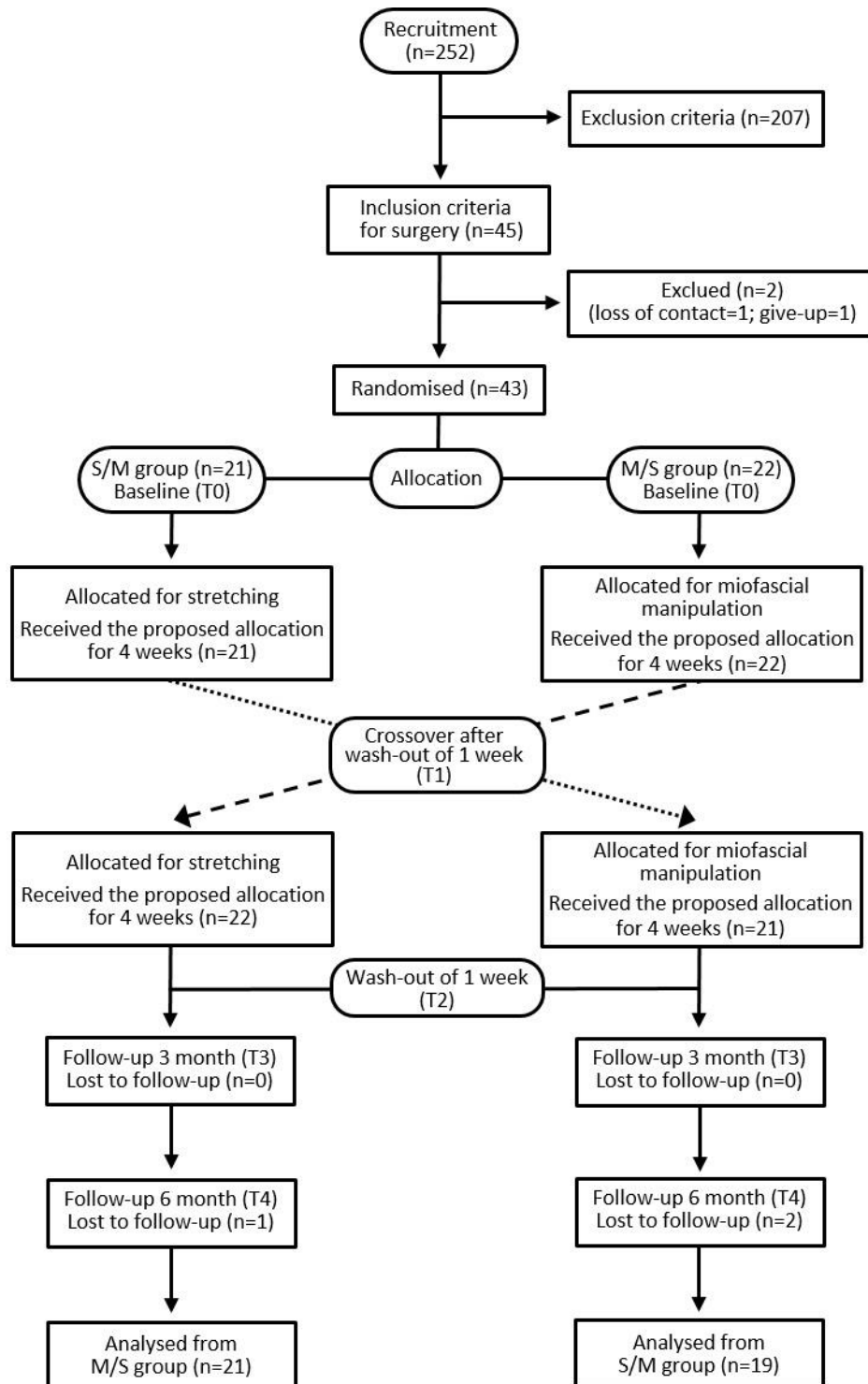


Table 1 presents the main information about the participants' profile according to the treatment sequences. In general, the groups were homogeneous in terms of characteristics. In the case of the severity of the operated hand, all cases were considered as severe, according to the research inclusion criteria.

Table 1: Sample profile by treatment sequence.

Variable	Category	Treatment sequence [n (%)]			Test	
		S/M [n = 21]	M/S [n = 22]	Total [n = 43]	χ^2/z	p-value
Sex	Female	19 (90.5)	21 (95.5)	40 (93.0)	0.410 [¥]	0.607
Ethnicity	White	13 (81.3)	14 (73.7)	27 (77.1)	0.282	0.700
Marital status	Married	16 (80.0)	15 (71.4)	31 (75.6)	0.408	0.719
Occupation	Housewife	6 (28.6)	11 (52.4)	17 (40.5)	2.471	0.208
Education	High school	14 (73.7)	13 (61.9)	27 (67.5)	0.631	0.511
Family income	Up to 1.000 BRL	9 (52.9)	14 (66.7)	23 (60.5)	0.741	0.509
BMI	Non-normal weight	19 (90.5)	17 (77.3)	36 (83.7)	1.374	0.412
Dominant hand	Right	19 (90.5)	20 (90.9)	39 (90.7)	0.002 [¥]	1.000
	Light	6 (28.6)	3 (13.6)	9 (20.9)		
Stevens NH	Moderated	9 (42.9)	5 (22.7)	14 (32.6)	5.322 [¥]	0.070
	Severe	6 (28.6)	14 (63.6)	20 (46.5)		
Age (years)	mean \pm SD	50.52 \pm 7.86	52.45 \pm 12.57	51.51 \pm 10.46	-0.207	0.836
Symptom time (years) OH	mean \pm SD	5.15 \pm 4.62	5.62 \pm 2.92	5.38 \pm 3.83	-1.27	0.205
Symptom time (years) NH	mean \pm SD	4.68 \pm 4.19	4.14 \pm 3.18	4.41 \pm 3.68	-0.345	0.730

NH = Non-operated hand; SD=Standard Deviation; S = Stretching; M = Miofascial mobilization; BRL = Brazilian Real; BMI = Body Mass Index. χ^2/z = Fisher's exact test (χ^2) and the Mann-Whitney test (z) [for age and symptom time]. The categories indicated in the table are the most frequent. [¥]Indicates that even with the reclassifications, an expected count of less than five was obtained in two cells.

3.2 ANOVA CROSS-OVER

Tables 2 to 4, in addition to bringing the results of the ANOVA Cross-Over, also indicate the required descriptions for replications of cross-over studies in meta-analysis, as recommended by Li and colleagues (2015) (27). Table 2 highlights the results for the objective outcomes (hand pressure strength and digital pinch) and Table 3 highlights the results for the subjective outcomes (VAS, BCTQ, and SF-12). Table 4 shows the results of the outcomes measured by hand, which aimed at assessing whether there was a difference in effects between the operated hand compared to the non-operated hand.

In the case of objective measures, we observed an effect of time for both hand pressure and pinch strength in both hands (Table 2). Evidence in favor of a treatment effect was also found for the digital pinch measure (in both hands), however, as the carryover effect was also shown to be significant, the results on the treatment effect are inconclusive. It is worth noting that the separability measure of treatment and carryover (1-Cramer' V) indicates that 50% of the variability can be individualized, that is, half of the variance is shared between treatment and carryover. These values refer to all outcomes.

Regarding subjective measures, the effect of period was highly significant for all outcomes (Table 3). The effect of sequence was found to be significant for the VAS of the non-operated hand and the physical and mental domains of the SF-12. Unlike the objective measures, in the case of the VAS of the operated hand and the mental domain of the SF-12, there was a significant effect of treatment and no effect of carryover, however, this conclusion should be cautiously interpreted and needs further investigation, as the carryover effect was marginally significant ($p=0.06$ and $p=0.09$ respectively). In the case of the BCTQ sensitive domain both treatment and carryover were significant.

Table 4 shows evidence that the combination of therapies in the period may have had a different effect between operated and non-operated hands with regard to the results of manual pressure strength and VAS. In addition, the sequence in the case of VAS was also significant, so as to cast suspicion that operated and non-operated hands may perform differently according to the allocation sequence.

Table 2: Objective outcomes (difference to baseline) from a two-treatment, four-period cross-over trial

Outcome	Treatment sequence S/M (n=81) M/S (n=87)	Treatment period Δ [mean (\pm SD)]				Effect F (p)			
		T1 (n=43)	T2 (n=43)	T3 (n=42)	T4 (n=40)	Sequence	Treatment	Carryover	Period
Hand grip strength (OH)	S/M	4.02 (4.08)	9.14 (5.98)	11.23 (6.12)	13.25 (5.72)	0.58	2.08	0.70	73.23
	M/S	5.92 (3.27)	9.91 (4.30)	12.32 (4.57)	13.17 (6.07)	(p=0.45)	(p=0.15)	(p=0.41)	(p<0.00)
Hand grip strength (NH)	S/M	3.49 (1.98)	7.06 (4.21)	9.70 (4.32)	10.32 (4.51)	0.73	0.79	1.61	65.73
	M/S	4.91 (3.28)	8.17 (3.90)	10.20 (4.19)	10.67 (5.15)	(p=0.40)	(p=0.38)	(p=0.21)	(p<0.00)
Tip pinch gauge (OH)	S/M	0.51 (0.45)	1.24 (0.57)	1.40 (0.66)	1.59 (0.78)	0.00	12.18	8.58	54.38
	M/S	0.73 (0.37)	1.17 (0.56)	1.29 (0.61)	1.27 (0.74)	(p=0.98)	(p<0.00)	(p<0.00)	(p<0.00)
Tip pinch gauge (NH)	S/M	0.45 (0.31)	1.17 (0.63)	1.32 (0.68)	1.51 (0.82)	0.24	9.54	6.71	52.42
	M/S	0.75 (0.38)	1.20 (0.56)	1.35 (0.62)	1.33 (0.75)	(p=0.63)	(p<0.00)	(p=0.01)	(p<0.00)

Δ =Difference; OH = Operated hand; NH = Non-operated hand; T = Period; SD = Standard Deviation; S = Stretching; M = Miofascial mobilization. Effect F (p) refers to F test (p-value) of the effects estimated from ANOVA Cross-Over. The values highlighted in bold are significant at 5%.

Table 3: Subjective outcomes (difference to baseline) from a two-treatment, four-period cross-over trial

Outcome	Treatment sequence S/M (n=81) M/S (n=87)	Treatment period Δ [mean (\pm SD)]				Effect F (p)			
		T1 (n=43)	T2 (n=43)	T3 (n=42)	T4 (n=40)	Sequence	Treatment	Carryover	Period
VAS (OH)	S/M	-3.67 (0.80)	-5.52 (0.81)	-6.00 (0.86)	-6.00 (0.88)	0.81	11.38	3.56	125.59
	M/S	-3.86 (0.56)	-5.14 (0.83)	-5.59 (0.73)	-5.76 (0.70)	(p=0.37)	(p<0.00)	(p=0.06)	(p<0.00)
VAS (NH)	S/M	-2.33 (0.80)	-3.57 (0.75)	-4.00 (0.79)	-4.11 (0.74)	4.56	1.10	1.08	68.93
	M/S	-3.09 (1.06)	-4.18 (1.30)	-4.59 (1.22)	-4.67 (1.24)	(p=0.04)	(p=0.30)	(p=0.30)	(p<0.00)
BCTQ (sensitive)	S/M	-14.81 (5.81)	-21.33 (5.70)	-23.10 (5.88)	-25.16 (6.99)	1.09	9.31	6.43	90.99
	M/S	-14.73 (4.71)	-19.14 (5.45)	-21.14 (4.94)	-22.14 (4.74)	(p=0.30)	(p<0.00)	(p=0.01)	(p<0.00)
BCTQ (function)	S/M	-7.76 (3.11)	-12.10 (3.71)	-14.75 (2.75)	-16.11 (3.70)	0.34	2.41	5.38	92.65
	M/S	-6.68 (3.50)	-10.50 (3.85)	-12.82 (4.08)	-13.14 (4.26)	(p=0.09)	(p=0.12)	(p=0.02)	(p<0.00)
SF-12 (physical)	S/M	-1.31 (5.05)	1.72 (4.87)	1.22 (5.52)	0.52 (5.58)	5.36	0.34	2.48	5.21
	M/S	0.97 (4.07)	3.83 (4.71)	5.20 (4.32)	4.88 (4.26)	(p=0.03)	(p=0.56)	(p=0.12)	(p<0.00)
SF-12 (mental)	S/M	10.63 (7.63)	16.82 (7.74)	20.43 (8.20)	22.26 (8.93)	5.15	3.80	2.94	24.46
	M/S	8.22 (4.68)	11.76 (6.56)	14.90 (7.23)	15.48 (7.92)	(p=0.03)	(p=0.05)	(p=0.09)	(p<0.00)

Δ =Difference; OH = Operated hand; NH = Non-operated hand; T = Period; S = Stretching; M = Miofascial mobilization; VAS = Visual Analogue Scale; BCTQ = Boston Carpal Tunnel Questionnaire; SF-12 = 12-Item Short Form Health Survey. Effect F (p) refers to F test (p-value) of the effects estimated from ANOVA Cross-Over. The values highlighted in bold are significant at 5%.

Table 4: Outcomes (difference to baseline between OH and NH) from a two-treatment, four-period cross-over trial

Outcome	Treatment sequence S/M (n=81) M/S (n=87)	Treatment period Δ [mean (\pm SD)]				Effect F (p)			
		T1 (n=43)	T2 (n=43)	T3 (n=42)	T4 (n=40)	Sequence	Treatment	Carryover	Period
Hand grip strength (OH - NH)	S/M	0.52 (3.69)	2.08 (5.60)	1.53 (5.72)	2.93 (4.82)	0.75	0.59	0.10	3.38
	M/S	1.02 (3.26)	1.74 (3.84)	2.12 (3.62)	2.51 (4.91)	(p=0.92)	(p=0.45)	(p=0.75)	(p=0.02)
Tip pinch gauge (OH - NH)	S/M	0.05 (0.48)	0.07 (0.51)	0.08 (0.51)	0.08 (0.47)	0.66	0.31	0.22	0.05
	M/S	0.02 (0.23)	-0.03 (0.26)	-0.06 (0.24)	-0.05 (0.28)	(p=0.42)	(p=0.58)	(p=0.64)	(p=0.99)
VAS (OH - NH)	S/M	-1.33 (1.06)	-1.95 (1.02)	-2.00 (0.92)	-1.89 (0.88)	6.09	2.60	0.31	3.04
	M/S	-0.77 (1.38)	-0.95 (1.50)	-1.00 (1.23)	-1.10 (1.26)	(p=0.02)	(p=0.11)	(p=0.58)	(p=0.03)

Δ =Difference; OH = Operated hand; NH = Non-operated hand; T = Period; SD = Standard Deviation; S = Stretching; M = Miofascial mobilization; VAS = Visual Analogue Scale. Effect F (p) refers to F test (p-value) of the effects estimated from ANOVA Cross-Over. The values highlighted in bold are significant at 5%.

3.3 EFFECT SIZE

In addition to the ANOVA Cross-Over models the Mann-Whitney and Wilcoxon tests were run as a counter test. To evaluate the treatment effect, the effect of carryover was completely excluded by only evaluating the first period (T0-T1). And in the case of the period effect, only the baseline period (T0) and the last period (T4) were considered, without capturing any other variability and control throughout physiotherapy. Concerning the sequence effect, despite carrying out the variability of the whole sample (differences of the outcomes in relation to the baseline period, period to period), no other control was used, as it is a bivariate test. At the same time, we calculated the effect size using Cohen's d (95%CI), whose values, when the Mann-Whitney and Wilcoxon tests were significant, are shown in Tables 5 and 6.

As displayed in Table 5, all period effects can be considered large, except for the SF-12 physical domain. In general, there is evidence that physical therapy acted positively in the improvement of patients who underwent surgery. This positive effect seems to be shared by both surgery and physical therapy procedures.

The point estimate of the treatment effect size for the digital pinch measurement and VAS of the non-operated hand can be considered large. Generically, IASTM performed better than stretching for digital pinch and pain reduction in the unoperated hand. Despite small and intermediate effect sizes the effect of the sequence was also significant for some outcomes: i) VAS of the non-operated hand; ii) function domain of the BCTQ; and iii) SF-12 in both domains. Thus, there are indications that starting with IASTM leads to a greater improvement in these items than starting with stretching for patients who underwent CTS surgery, although the effect size is not large.

Table 5: Effect size by sequence, treatment and period

Outcome	Measure	Cohen's <i>d</i> (IC95%)		
		Sequence	Treatment	Period
Hand grip strength	OH	–	–	1.93 (1.40 ; 2.46)
	NH	–	–	2.55 (1.96 ; 3.14)
Tip pinch gauge	OH	–	–	2.68 (2.08 ; 3.29)
	NH	–	-0.86 (-1.49 ; -0.24)	3.08 (2.43 ; 3.73)
VAS	OH	–	–	-6.78 (-7.92 ; -5.64)
	NH	0.53 (0.23 ; 0.84)	0.80 (0.18 ; 1.43)	-3.67 (-4.39 ; -2.96)
BCTQ	Sensitive	–	–	-5.01 (-5.91 ; -4.12)
	Function	-0.39 (-0.70 ; -0.09)	–	-5.13 (-6.03 ; -4.22)
SF-12	Physical	-0.64 (-0.95 ; -0.33)	–	0.50 (0.06 ; 0.95)
	Mental	0.59 (0.28 ; -0.90)	–	2.07 (1.52 ; 2.61)

OH = Operated hand; NH = Non-operated hand; VAS = Visual Analogue Scale; BCTQ = Boston Carpal Tunnel Questionnaire; SF-12 = 12-Item Short Form Health Survey. The cell values indicate that the respective bivariate tests (Mann-Whitney for sequence and treatment, and Wilcoxon for period) were significant at the 5% level. For the sequence we considered all periods [i.e., M/S (n=87) and S/M (n=81)]. For treatment we considered the baseline difference of the outcome in the first period between the groups [i.e., M (n=22) and S (n=21)]. And to assess the effect of period we took the endpoint value at baseline and the endpoint value at the fourth period as paired samples (i.e., n = 40).

The results in Table 6 indicate that the combinations of therapies, that is, the effect of the period after surgery, had a greater impact on the operated hand than on the non-operated hand. This effect can be considered intermediate in the case of grip strength and large for pain reduction (VAS).

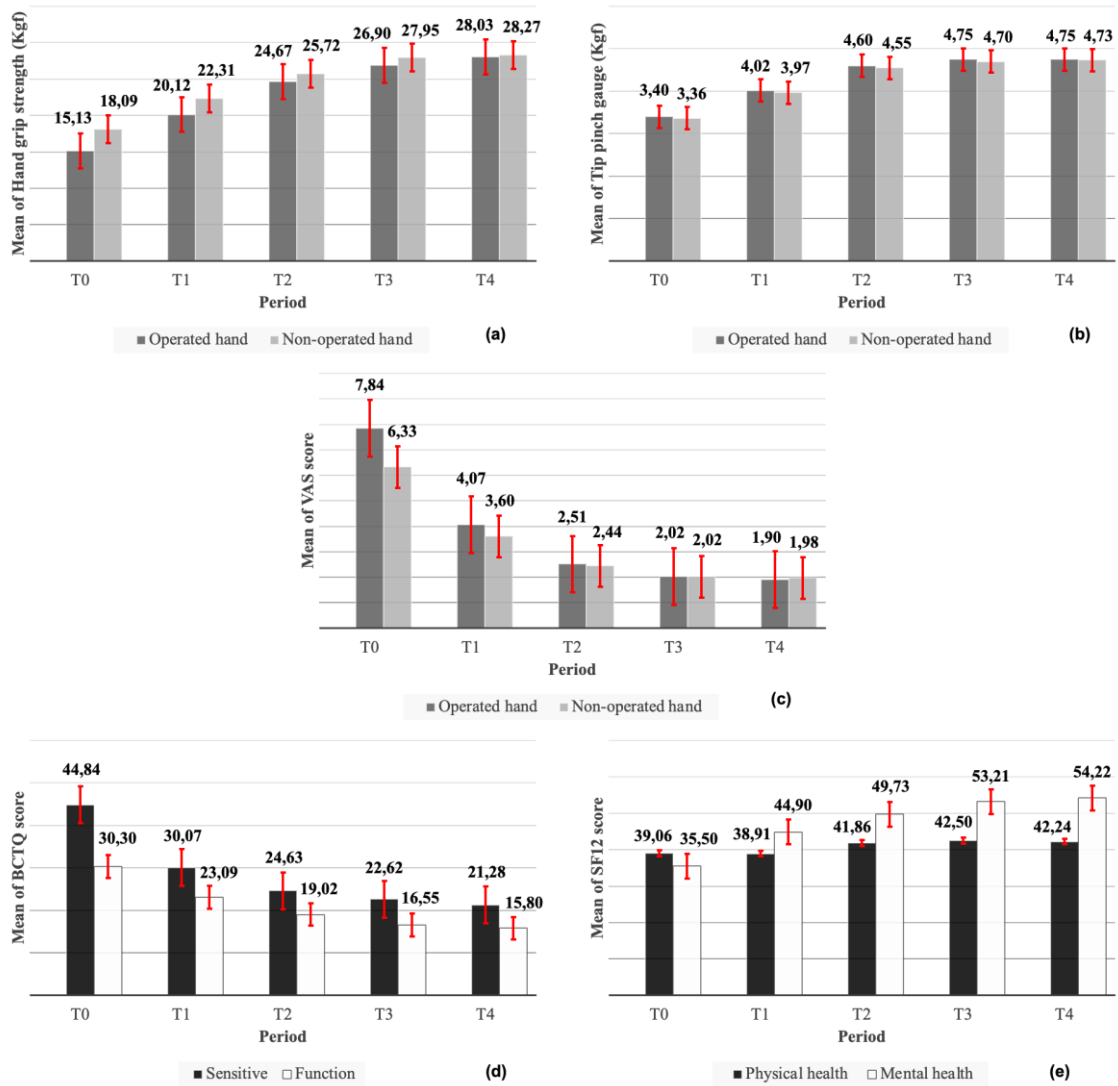
Table 6: Effect size (OH - NH) by sequence, treatment and period

Outcome	Cohen's <i>d</i> (IC95%)		
	Sequence	Treatment	Period
Hand grip strength	–	–	0.50 (0.05 ; 0.94)
Tip pinch gauge	–	–	–
VAS	-0.71 (-1.02 ; -0.40)	–	-1.14 (-1.62 ; -0.67)

OH = Operated hand; NH = Non-operated hand; VAS = Visual Analogue Scale. The cell values indicate that the respective bivariate tests (Mann-Whitney for sequence and treatment, and Wilcoxon for period) were significant at the 5% level. For the sequence we considered all periods [i.e., M/S (n=87) and S/M (n=81)]. For treatment the difference from baseline of the outcome in the first period between groups was considered [i.e., M (n=22) and S (n=21)]. And to evaluate the effect of period, we considered the endpoint value at baseline and the endpoint value at the fourth period as matched samples (i.e., n = 40). The endpoints refer to the original measurements of the operated hand (OH) except the non-operated hand (NH).

This finding can be viewed in Figure 2(a) and Figure 2(c), respectively. It can be seen that for almost the same level of the operated and non-operated hand in the outcomes of grip strength (≈ 28) and VAS (≈ 2) in the fourth period, the operated hand has a lower level of grip strength (15.1 versus 18.1) and higher VAS score (7.8 versus 6.3) in the baseline period (i.e., the difference between the fourth period and baseline period was greater for the operated hand than the non-operated hand).

Figure 2: Outcomes means by period

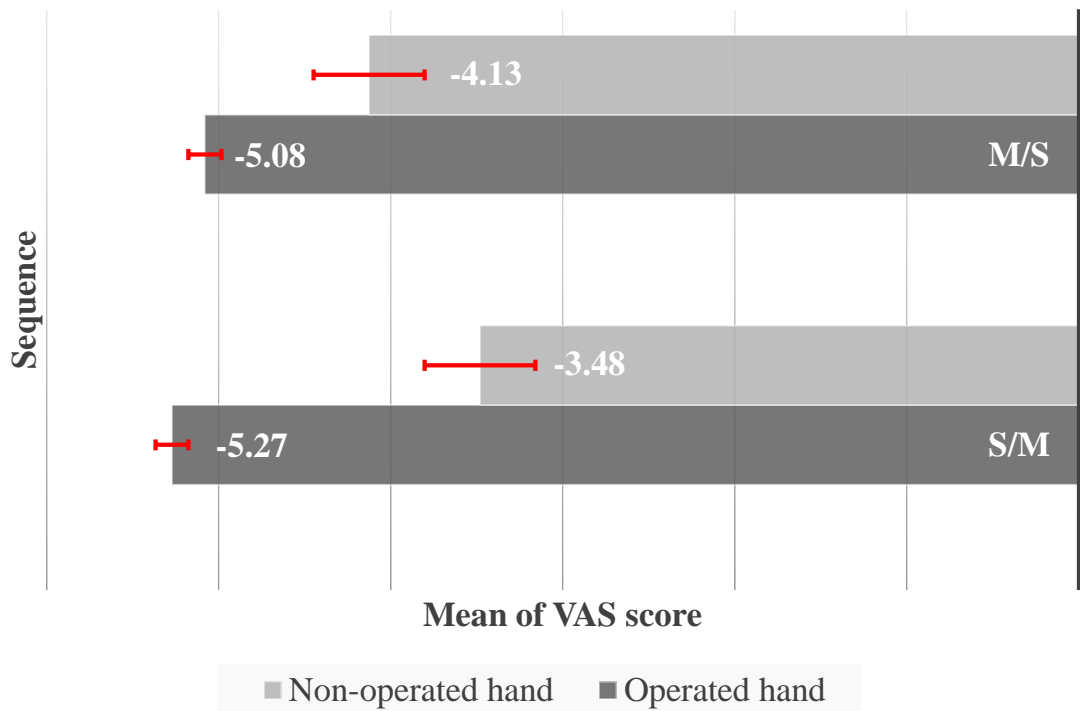


VAS = Visual Analogue Scale; BCTQ = Boston Carpal Tunnel Questionnaire; SF-12 = 12-Item Short Form Health Survey. The graphs illustrate the positive development of the outcomes throughout physiotherapy, supported by the statistical analyses carried out in the research and the effect sizes shown in Table 5 and 6. The values refer to the original measures and not to the baseline differences, since the baseline differences were evidenced in Table 2 and 3.

Still in relation to the results of Table 6, a large effect between the sequences was found in terms of the differences between the operated and non-operated hand regarding pain reduction (VAS). This difference can be better seen in figure 3: the difference for the non-operated hand is greater in the M/S sequence (-4.13) than in the S/M sequence (-3.48), i.e. the effect of the sequence (start with myofascial manipulation = M/S) contributed more to pain reduction in the non-operated hand. This is not the case for the operated hand when evaluating the irrelevant differences

between the sequences (-5.08 versus -5.27) in figure 3 and the non-significant tests in Tables 3 and 5. The combination of therapies (stretching +IASTM) contributed more to pain reduction for the OH, however, starting with the sequence M(IASTM)/S contributed more to pain reduction for the non-operated hand.

Figure 3: VAS mean score by sequence



VAS = Visual Analogue Scale. The graph illustrates the difference in mean VAS score between the sequences and between T1 and T4, supported by the statistical analyses performed in the research and the effect sizes shown in Table 5 and 6. The values refer to the baseline differences.

4 DISCUSSION

The argument on the results found was divided into two stages, initially analyzing the repercussions of the combined therapies in relation to the groups (S/M *versus* M/S) and, later, the differences in response between the operated hand (OH) and the non-operated hand (NH) in relation to the group of therapies used.

The groups were analyzed for several different outcomes, with punctual results found in the sequences and treatments for both OH and NH in relation to some variables, however, the period was the most significant outcome for all variables.

The following considerations stand out when evaluating each of the outcomes in the period: the improvement in hand grip strength is related to the general state of muscle strength and power, being an indicator of quality of life (28, 29); the increase in digital grip strength translates, in part, into an improvement in the function of the abductor pollicis brevis muscle (30, 31); decreases of 2 or more points on the EVA represent a clinically significant improvement as a result of therapies used for chronic pain (32); increases in Boston Sensitive and Function from baseline report a decrease in STC impact, however, there is no consensus in the literature on values of clinically significant difference for Boston that can be used (33); and increases in the values of the physical and mental constructs of the SF12 reflect an improvement in the perception of the patient's quality of life, but the results indicated must be interpreted with caution, as their normal values are constituted in relation to the specific conditions of a population (24). Therefore, it was found in the present study that the instruments used to analyze the object of study had an association of significant results with large effect sizes, suggesting the effectiveness of the implemented therapeutic strategy (34, 35).

Regarding the therapies implemented, the isolated use of stretching in the postoperative rehabilitation of STC in CA with palmar incision was described by Nathan et al. (1993). The authors performed a dynamic wrist stretch for two weeks and obtained satisfactory results (36). Schmid et al. (2012) evaluated the physical therapy treatment with mobilization exercises in tendons and NM in the postoperative period of CA with palmar opening. The authors observed a beneficial effect after one week of physical therapy, with a reduction in edema in the MN in the OH verified by magnetic resonance imaging (37).

The benefits observed by the use of stretching in STC may be due to the following factors: improvement of the viscoelastic properties of musculoskeletal tissue (38), restoration of dysfunctional proprioceptors and nociceptors patterns at both the central and peripheral nervous system levels (39), and the remodeling of subsynovial connective tissue (SSCT) that restores its functional integrity (40).

The unique use of myofascial mobilization in the postoperative rehabilitation of STC has not yet been reported in the literature, although this therapy is indicated in SSCT disorders, such as: painful fascia syndromes, low back pain, plantar fasciitis and myofascial trigger points (41). The beneficial effects of myofascial mobilization on the

SSCT would be related to the following causes: release of existing adhesions between the connective tissue and the NM, allowing its free sliding along the fascia, and biomechanical restructuring, both locally and remotely, restoring the tensional network of the body and stimulating the proliferation of fibroblasts that triggers an increase in the synthesis, maturation and alignment of collagen reconstituting the SSTC (42-44).

Thus, the present study, when using the combination of stretching and IASTM, obtained an additive effect of these therapies, justifying, in part, the good results achieved with this strategy (45-47).

It was found in this study, that both hands responded positively to the combination of therapies used, regardless of the degree of NH severity. A difference was found between OH and punctual NH for sequence compared to the NH hand for EVA. Nevertheless, the most significant outcome of the difference between the hands was in relation to the period, with a greater impact on the OH hand in the variables palmar grip and EVA. Structural changes in the NM resulting from the procedure may result in an improvement in the clinical picture (48).

The results of surgery without postoperative physical therapy rehabilitation are controversial in the literature for both OH and NH (10, 49, 50). Although long-term results for OH in CA for bilateral STC have not been described in the literature, satisfactory outcomes with 3 months of evolution for Boston SSS and FSS have been described in the literature (51, 52). Bland (2007) analyzed the outcome for OH in a cohort study of 32,936 CA for STC between 2000 and 2006 with follow-up times ranging from weeks to years. The author reported satisfactory outcomes in 75% of the OH, however, poor results and worsening of the clinical picture were evidenced in 25% of the patients, and the causes indicated for this failure were multifactorial, not showing a linear correlation between them (53). Matsuura and colleagues linked the poor post-surgical outcome in STC to an impairment of the SSCT, which would maintain NM dysfunction (54).

The outcomes of surgery on the NH hand were evaluated by Unno et al (2015) in patients with bilateral STC operated on only one hand. The authors described improvement of the NH hand both in the immediate postoperative period and in the follow-up for 6 months after surgery, regardless of the NH severity (11).

According to Agrawal and Southern (2010), the evolution of NH in cases of bilateral STC showed a spontaneous improvement of 37% of patients after six months

of follow-up. However, there is disagreement regarding the results of surgery on NH, as shown by the work of Afshar et al. (2007). They reported that NH remained unchanged after six months of follow-up in a bilateral STC sample containing 24% of NH hands classified as severe according to the Stevens' ENMG criteria (55).

The reasons for the improvement in the NH hand after performing the contralateral surgery may be related to the decrease in the persistent paresthesia stimulus that deactivates the interneurons located in the spinal cord and brainstem (56), disinhibiting the sensory pathways (57). These precepts are based on the hypothesis that STC is a complex neuropathy with involvement of the peripheral and central nervous systems. Nevertheless, there is a need for future investigations in order to clarify in more detail the mechanisms involved in bilateral STC (58).

The use of post-surgical physical therapy is an indicated strategy in an attempt to improve surgical outcomes (59, 60). However, there are divergences in the literature regarding its validity, which is due, in part, to the following limitations: few studies containing exclusive samples from patients with idiopathic bilateral STC (61); low quality of evidence on the benefits of different types of rehabilitation resulting from methodological and statistical analysis problems arising from the bilaterality of the data (59, 62); lack of standardization of rehabilitation programs worldwide (14) and the lack of a gold standard instrument for evaluating the results of the therapies employed, which entails the use of many different measures of outcome, making difficult the comparison of results between studies (63).

Therefore, future studies are necessary to clarify the limitations found in the literature regarding the indication of physiotherapy in the postoperative period of STC, such as: randomized clinical trials using samples containing exclusively patients with idiopathic bilateral STC with allocation being made by participant and not by wrist; the use of appropriate statistical analysis in face of the repetition of data by bilaterality in order not to produce overvalued results; establishing a standardization of both the therapies used and the outcome measures to allow comparison between studies; and implementing rehabilitation therapies throughout the NM, no longer considering STC as a focal mononeuropathy.

The limitations of this study were based on its performance in a single center, which compromises its external validity and on the absence of a control group without physical therapy in order to compare the results obtained.

The results produced by the present study were robust and demonstrated that the therapeutic combination used in the postoperative period of idiopathic bilateral STC, as well as its use throughout the entire NM, brought good results during its performance, in addition to maintaining the effects obtained by a six-month follow-up. There was also an improvement in both OH and NH in terms of functionality and sensitivity, with the greatest impact being observed in OH.

Although the beneficial effects of physical therapy and surgery are difficult to dissociate, the performance of the outcome over time shows that surgery followed by a combination of the proposed treatments or some interaction between them was an effective strategy for this population. However, other studies are needed to confirm the findings.

5 CONCLUSION

The present study presented robust results for objective and subjective measures in the postoperative rehabilitation of patients with idiopathic bilateral STC, demonstrating that the proposed therapeutic model was effective.

Comparing the responses between OH and NH to the combined therapies, positive effects were found for both hands, demonstrating that in the presence of bilateral idiopathic STC the option of operating on the severe hand and treating both hands with the combination of recommended therapies was valid strategy.

The benefits of physical therapy and surgery are difficult to dissociate, however the results obtained suggest a positive interaction between them.

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9. CONSIDERAÇÕES FINAIS

Apesar da STC ter sido descrita em 1854 por Sir James Paget, o seu reconhecimento na área médica só ocorreu em 1950 em consequência dos trabalhos de Phalen. Transcorridos setenta e dois anos de pesquisa as opções de tratamentos clínicos e cirúrgicos para essa patologia permanecem incertas, tornando o seu estudo um tema instigante. A presente tese enfrentou o desafio de tecer um panorama atual sobre a STC bilateral idiopática ressaltando as características clínico-funcionais que a diferenciam das outras compressões do nervo mediano no túnel cárpico.

Foi realizado o tratamento de casos leves e moderados, bem como a reabilitação após o tratamento cirúrgico utilizando-se a combinação de duas terapias implementadas ao longo de todo o nervo mediano, em ambos os lados, sendo tal proposta inédita na literatura. O pensamento terapêutico utilizado para direcionar esse projeto excedeu a noção de que a STC é uma patologia restrita ao carpo e passou a interpretá-la como uma neuropatia complexa com envolvimento do sistema nervoso periférico e central.

Com base nos resultados desta tese, pode-se concluir que a utilização de métodos fisioterapêuticos direcionados para o tecido conectivo subsinovial são úteis na reabilitação da STC. O emprego combinado de alongamento/IASTM demonstrou ter um efeito aditivo no tratamento clínico de STC bilateral idiopática. O uso de gabapentina preventiva foi eficaz na redução da dor pós-operatória. Além disso, a utilização da combinação alongamento/IASTM foi efetiva no tratamento pós-cirúrgico. Vale ressaltar ainda que a mão não operada teve uma melhora expressiva, independentemente da sua gravidade, o que demonstra que a estratégia utilizada foi válida para essa população.

Os desfechos obtidos utilizando-se o modelo de estudo *cross-over* e a análise dos dados com ANOVA *Cross-Over* foram consistentes nas avaliações terapêuticas dessa patologia bilateral. Não foi possível comparar os resultados encontrados na presente tese com a literatura, tanto em relação ao tratamento clínico como ao seu emprego na reabilitação pós-cirúrgica, devido à baixa quantidade de artigos com amostras contendo STC bilateral idiopática associada à fragilidade nos resultados

apresentados por esses trabalhos ao desconsiderarem os problemas metodológicos e estatísticos ao reportarem os desfechos de patologias com envolvimento bilateral.

No campo acadêmico-científico as considerações traçadas no presente estudo podem servir de orientação para que estudos futuros sejam realizados com maior rigor, produzindo resultados robustos a fim de consolidar as indicações terapêuticas direcionadas à melhora da saúde e da qualidade de vida de pacientes com STC bilateral idiopática

10. APÊNDICE A – FICHA DE IDENTIFICAÇÃO DO PARTICIPANTE DA PESQUISA

FICHA DE IDENTIFICAÇÃO DO PARTICIPANTE DA PESQUISA.

Nome do paciente: _____	ID: _____
Data: ____/____/____	

Dados pessoais

Iniciais: _____ Sexo () M () F Contato: () _____
 DN: ____/____/____ Idade: _____ Etnia: _____

Profissão / Ocupação: _____
 Mão dominante: _____
 Peso e altura aproximados: _____

Escolaridade:	sem ensino ()	fundamental ()	médio ()	graduação ()	pós-graduação ()
Situação conjugal:	casado ()	separado ()	divorciado ()	solteiro ()	outros ()
Renda familiar aproximada:	menos 1000,00 ()		1000,00 a 2000,00 ()		maior de 3000,00 ()
Procedência:	_____				

Anamnese

1). Quando os sintomas tiveram início (em anos)? mão direita () mão esquerda ()

Mão direita:	dor ()	dormência só noturna ()	dormência diurna ()	dormência no repouso ()
	perda sensitiva ()	déficit motor / queda de objetos ()	completa atrofia tenar / plegia ()	
Mão esquerda:	dor ()	dormência só noturna ()	dormência diurna ()	dormência no repouso ()
	perda sensitiva ()	déficit motor / queda de objetos ()	completa atrofia tenar / plegia ()	

2). Qual foi o serviço de saúde que o encaminhou? Por quem? Quanto tempo?

3). Que tipo de tratamento foi realizado anteriormente para o seu problema?

1. Nenhum () 2. Algum () Qual?

4). Já realizou fisioterapia para este problema?

1. Não () 2. Sim () Quanto tempo?

5). Antecedentes pessoais

Alergia a medicação:	Não ()	Sim ()	Qual?
Diabetes Mellitus:	Não ()	Sim ()	Tipo, tempo e medicação?
Doença Reumática:	Não ()	Sim ()	Qual?
Alterações cervicais:	Não ()	Sim ()	Qual?
Doença Neurológica:	Não ()	Sim ()	Qual?
Doenças ortopédicas:	Não ()	Sim ()	Qual?
Doença da tireoide:	Não ()	Sim ()	Qual?
Fumante:	Não ()	Sim ()	Quantos / dia?
Crise convulsiva:	Não ()	Sim ()	Qual medicamento usa?
Bebidas alcoólicas:	Não ()	Sim ()	Frequência diária e quantidade?
Hipertensão arterial:	Não ()	Sim ()	Medicação?

Nome do paciente: Data: ____/____/____	ID:
---	------------

6). Sintomas que apresenta no momento

Dores musculares:	Não ()	Sim ()	
Tonturas:	Não ()	Sim ()	
Perda de equilíbrio e coordenação:	Não ()	Sim ()	
Tremores:	Não ()	Sim ()	
Cefaleia:	Não ()	Sim ()	
Náuseas:	Não ()	Sim ()	
Problemas de sono relacionados STC:	Não ()	Sim ()	Quanto tempo? Frequência semanal?
Irritado:	Não ()	Sim ()	
Deprimido:	Não ()	Sim ()	

7). Exames Complementares Anteriores:

- 1) ENMG _____
- 2) USG _____
- 3) Ressonância magnética _____

11. APÊNDICE B - TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO (TCLE)

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO (TCLE)

Prezado(a) Senhor(a):

Título do Projeto: Caracterização clínico-funcional e avaliação da eficácia do tratamento de pacientes portadores da síndrome do túnel do carpo.

Pesquisador Responsável: Dr. Sérgio Murilo Georgeto

Instituição: Irmandade da Santa Casa de Londrina (ISCAL)

Telefones para contato: (43) 99111 0088/ (43) 33742540

E-mail: georgetosm@gmail.com

Nome do voluntário: _____

Idade: _____ RG: _____

O senhor(a) está sendo convidado a participar da pesquisa denominada "**Caracterização clínico-funcional e avaliação da eficácia do tratamento de pacientes portadores de síndrome do túnel do carpo**", a ser realizado ambulatório de neurocirurgia da Irmandade da Santa Casa de Londrina, localizado na rua Senador Souza Naves, 219, Londrina, Paraná.

O objetivo da pesquisa é caracterizar o impacto da Síndrome do Túnel do Carpo sobre aspectos funcionais, psicológicos e de qualidade de vida, assim como testar novas alternativas terapêuticas para melhora do quadro.

Após a avaliação clínica, os voluntários com quadro leve ou moderado serão convidados para participar da etapa de tratamento clínico, enquanto os pacientes com grau severo da doença serão convidados para participar do grupo cirúrgico.

As coletas de informações serão realizadas por meio de entrevista com os voluntários em uma sala reservada antes e após o tratamento. Por meio de questionários e escalas será feita uma caracterização clínico-funcional, levantando dados sobre a doença, intensidade e caracterização da dor, limitações nas atividades de vida diárias e comprometimento da qualidade de vida.

Com a participação na pesquisa, o senhor(a) poderá esperar alguns benefícios, tais como: acesso, de forma gratuita, à medicação (Gabapentina) sem qualquer custo no grupo de tratamento clínico e como estratégia para a prevenção da dor no grupo cirúrgico. Além disso, o grupo do tratamento cirúrgico poderá se beneficiar da fisioterapia de pós-operatório.

Sua privacidade será respeitada mediante anonimato e não serão revelados quaisquer dados de identificação. Os dados serão mantidos em completo sigilo. Para evitar constrangimento, as entrevistas serão feitas em consultório reservado.

RUBRICA DO PESQUISADOR.

O senhor(a) poderá se recusar a participar do estudo, ou seu consentimento a qualquer momento, sem necessidade de justificativa prévia. Caso deseje sair da pesquisa, não sofrerá qualquer prejuízo à assistência recebida.

É assegurada a assistência durante toda a pesquisa, bem como é garantido o livre acesso a todas as informações e esclarecimentos adicionais sobre o estudo e suas consequências a qualquer tempo.

As informações da presente pesquisa serão armazenadas de forma anônima sob responsabilidade do Dr. SERGIO MURILO GEORGETO. Enfim, tendo sido orientado quanto ao teor de todo o aqui mencionado e compreendido a natureza e o objetivo do já referido estudo, manifesto meu livre consentimento em participar, estando totalmente ciente de que não há nenhum valor econômico, a receber ou a pagar, por minha participação.

Esse termo será preenchido em duas vias de igual teor, sendo uma delas, devidamente preenchida, assinada e entregue a mim.

Em caso de reclamação ou qualquer tipo de denúncia sobre este estudo, devo ligar para o CEP BIOISCAL (43) 3374-2540 ou mandar um e-mail para bioiscal@iscal.com.br

Declaro que concordo em participar desse estudo. Recebi uma cópia deste termo de consentimento livre e esclarecido e me foi dada a oportunidade de ler e esclarecer as minhas dúvidas. Declaro ter sido informado e concordo em participar, como voluntário, do projeto de pesquisa acima descrito, e pelo presente afirmo:

Londrina, de de 2018.

Nome e assinatura do sujeito da pesquisa:

Nome do voluntário

Assinatura do voluntário da pesquisa

RG: _____

Dr. Sérgio Murilo Georgeto – Pesquisador Responsável

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RUBRICA DO PESQUISADOR

12. APÊNDICE C - SEQUÊNCIA DE ALONGAMENTO

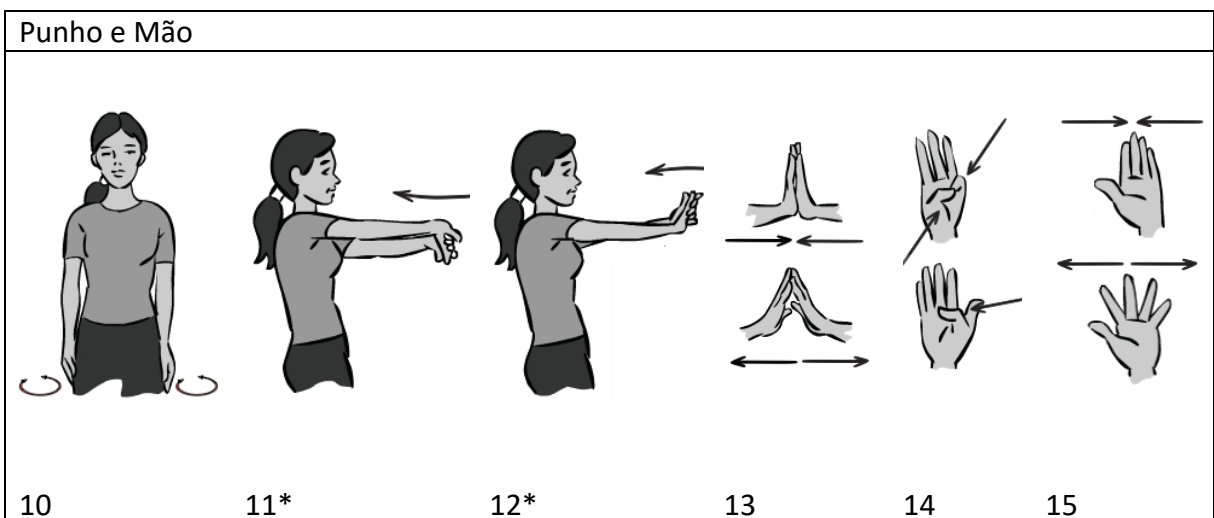
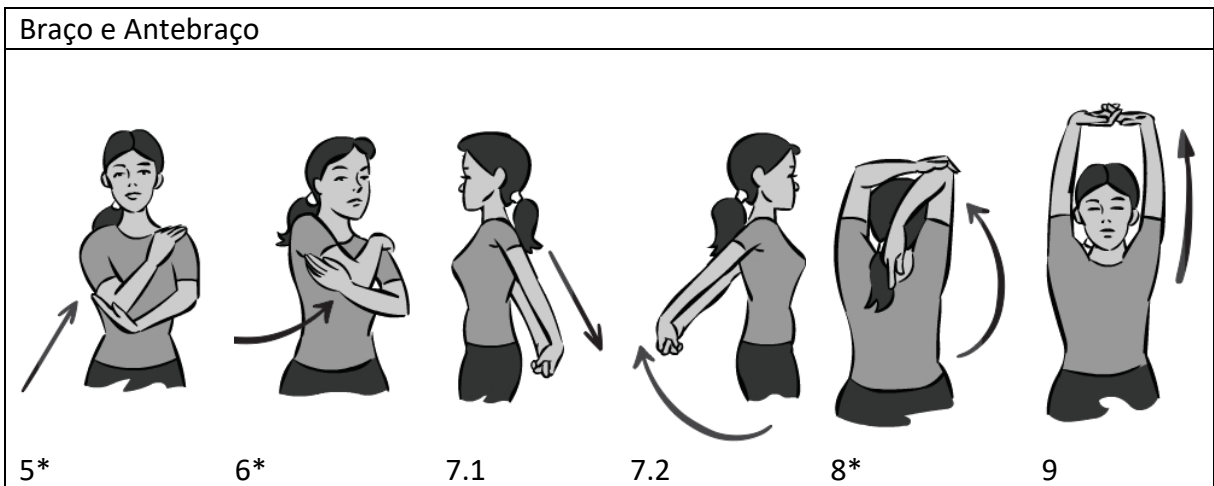
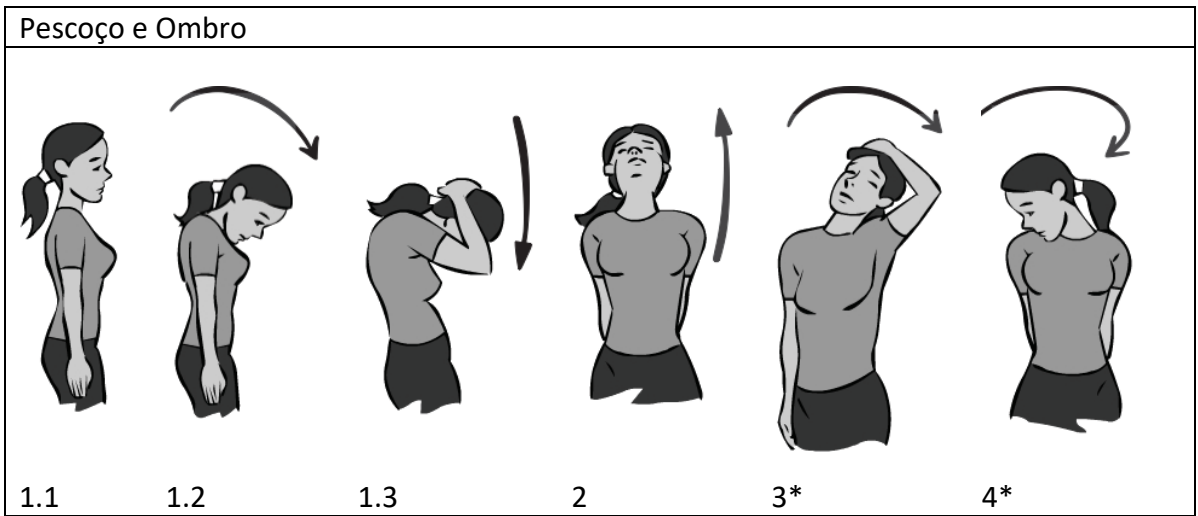


Figura 10: Sequência de Alongamento. *= movimento para ambos os lados

13. APÊNDICE D - SEQUÊNCIA DE MANIPULAÇÃO MIOFASCIAL

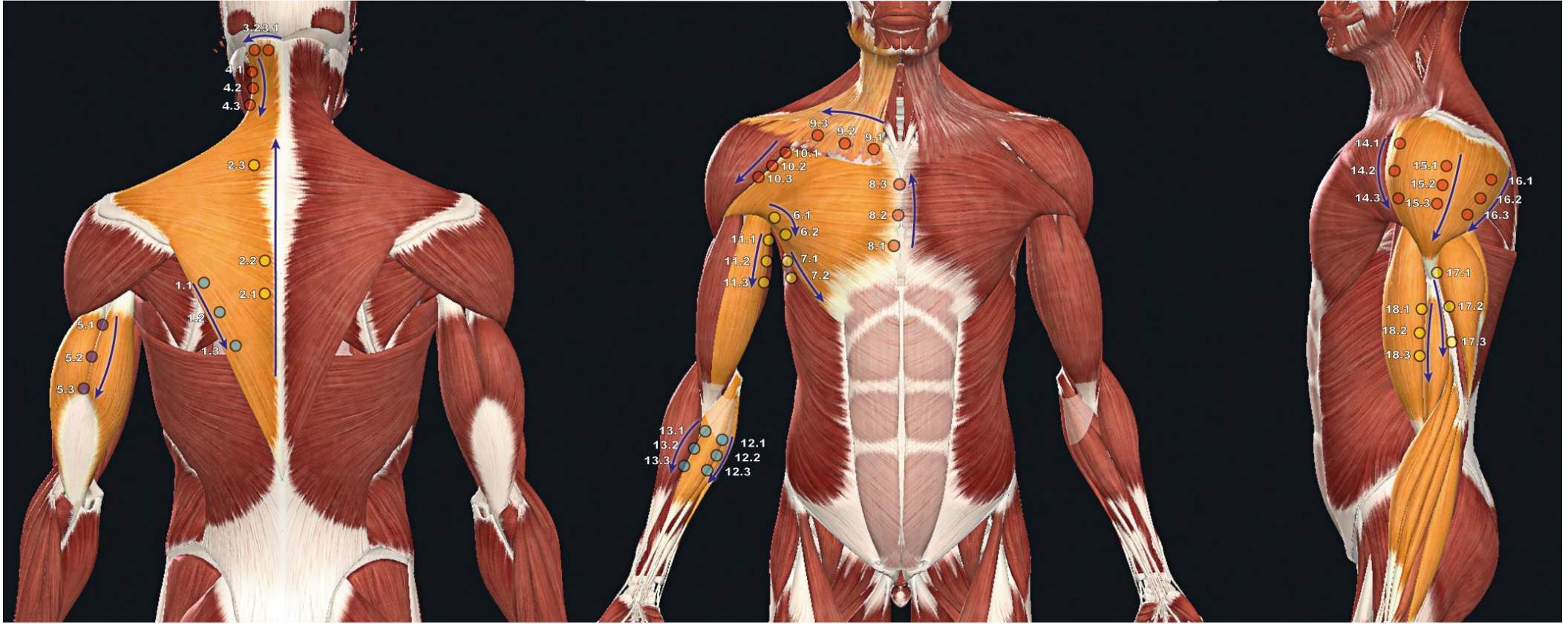


Figura 11: Sequência de Manipulação Miofascial.

14. APÊNDICE E: STUDY DESIGNS AND STATISTICAL APPROACHES FOR BILATERAL CARPAL TUNNEL SYNDROME: AN OVERVIEW.

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ABSTRACT

Background: Pathologies with bilateral involvement, such as carpal tunnel syndrome (CTS), are relatively common in clinical practice. However, some published data are misleading, as many articles consider only one hand in data analysis. **Objectives:** This article aims to briefly propose a study design and statistical approach for data analysis of bilateral CTS. **Method:** Statistical reporting. **Results:** Although the results of clinical and surgical interventions are usually reported by randomized clinical trials, the main guidelines do not offer recommendations on how to proceed in cases of interventions in patients with bilateral conditions. Additionally, crossover trials may be an alternative, particularly when comparing different interventions in these patients. Considering the statistical approach, traditional tests are not suitable for bilateral conditions, and result in an overestimation of the results. In contrast, regression models, mixed effects analysis, generalized estimating equations, and multilevel modeling analysis are more reliable. Furthermore, in the case of crossover trials, an ANOVA suitable for crossover design should be chosen with normally distributed data of two groups, while a variance-balanced design is the ideal choice for three or more treatments and Cochran's Statistics. **Conclusions:** When considering the comparison of different therapeutic intervention/rehabilitation techniques in patients with CTS or other peripheral nerve pathologies, the choice of the most appropriate study design and statistical analysis will provide more reliable evidence.

Keywords: Carpal tunnel syndrome; statistical methods; crossover trial; rehabilitation; surgical treatment; clinical treatment

1. INTRODUCTION

Bilateral Carpal tunnel syndrome (CTS) has clinical implications and therapeutic results that differ from unilateral NM compression (1). In addition, the presence of bilateral symptoms generates an interrelationship between the outcome measures, which, if not properly considered in the interpretation of the data, causes an effect of repetition of information, which can bias the statistical analysis (2). However, despite the high prevalence of bilateral CTS, there is lack of studies that demonstrate the best way to manage these cases, both in relation to clinical (3) and surgical treatment (4).

Even the main guidelines for randomized clinical trials (RCTs), researchers lack guidance on how to work with pathologies of bilateral involvement (5, 6), both in relation to the allocation of participants and the statistical analyzes that should be implemented, considering the interdependence of the data produced by bilaterality (7). The allocation of patients with bilateral CTS should be made by individual and not by affected hand. At traditional statistical tests, when analyzing results by wrist and not by individual, lead to an overestimation of results due to repetition of information (8). Therefore, it is necessary to use more reliable statistical models to manage the repetition of data resulting from the inclusion of the same participant more than once. Therefore, this study aims to discuss aspects related to study designs for the allocation of participants with bilateral CTS and their respective statistical analysis.

2. CARPAL TUNNEL SYNDROME (CTS)

CTS is a compressive neuropathy of the upper limbs, representing 90% of peripheral compressive neuropathies, and is the most common neuropathy in the general population (9). It has been reported that CTS affects 10% of the global population, with 3 to 4 new cases per 1.000 inhabitants per year (10).

In the United States, the prevalence of CTS is nearly 5%, with an incidence of 1 to 3 cases per 1.000 inhabitant (11). CTS has a higher incidence in women aged 45–65 years and tends to be bilateral in 60%–65% of cases (12). Additionally, there is an increase in the prevalence and severity of this pathology with aging (13).

Clinical signs of CTS, such as pain, numbness, and tingling at the median nerve of the upper limbs, may be associated with muscle weakness and atrophy, with a marked impairment of manual abilities and health-related quality of life (10).

It has been reported that surgical treatment of CTS carries an annual cost of more than 2 billion dollars (14). In Brazil, the estimated cost of CTS surgeries at the Unified Health System is nearly 30 million reais (15).

The main factors associated with CTS are older age, sex, obesity, diabetes mellitus, rheumatic arthritis (16), and manual labor, particularly jobs that require manual strength and physical activity (17).

Treatment for CTS may be clinical or surgical, the choice of which is based on disease severity. The use of clinical therapies is indicated for the treatment of CTS with mild or moderate impairment (18). Therapeutic approaches include modification of daily life activities, low-level laser therapy, ultrasound therapy, stretching, and myofascial manipulation (19-21). However, surgical treatment of this neuropathy is indicated when severe involvement of the median nerve is observed during clinical evaluation or electroneuromyography (22). Open or endoscopic surgery can also be used, despite several studies indicating no statistical difference when comparing the outcomes of both techniques in this patient group (23). The high incidence of CTS in both developed and developing countries, as well as the clinical features and negative impact of the disease, demonstrates the relevance of this topic, which is confirmed by several published articles involving different aspects of the management of such cases (24).

3. STUDY DESIGNS IN BILATERAL CTS

Although CTS is mostly bilateral, insufficient studies have used samples composed exclusively of this population. Individuals with bilateral CTS have peculiar clinical characteristics that influence both the therapeutic results (25) and data analysis. Moreover, statistical methods that do not consider each hand as an interrelated event overestimate the outcome (7).

The results of clinical and surgical interventions are usually reported in randomized clinical trials. Considering the need for improvement in the methods of randomized clinical trials, guidelines such as Consolidated Standards of Reporting Trials – CONSORT (5) and Physiotherapy Evidence Database - PEDro (6), and Hooked on Evidence (26) the

latter two being developed specifically for rehabilitation studies. However, there is no recommendation in these guidelines on how to deal with bilateral conditions, which are relatively common in medical practice.

Crossover trials may be an alternative to randomized double-blind studies. Crossover designs are useful for studies where the patients receive a prespecified sequence of treatments during consecutive periods of time for evaluation (27). The patients' outcomes are measured during each period and the patients serve as their own control, assuming similar conditions for evaluation across treatment periods for each patient (28). Additionally, it is possible to implement a washout period between consecutive periods so that the preceding treatment does not influence the response to the next treatment, allowing any residual effects of treatments to be minimized (29). Briefly, the crossover trial is a "within subject" study design, which seems to be a reliable option, particularly for research studies that aim to compare different interventions in the same individuals. The crossover design has numerous advantages that investigators may wish to use for early-stage trials. The strength of this design is that the interventions under investigation are evaluated within the same patients, thus eliminating between-subject variability (30). Furthermore, this trial design permits head-to-head trial opportunities, and patients receiving multiple treatments can express preferences for or against treatments (31).

Crossover studies are extremely popular for the study of new and developmental drugs (32) and are most appropriate in studies where the effects of the treatment(s) are short-lived and reversible, and are best suited to trials related to symptomatic conditions or diseases (33, 34).

4. STATISTICAL ANALYSIS IN BILATERAL CTS

CTS is usually a bilateral pathology, in which the dominant hand has a worse severity status. Statistical approaches that do not consider the bilateral interdependence of the data do not consider the real physio-pathological expression of CTS. CTS has a complex pathology, with clinical implications on both sides, involving both the central and peripheral nervous systems instead of a simple compression that affects the median nerve in both hands (35).

However, some of the published literature regarding these cases is misleading for several reasons. First, many articles about clinical or surgical interventions only consider one hand in the data analysis, even if the patient reports pain in both hands (4). Moreover, many studies do not consider the effect of repeated information, which may introduce bias in the data analysis if a proper statistical approach is not applied (2). Additionally, some studies have described bilateral data instead of considering bilateral information in the statistical analysis (7).

To consider the continuous or categorical characteristics between interdependent groups, the use of traditional tests, such as the t-test, chi square test, ANOVA, Kruskal–Wallis, and Mann–Whitney test, are unsuitable for bilateral conditions, and create an overestimation of the results (36). Additionally, the description of only one hand for the analysis, or the inclusion of both hands from the same individual creates an artificial increase in the sample size, which predisposes the results to a type I error (2).

A better option to analyze the repeated data arising from bilateral pathologies would be the use of regression models (37) and the analysis of mixed effects (38). Additionally, the generalized estimating equation (GEE) is a less used but still suitable option that is found in some statistical software; the GEE allows the results from both hands to be grouped and the models to be compared considering the correlations between observations for everyone (Johnson, 2010). Additionally, multilevel modeling analysis is a method that analyzes data with multilevel variability. Multilevel models can connect dependent observations that lay bilateral characteristics (39).

Furthermore, while crossover trials are supposed to reduce the standard errors for treatment comparisons, a problem may occur if there are carryover or residual effects from a treatment given in one period to a treatment given in a subsequent period. Carryover exists when a treatment (or intervention) “A” is given in the first period and continues to affect treatment “B”, which is given in the subsequent period (28).

For the analysis of more complicated designs and further investigation of carryover effects, as well as interactions involving treatment effects, models that address conditional distributions of responses within patients can be applied. This potential source of bias is akin to confounding in an epidemiological study and implies that, to some extent, the analysis of data from a crossover trial will inevitably rely more on assumptions and modeling, and less directly on the randomization, than a conventional parallel group study (40).

A crossover trial has a special type of repeated measures design, and the variance-covariance structure of the repeated measures should be taken into consideration when analyzing the collected data.

Crossover data are examples of repeated measurements. Consequently, a key concept in the design and analysis of crossover trials is between-subject and within-subject information. Between-subject information is contained in the total (or mean) of the measurements from a subject, while within-subject information is contained among all differences in the measurements from a subject (40). Statistical analysis of data repeated in the same individuals because of bilateral involvement is done by a specific ANOVA for crossover design (Tudor et al., 2000)

In cases with three or more treatments, there will be more than one possible contrast between the treatment effects. In such situations, a variance-balanced design is the ideal choice because the variance of every estimated pairwise comparison is equal to the same constant value, such as in the Williams design (41) The Williams design also possess a combinatorial balance in the sense that every treatment follows every other treatment (except itself) the same number of times, and is a special case of sequentially counterbalanced Latin squares (42).

Additionally, the analysis of non-normal crossover data falls into the class of analyses of non-normal clustered or dependent data. Such analyses are more complex than those for continuous data based on a linear model (43). There are two main reasons for this. First, there is no single “natural” choice of multivariate model in such settings for which to parallel the multivariate normal linear model. Second, for most problems in this class, it is appropriate to assume a non-linear relationship between the mean or expectation of an observation and the linear predictor with various fixed effects [(43, 44). Therefore, a straightforward nonparametric method can be used for the comparison of treatments in situations where one can assume that neither carryover nor period effects are present (27). In such cases, Mantel-Haenszel statistics or Cochran analyzes can be used if the response variable is dichotomous. It is based on Mantel–Haenszel statistics with the respective patients as strata, within which the association between treatments and ordinal outcomes is assessed (Tudor et al., 2000). In addition, the dichotomous response variable is comparable to Cochran’s statistics (45).

5. CONCLUSIONS

Although randomized controlled trials are the primary choice for comparing different interventions, considering the frequent bilateral condition in CTS, crossover trials may be another suitable option, particularly when comparing different interventions in these patients. Considering the statistical approach, traditional tests are not suitable for bilateral conditions and result in an overestimation of the results. Regression models, mixed effects analysis, generalized estimating equations, and multilevel modeling analysis are more reliable methods for this condition.

In the case of crossover trials an ANOVA that is suitable for the crossover design should be chosen. However, when there are three or more treatments, a variance-balanced design is the ideal choice, whereas Cochran's statistics may be chosen for dichotomous response variables.

Therefore, when considering the comparison of therapeutic interventions or different rehabilitation techniques in patients with CTS or other peripheral nerve pathologies, the choice of the most appropriate study design and statistical analysis will provide more reliable evidence.

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15. ANEXO A – QUESTIONÁRIO DO TÚNEL DO CARPO

Nome do paciente:	ID:
Data: ____/____/____	

QUESTIONÁRIO DE BOSTON

AS QUESTÕES A SEGUIR REFEREM - SE AOS SEUS SINTOMAS, NUM PERÍODO TÍPICO DE 24 HORAS, DURANTE AS ÚLTIMAS DUAS SEMANAS.
(Assinale uma resposta para cada pergunta)

- 1) Qual a intensidade da dor na mão ou punho que você tem à noite?
 - 1- Eu não tenho dor na mão ou no punho à noite.
 - 2- Pouca dor
 - 3- Dor moderada
 - 4- Dor intensa
 - 5- Dor muito intensa
- 2) Quantas vezes a dor na mão ou punho acordou você durante uma noite típica nas duas últimas semanas?
 - 1- Nenhuma
 - 2- Uma
 - 3- Duas a três vezes
 - 4- Quatro a cinco vezes
 - 5- Mais que cinco vezes
- 3) Você usualmente tem dor na mão ou punho durante o dia?
 - 1- Eu nunca tenho dor durante o dia
 - 2- Eu tenho pouca dor durante o dia
 - 3- Eu tenho dor moderada durante o dia
 - 4- Eu tenho dor intensa durante o dia
 - 5- Eu tenho dor muito intensa durante o dia
- 4) Com que frequência você tem dor na mão ou punho durante o dia?
 - 1- Nunca
 - 2- Uma ou duas vezes por dia
 - 3- Três a cinco vezes por dia
 - 4- Mais que cinco vezes por dia
 - 5- A dor é constante
- 5) Quanto tempo, em média, duram os episódios de dor durante o dia?
 - 1- Eu nunca tenho dor durante o dia
 - 2- Menos que 10 minutos
 - 3- De 10 a 60 minutos
 - 4- Mais que 60 minutos
 - 5- A dor é constante durante o dia
- 6) Você tem adormecimento (perda da sensibilidade) em sua mão?
 - 1- Não
 - 2- Eu tenho pouco adormecimento
 - 3- Eu tenho adormecimento moderado
 - 4- Eu tenho adormecimento intenso
 - 5- Eu tenho adormecimento muito intenso
- 7) Você tem fraqueza na sua mão ou punho?
 - 1- Sem fraqueza
 - 2- Pouca fraqueza
 - 3- Fraqueza moderada
 - 4- Fraqueza intensa
 - 5- Fraqueza muito intensa

- 8) Você tem sensação de formigamento em sua mão?
 - 1- Sem formigamento
 - 2- Pouco formigamento
 - 3- Formigamento moderado
 - 4- Formigamento intenso
 - 5- Formigamento muito intenso

- 9) Qual a intensidade do adormecimento (perda da sensibilidade) ou do formigamento à noite?
 - 1- Eu não tenho adormecimento ou formigamento à noite
 - 2- Pouca
 - 3- Moderada
 - 4- Intensa
 - 5- Muito intensa

- 10) Com que frequência o adormecimento ou o formigamento acordaram você durante uma noite típica nas duas últimas semanas?
 - 1- Nenhuma
 - 2- Uma
 - 3- Duas a três vezes
 - 4- Quatro a cinco vezes
 - 5- Muito intensa

- 11) Você tem dificuldade em pegar e usar pequenos objetos, tais como chaves ou canetas?
 - 1- Sem dificuldade
 - 2- Pouca dificuldade
 - 3- Dificuldade moderada
 - 4- Dificuldade intensa
 - 5- Dificuldade muito intensa

UM DIA TÍPICO, DURANTE AS DUAS ÚLTIMAS SEMANAS, OS SINTOMAS DA SUA MÃO OU PUNHO TÊM CAUSADO A VOCÊ ALGUMA DIFICULDADE EM FAZER AS ATIVIDADES LISTADAS ABAIXO?

Por favor circule o número que melhor descreva sua habilidade para fazer atividade.

Atividade	Grau de Dificuldade				
	1	2	3	4	5
Escrever	1	2	3	4	5
Abotoar as roupas	1	2	3	4	5
Segurar um livro enquanto lê	1	2	3	4	5
Segurar o telefone	1	2	3	4	5
Trabalhos domésticos	1	2	3	4	5
Abrir tampa de um vidro	1	2	3	4	5
Carregar saco de supermercado	1	2	3	4	5
Tomar banho e vestir-se	1	2	3	4	5

Nenhuma dificuldade 1
 Pouca dificuldade 2
 Dificuldade moderada 3
 Dificuldade intensa 4
 Não pode realizar atividade de jeito nenhum, por causa dos sintomas das mãos e punhos 5

Opinião do observador:

16. ANEXO B - SF12 - QUESTIONÁRIO DE QUALIDADE DE VIDA

Nome do paciente:	ID:
Data: ____/____/____	

SF 12

1 - Em geral você diria que a sua saúde é: (circule uma)

EXCELELENTE	MUITO BOA	BOA	RUIM	MUITO RUIM
1	2	3	4	5

Os seguintes itens são sobre atividades que você poderia fazer atualmente durante um dia comum. Devido à sua saúde, você teria dificuldade para fazer essas atividades? Neste caso, quanto? (Circule um número para cada linha)

ATIVIDADES	SIM, DIFICULTA MUITO	SIM, DIFICULTA POUCO	NÃO DIFICULTA DE MODO ALGUM
2. Atividades moderadas, tais como mover uma mesa, passar aspirador de pó, jogar bola, varrer a casa.	1	2	3
3. Subir vários lances de escada	1	2	3

Durante as últimas quatro semanas, você teve algum dos seguintes problemas com seu trabalho ou com alguma atividade diária regular, como consequência de sua saúde física? (Circule uma em cada linha)

4. Realizou menos tarefas do que gostaria?	SIM	NÃO
5. Esteve limitado no seu tipo de trabalho ou em outras atividades?	SIM	NÃO

Durante as últimas quatro semanas, você teve algum dos seguintes problemas com seu trabalho ou com alguma atividade diária regular, como consequência de algum problema emocional (como sentir-se deprimido ou ansioso?) (Circule uma em cada linha)

6. Realizou menos tarefas do que gostaria?	SIM	NÃO
7. Não trabalhou ou não fez qualquer das atividades com tanto cuidado como geralmente faz?	SIM	NÃO

Nome do paciente:	ID:
Data: ___/___/___	

8. Durante as últimas quatro semanas, quanto a presença de dor interferiu com o seu trabalho normal (incluindo tanto o trabalho fora de casa e dentro de casa)? (circule uma)

DE MANEIRA ALGUMA	UM POUCO	MODERADAMENTE	BASTANTE	EXTREMAMENTE
1	2	3	4	5

Estas questões são sobre como você se sente e como tudo tem acontecido com você durante as últimas quatro semanas. Para cada questão, por favor, dê uma resposta que mais se aproxime da maneira como você se sente. Em relação as últimas quatro semanas (circule um número para cada linha)

	Todo Tempo	A maior parte do tempo	Uma boa parte do tempo	Alguma parte do tempo	Uma pequena parte do tempo	Nunca
9. Quanto tempo você tem se sentido calmo ou tranquilo?	1	2	3	4	5	6
10. Quanto tempo você tem se sentido com muita energia?	1	2	3	4	5	6
11. Quanto tempo você tem se sentido desanimado e abatido?	1	2	3	4	5	6

12. Durante as últimas quatro semanas, quanto do seu tempo, a sua saúde física ou problemas emocionais interferiram nas suas atividades sociais (como visitar amigos, parentes, etc.) (circule uma)

TUDO O TEMPO	A MAIOR PARTE DO TEMPO	ALGUMA PARTE DO TEMPO	UMA PEQUENA PARTE DO TEMPO	NENHUMA PARTE DO TEMPO
1	2	3	4	5

17. ANEXO C - ESCALA VISUAL ANALÓGICA (EVA) DA DOR



Figura 12: Escala EVA.

18. ANEXO D – COMITÊ DE ÉTICA



Ilmo. Sr.
Dr. Sergio Murilo Georgeto

Londrina, 22 de novembro de 2017.

CEP PB 09/17 – CAAE: 74741317.4.0000.0099
Ofício nº. 36/17 BIOISCAL

O Comitê de Bioética e Ética em Pesquisa da Irmandade Santa Casa de Londrina – BIOISCAL, de acordo com orientações da Resolução 466/12 do Conselho Nacional da Saúde/MS e Complementares, **APROVA** a realização do Projeto: **“Caracterização clínico-funcional e avaliação da eficácia do tratamento de pacientes portadores da síndrome do túnel do carpo”**.

E informamos que deverá ser comunicado, por escrito, qualquer modificação que ocorrer no desenvolvimento da pesquisa, e segundo a resolução citada, *no art. XI item d*, deve ser encaminhado a este Comitê, **relatório parcial semestral e final da pesquisa**.

Desejamos sucesso e êxito na realização do mesmo que contribuirá no aprimoramento da assistência à saúde.

Atenciosamente,

Karen Barros Parron Fernandes

Karen Barros Parron Fernandes
Coordenadora do BIOISCAL.

