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Terapia Manual na Síndrome do Túnel do Carpo: uma Revisão Sistemática

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Terapia Manual na Síndrome do Túnel do Carpo: uma Revisão Sistemática

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RESUMO

Terapia Manual na Síndrome do Túnel do Carpo: uma Revisão Sistemática

A síndrome do túnel do carpo (STC) é uma neuropatia periférica, causada pela compressão e tensão do nervo mediano ao nível do carpo. Os sintomas são de dor, parestesia, hipoestesia, formigamentos dos três primeiros dedos e atrofia da eminência tenar. Essa condição pode afetar atividades de vida diária e qualidade de vida. Os pacientes classificados com STC leve a moderada tem indicação ao tratamento conservador. Dentre as opções de tratamento conservador aplicadas a STC atualmente são órteses, medicações anti-inflamatórias, injeções de corticoesteróides, termoterapia, eletroterapia, exercícios e as terapias manuais.

Esta revisão sistemática tem como objetivo demonstrar os efeitos da terapia manual nos sintomas de dor, sensibilidade, força de preenção e pinça nos pacientes com síndrome do túnel do carpo idiopática de leve a moderada, quando comparados com placebos ou outras intervenções.

Essa revisão sistemática foi planejada e conduzida conforme as normas do PRISMA. As buscas foram feitas em três base de dados (MEDLINE, EMBASE e PeDRO) finalizadas em abril de 2017. Os critérios de inclusão e exclusão desta revisão sistemática foi ensaios clínicos randomizados que aplicaram terapia manual em pacientes com STC idiopática de leve a moderado grau, sem presença de doença sistêmica. A qualidade dos estudos foi avaliada através do instrumento de controle de viés da Cochrane.

Doze estudos foram incluídos na revisão sistemática, dez dos doze ensaios clínicos randomizados incluídos na revisão avaliaram dor, destes todos estudos relataram melhora significativa da dor após intervenção com terapia manual. A força de preensão palmar teve melhora significativa após as intervenções de massagem, mobilização carpal e mobilização de tecidos moles. Dois estudos avaliaram a sensibilidade, a mobilização neurodinâmica associada a massagem obteve melhora superior a mobilização neurodinâmica sozinha.

Os resultados apresentados na revisão sistemática permitem concluir que o uso de terapias manuais podem ser a abordagem para alívio da dor nos casos de síndrome do túnel do carpo idiopática de leve e moderado graus quando comparados a órtese, termoterapia, eletroterapia e cirurgia.

Revisão sistemática foi registrada no PROSPERO sob número CDR 42016053281.

Palavras-chave: síndrome do túnel carpal; nervo mediano; manipulações musculoesqueléticas; reabilitação.

ABSTRACT

Manual Therapy for the carpal tunnel syndrome: a systematic review
Carpal tunnel syndrome (CTS), caused by compression of the median nerve at the wrist, is the most common peripheral neuropathy. Symptoms of CTS include pain, paresthesia, hypoesthesia, tingling involving the first three fingers and atrophy of the thenar eminence. This condition affects daily activities and quality-of-life. Patients with mild to moderate CTS symptoms are usually treated conservatively. The current conservative interventions prescribed for CTS consists of wrist splinting, activities modification, nonsteroidal anti-inflammatory drugs, thermotherapy, electrotherapy, exercises and manual therapies. The purpose of this review was to assess pain, sensibility, grip and pinch strength on patients with mild and moderate idiopathic carpal tunnel syndrome (CTS) treated with manual therapy when compared with termo, electro modalities, splint and surgery.
This systematic review was planned and conducted by the PRISMA statement, three electronic databases (MEDLINE, EMBASE and PeDRO) were searched, completed in april 2017 and identified 12 randomized controlled trials that met the inclusion/exclusion criteria, wich were: manual therapy treatment for individuals diagnosed with idiopathic CTS, absence of systemic diseases and no previous surgery. Appreciation of the quality of studies was done by Cochrane risk of bias tool. Twelve randomized controlled trials met the inclusion criteria for this review. Ten of twelve studies included rated pain and those studies showed significant betterment of pain after manual therapy. Grip strength had significant improvement after massage, carpal mobilization and soft tissue mobilization. Two trials evaluated sensitivity, the neurodinamic mobilization associed with massage was superior to single neurodinamic mobilization. This systematic review suggest that manual therapies might be the approach to reduce pain in mild and moderate idiopathic carpal tunnel syndrome when compared with termoand electro modalities, splint and surgery .
This review was registrated on Prospero CDR 42016053281.

Key-words: carpal tunnel syndrome; median nerve; nerve injuries; manual Therapy; rehabilitation.

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LISTA DE ABREVIATURAS E SIGLAS

AAOS - *American Academy of Orthopedic Surgeons*

AAHT - *American Association of Hand Therapists*

DASH - *Disability of arm shoulder and hand Questionnaire*

ENMG - Eletroneuromiografia

STC - Síndrome do túnel do carpo

MEDLINE- *Medical Literature Analysis and Retrieval System Online*

PRISMA - *Preferred Reporting Items for Systematic Reviews and Meta-Analysis*

PROSPERO – *International Prospective register of systematic reviews*

RCT – *Randomized controlled trials*

SUMÁRIO

1 INTRODUÇÃO

A síndrome do túnel do carpo (STC) é uma condição clínica de dor na mão causada por uma variedade de condições que culminam com o aumento da pressão sobre o nervo mediano ao nível do túnel carpal, que é formado pelos ossos do carpo dorsal e pelo ligamento retinacular volar (CARNEIRO, 1999). As primeiras descrições da patologia remontam ao início do século passado, evidenciando um problema de origem neural ao nível do carpo (MARIE; FOIX, 1913).

Trata-se de uma condição com maior prevalência na população feminina em relação a população masculina. Em um estudo realizado em 3 hospitais de Porto Alegre (RS-Brasil) 2555 voluntários foram avaliados na qual 31% teve o diagnóstico de STC, a relação dos casos foi de 7.4:1, mulheres:homens. (BECKER *et al*., 2002). No Reino Unido, Bland *et al.* (2003) encontraram uma incidência anual de 139 casos para cada 100.000 mulheres e 67 novos casos para cada 100.000 homens, uma taxa de novos casos 2:1 (relação mulher:homem), o que demonstra também a maior ocorrência do problema em indivíduos do sexo feminino. Uma explicação para essa maior incidência foi sugerida por Becker *et al.* (2002) que mostrou a obesidade e a idade entre 41 e 60 anos são fatores de riscos para STC na análise estratificada para o sexo feminino.

A STC possui a mais alta prevalência dentre todas as formas de compressão neuropática. De acordo com a *American Academy of Neurology* (2012), diferentes níveis compressivos sobre o nervo mediano ao nível do carpo podem afetar aproximadamente até 10% da população adulta. O pico de incidência da doença é no final dos 50 anos e a população idosa apresenta o chamado “síndrome do túnel do carpo senil” que acarreta na diminuição do diâmetro do túnel que o nervo mediano atravessa (CARNEIRO, 1999).

Além de sua alta prevalência a STC também impacta significativamente a vida diária das pessoas acometidas por essa síndrome. Tanaka *et al.* (1994) relata que os pacientes com esse diagnóstico sofreram em média 12 semanas consecutivas com desconforto na mão. Dentre os indivíduos desta população 73% relataram problemas de sono, 21% faltas ao trabalho, 18% mudanças nas

tarefas do trabalho e 17% mudança de emprego. Relatou a prevalência de STC auto estimada de 1.55% (2,65 milhões) revelada por questionário auto preenchido e diagnosticada por um médico clínico de 0.43%. Estes dados demonstram o quão incapacitante essa patologia pode ser, causando além da incapacidade, perda de produtividade e aumento dos custos no mercado de trabalho. Atroshi *et al.* (1999) mostraram uma prevalência entre 2.7-14.4%, a STC afeta pessoas em idade produtiva e que realizavam força excessiva ou força com tensão do punho em flexão ou extensão. Esses dados reforçam o papel da ocupação na prevalência do STC.

A incidência de acometimento conforme atividade laboral recai sobre indivíduos expostos a atividades manuais prolongada com punho em flexão ou extensão, uso repetitivo dos tendões flexores e exposição a vibração (LECLERC *et al.* 1998; ROQUELAURE *et al*. 2001; MAHTO; OMAR, 2015) condições como aumento do índice de massa corporal (ATROSHI *et al.*, 1999, BLAND, 2005) e a combinação de estresse físico e mental (VOGELSANG *et al*., 1994). A combinação de mudanças isquêmicas e pressão mecânica, com o passar do tempo, geram mudanças na bainha de mielina e ocasionalmente resulta em lesão do axônio que pode ser detectado com estudo eletrofisiológico da velocidade de condução nervosa, motora e sensitiva (WERNER; ANDARY, 2002).

Em razão da complexidade e elevados níveis de prevalência e incidência, esta condição do membro superior pode ser tratada conservadoramente ou cirurgicamente. Nos casos da graduação da ENMG (eletroneuromiografia) ser de leve a moderada intensidade a indicação dos tratamentos conservadores devem estar sempre à frente da indicação cirúrgica (PRATELLI *et al.*, 2015) e podem reduzir o número de pacientes que necessitem de intervenção cirúrgica (GOODYER-SMITH; ARROL, 2004). O *guideline* da *American Academy of Orthopedic Surgeons* (AAOS) para STC recomenda tanto cirurgia quanto tratamento conservador. Aconselha que o tratamento inicial deve ser conservador e na ausência de denervação do nervo mediano. Cirurgia pode ser considerada nos casos severos onde há denervação ou se é preferência do paciente. A cirurgia pode ser via aberta ou endoscópica (minimamente invasiva), realiza-se uma secção do retináculo dos flexores (retinaculotomia), retirando a pressão sobre o túnel carpal (CHAMMAS *et al.*, 2014).

A cirurgia de liberação do túnel do carpo geralmente resulta em completo alívio dos sintomas, porém o tratamento cirúrgico apresenta uma falha de 1-25% no que diz respeito a complicações ou eventos adversos e com uma taxa de reintervenção de 12% (NEUHAUS *et al.*, 2012), devendo-se também considerar o custo-efetividade deste tratamento frente ao tratamento conservador (MOHER et al., 2009).

Ainda não existe um tratamento aceito universalmente para síndrome do túnel do carpo e as revisões existentes sobre os tratamentos conservadores ainda são pouco conclusivas (DUYMAZ, 2012). Quando o paciente busca o alívio dos sintomas e uma melhora funcional há uma extensa gama de tratamentos conservadores que podem ser utilizados, tais como medicações, infiltrações, eletroterapia, termoterapia, exercícios, terapia manual e órteses. Exercícios ativos são indicados para a STC e incluem deslizamento tendinoso e neural (ROZMARYM *et al*., 1998). As órteses amplamente avaliadas quanto ao seu uso diurno e ou noturno são indicadas por prevenir a elevação da pressão dentro do canal do carpo (WALKER *et al*., 2000).

A terapia manual é definida como uma abordagem clínica que inclui diagnóstico fisioterapêutico e tratamento direcionado às articulações e tecidos moles. O objetivo da terapia manual inclui diminuição de dor, aumento de movimento articular em quantidade e qualidade, promover estabilidade, promover tensão e mobilidade no nervo e melhorar função. Fisioterapeutas aplicam a terapia manual para atingir vários tecidos incluindo nervos, músculos, ossos e fáscia (SMITH Jr., 2007). As terapias manuais mais utilizadas são mobilização articular, mobilização de tecidos moles e massagem (MITKEN *et al*., 2008).

Dentro das opções citadas acima, os recursos manuais são uma das opções terapêuticas com baixo custo e não invasivo (GÜNAY; ALP, 2015). No entanto não se sabe ainda quais seriam os reais benefícios das intervenções baseadas em terapia manual no tratamento de indivíduos acometidos pela STC no que diz respeito ao alívio das dores.

Alguns estudos têm mostrado que as manobras de neuromobilizações, uma forma de terapia manual, são auxiliares na restauração do movimento longitudinal do nervo afetado pela STC (KOSTOPOULOS, 2004). Estudos que comparam terapia manual com recursos eletrofísicos como Pratelli *et al*. (2014)

e Wolny[1] *et al*. (2017), apresentaram superioridade nos grupos de intervenção com terapia manual sobre os recursos de Laser de baixa intensidade e ultrassom.

Ensaios clínicos randomizados de tratamento conservador versus o cirúrgico (FERNANDEZ-DE-LAS-PEÑAS, 2015 e 2017) constataram que até o terceiro mês após acompanhamento, as melhoras clínicas com o tratamento conservador mostraram-se significativamente superior a cirurgia.

Estudos recentes têm mostrado que o uso de tratamentos conservadores para tratar a Síndrome do Túnel do Carpo afeta positivamente uma parcela importante da população estudada quando essa é comparada com os efeitos gerados pelo tratamento cirúrgico (SHI; MacDERMID, 2011).

Apesar da existência de várias revisões sistemáticas sobre os tratamentos para a STC Ellis *et al* (2008), Page *et al*. (2012), Ballestero-Péres (2016), Jiménez del Barrio *et al*. (2016), ainda assim não encontramos uma revisão que respondesse quais os benefícios do uso das terapias manuais sobre os outros tratamentos como eletroterapia, termoterapia, órtese, placebo e cirurgia. Uma revisão sistemática sobre esse assunto pode indicar qual a melhor diretriz a ser seguida para o uso combinado ou não dessas terapias manuais quanto aos sintomas de dor, sensibilidade, força de preensão e da pinça polpa a polpa.

(1) Red Laser emitido a 658nm de luz a 50 W, a duração da bioestimulação foi de 1 minuto e 40 segundos para dose de 5J e após um Laser infravermelho emitindo 658nm de luz a 400mW com a duração de 1 minuto e dose de 24J.
Ultrassom na frequência de 1MHz, intensidade de 1.0W/cm e pulsado a 75% por 15 minutos.

2 REVISÃO DE LITERATURA

2.1 SÍNDROME DO TÚNEL DO CARPO

O túnel do carpo é um compartimento anatômico no punho que inclui no seu interior o nervo mediano e os nove tendões flexores (quatro tendões flexores superficiais dos dedos, quatro tendões flexores profundos dos dedos e o tendão flexor longo do polegar) delimitado pelos ossos do carpo escafoide, trapézio e hamato e pelo ligamento transverso do carpo que juntos formam um arco (McCARTAN *et al.* 2012).

A síndrome do túnel do carpo (STC) é neuropatia causada pela compressão e tração do nervo mediano ao nível do túnel do carpo (ALFONSO *et al.* 2010). A STC é classificada como neuropatia periférica compressiva do membro superior, dentre as compressões, a mais comum. O nervo mediano é composto na sua estrutura de ramos sensitivos e motores. Os sintomas podem estar relacionados a seu ramo sensitivo e ou motor, eles são de dor, parestesia, formigamento e fraqueza muscular distal ao punho principalmente nos três primeiros dedos. Szabo *et al* (1999) achou correlação da STC com dor noturna. Pagnanelli e Barrer (1991) reportaram que a parestesia noturna estava presente em 91.5% das mãos de pacientes com STC idiopática, sem causa definida, e era o sintoma mais confiável para realizar o diagnóstico. O aumento da pressão no canal do carpo durante a noite pode ser o resultado de vários fatores que incluem: redistribuição dos fluidos no membro superior na posição supina, falta do mecanismo de contração muscular que contribui para drenagem dos líquidos intersticiais, tendência de posicionar o punho em flexão, aumento da pressão sanguínea na segunda metade da noite e baixa nos níveis de cortisol (CHAMMAS, 2014).

Há inúmeras causas para STC aguda e entre elas estão a traumática, hematológica, reumatológica, anatômica, homeostática e infecciosa (TOSTI; ILYAS, 2012) (Quadro 1). No entanto todas seguem uma mesma sequência de eventos como ocupação de mais espaço dentro do túnel e este acaba por aumentar a pressão intracanal (SZABO, 1998). A STC idiopática também acontece devido à incompatibilidade entre o tamanho do nervo mediano e o conteúdo do túnel do carpo na qual leva a um aumento da pressão no túnel e desequilíbrio do fluxo sanguíneo do nervo mediano (GELBERMAN *et al.*, 1998).

Além das causas acima, fatores de risco como idade, sexo, genético e fatores antropométricos do túnel podem implicar no desenvolvimento da STC (BECKER, *et al.* 2002, CHAMMAS *et al.* 2014).

Tabela 1 – Causas da STC aguda

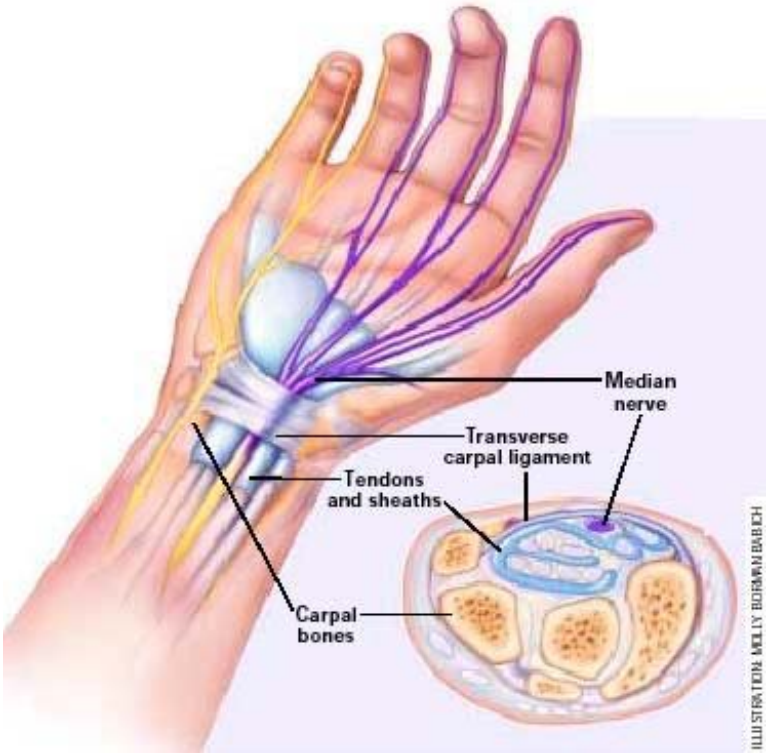
TRAUMA	INFECÇÃO	INFLAMAÇÃO
Fratura do rádio distal	Tenossinovite Infecciosa	Overuso (sinovite flexora)
Fratura Metacarpos	Artrite Séptica	Pseudogota
Fratura Carpal	Celulite	Gota
Deslocamento do Escafóide	Infecção Filarial	Tendinite Calcárea
Deslocamento do Semilunar	Osteomielite Metacarpal	Deposição de Alendronato
Deslocamento do	Parvovirose	Deposição de Hidroxiapatita
Injeção em alta-pressão	Síndrome do choque tóxico	Artrite Reumatóide
Laceração	Sepse do canal intracarpal	**ANATOMIA**
Mordida de animal	Hanseníase	Malformação Venosa
TUMOR	**MUDANÇAS DE FLUIDOS**	Lumbricais Anômalos
Tumor de células gigantes	Gravidez	Trombose artéria mediana
Hemangioma	Queimaduras	Aneurisma artéria mediana
Mixofibrosarcoma	Toxina de stonefish	Ruptura da artéria mediana
IATROGÊNICO	Veneno de cobra	**COAGULOPATIA**
Hematoma Cirúrgico	Transplante de Pâncreas	Doença de Von Willebrand
Hiperflexão após fixação externa		Hemofilia
Fluido tumescente		Varfarina

Fonte: Tosti e Ilayas, 2012

2.2 PATOFISIOLOGIA

O aprisionamento do nervo periférico ocorre como resultado da diminuição de seu compartimento anatômico. Este torna-se estenosado causando disfunção e lesão neste ponto de passagem do nervo (MILLESI *et al.*, 1990). A neuropatia compressiva é um fenômeno combinado de compressão e tração. A compressão do nervo e tração pode causar disfunção na microcirculação intraneural, lesão na bainha de mielina do axônio assim como alterações nos tecidos conectivos de suporte, formação de edema e em última análise isquemia e lesão nervosa (ABOONQ, 2015). Anatomicamente o túnel pode sofrer compressão em dois pontos: na borda proximal do túnel carpiano causada pela flexão do punho e devido as chances de engrossamento e rigidez entre a fáscia antebraquial e o retináculo dos flexores e o outro ponto é no gancho do hamato em sua porção mais estreita (Figura 1) (WERNER; ANDARY, 2002).

Figura 1: Desenho do Túnel do Carpo



O movimento do punho tem estreita relação de pressão sobre o túnel, BAUMAN *et al.* (1981) demonstraram que quando estamos com o punho em posição neutra a pressão média é de 32mmHg, quando o punho está em flexão a pressão alcança 94mmHg e em extensão 110mmHg, comprovando que em algumas ocupações e ou tarefas os sujeitos estão mais expostos ao risco de desenvolver a síndrome do túnel do carpo.

Somado a pressão, Nakamishi (1995) mostrou que os punhos dos pacientes com STC tinham significativamente menos deslizamento (0.37±0.34 mm; *P*=0.0001), o que indica que fisiologicamente o movimento do nervo fica restrito. A diminuição da mobilidade do nervo deve fundamentar a patofisiologia da síndrome.

Movimentos ou posições que expõe tecidos neurais a estímulos de compressão, fricção, tensão ou vibração podem provocar sintoma de dor neuropática, esse fenômeno pode ser descrito como hiperalgesia/alodínia. A dor neuropática periférica é termo usado para descrever situações onde raízes de nervos periféricos sofreram lesão por estímulos mecânicos e ou químicos que excedem a capacidade física do sistema nervoso (NEE; BUTLER, 2006).

2.3 DIAGNÓSTICO

O diagnóstico da STC não possui padronização e não há concordância do padrão-ouro (MacDERMID; DOHERTY, 2004), ele consiste de exame físico e de teste eletroneuromiográfico para sua confirmação (WERNER; ANDARY, 2002).

Para o exame físico realizam-se testes provocativos dos sintomas, como os testes de Tinel, Phalen e Durkan. Observa-se diminuição de sensibilidade e a presença de atrofia nos músculos inervados pelo nervo mediano. Phalen descreve que a atrofia da eminência tenar é quase sempre precedida de hipoestesia na distribuição do nervo mediano por muitos meses ou anos. A atrofia que ocorre nos músculos oponente do polegar, abdutor curto do polegar e no flexor curto do polegar pode ser observada em diferentes intensidades. Phalen (1966) avaliou 439 pacientes com STC, e, destes, 41% apresentavam atrofia da eminência tenar. Essa atrofia está associada à fraqueza do segmento acometido (SZABO *et al.* 1999).

No exame físico o teste Phalen consiste em manter os punhos em flexão por aproximadamente 1 minuto. Nesta posição o nervo mediano é comprimido entre a borda proximal do ligamento transverso do carpo e os tendões flexores. Essa manobra causa aumento da pressão dentro do túnel do carpo e consequentemente o nervo mediano responde rapidamente com bloqueio da condução e reprodução dos sintomas (WERNER; ANDARY, 2002). Manter essa posição durante longos períodos causa amortecimento e parestesia ao longo da distribuição do nervo mediano mesmo em mãos normais. A sensibilidade de 68% para este teste foi atingida em 3000 casos, isso demonstra uma forte evidência de que pode ser usado no diagnóstico da STC, o que não impede de gerar resultados falsos-negativos (MacDERMID; DOHERTY, 2004).

O sinal de Tinel é uma leve percussão sobre o nervo mediano, que está localizado logo medialmente ao tendão flexor radial do carpo na parte mais proximal da palma da mão. O resultado do teste é positivo quando o paciente reporta dor, choque ou formigamento nos três primeiros dedos (PHALEN, 1966).

O teste de Durkan provova uma pressão direta sobre o túnel do carpo, o examinador realiza pressão sobre o retináculo flexor com ambos polegares, este teste mostrou-se mais sensível e específico que o teste de Phalen e Tinel (DURKAN, 1991).

A eletroneuromiografia (ENMG) permite estudar a condução nervosa sensitiva e motora do nervo mediano. Este exame pode ser complementado testando a amplitude e a duração das respostas do nervo e deve ser comparada ao membro contralateral. O exame utiliza uma classificação quanto a gravidade da compressão que está diretamente relacionada com a passagem do nervo pelo túnel do carpo (CHAMMAS *et al*., 2014). Essa graduação pode variar de mínima, moderada e grave. O achado é latência terminal prolongada do nervo sensório-motor nas mãos com STC, que é influenciada pela desmielinização e degeneração (MACKINNON, 1985) que resulta no bloqueio e diminuição da condução nervosa. A maioria dos ensaios clínicos randomizados realizam este teste para confirmação do diagnóstico e inclusão de pacientes com STC na população a ser estudada, os valores de corte (Tabela 2) possuem algumas diferenças conforme referências usadas pelos autores.

Tabela 2 - Valores de referência para diagnóstico e inclusão de pacientes com STC

ESTUDO	LATÊNCIA MOTORA DISTAL
BURKE, 2007	>4.20m/s
OSKOUEI, 2014	>4.40m/s
FERNANDEZ-DE-LAS PEÑAS, 2015, 2017	>4.00m/s
WOLNY, 2016, 2017	4.20m/s

Além dos testes acima, os pacientes são também avaliados com relação à dor, hipoestesia e fraqueza.

A dor é avaliada na maioria dos estudos através da escala visual analógica (EVA) (BURKE *et al*. 2004, OSKOUEI *et al.* 2014, TAL-AKABI; RUSHTON 2000, GÜNAY; ALP 2015), onde o paciente relata sua dor numa escala de zero (sem dor) a dez (pior dor possível). Pratelli *et al.* (2014) encontrou nos pacientes avaliados com STC dor em 82% na mão dominante.

Os monofilamentos de *Semmes-Weinstein* são utilizados para verificar a presença ou não da hipoestesia (LEHMAN *et al*, 1996). O paciente é examinado no polegar, dedo indicador e médio, com os olhos fechados, é solicitado a relatar verbalmente o momento que sentir o monofilamento. Este em contato com a pele realiza uma pressão e conforme espessura do monofilamento percebe diferenças de pressão. Pessoas com a sensibilidade normal percebem monofilamentos de 0.05 a 0.2g de resistência. Um paciente afetado severamente conseguirá sentir filamentos de 2g ou mais (MacDERMID, 2004). No estudo de Wolny *et al.* (2016) foi utilizado os discos de discriminação de dois pontos (disco de Dellon) para detectar a qualidade da sensibilidade tátil. Cada disco tem séries de pinos de metal separados a distâncias diferentes que variam de 1 a 15mm. Ele é posicionado perpendicularmente na pele exercendo pressão suficiente a causar estimulação, mas não dor. A determinação foi considerada completa quando duas respostas idênticas ocorriam em três testes consecutivos. Normalmente as pessoas conseguem distinguir 2 pontos com 0.4mm de afastamento, quando passa a 0.6mm representa déficit sensório leve e 0.8mm déficit moderado (DELLON, 1978).

Já a fraqueza apresentada pelos pacientes com STC é resultante da atrofia da eminência tenar e pode ser mensurada através do dinamômetro de preensão ou pelo dinamômetro de pinça. A mensuração da preensão palmar consiste na quantificação da capacidade de produção de força (SZABO *et al*., 2000). Segundo AAHT (*American Association of Hand Therapists)* o teste deve ser feito em posição padronizada com o ombro aduzido, cotovelo em 90° de flexão e punho neutro. A média de três medidas consecutivas deve ser considerada (BOHANNON *et al*, 2006). Considerando a musculatura tenar mais envolvida na patologia da STC, a medida de força de pinça simples é a mais sensível entre as duas opções (GEERE *et al,*2007).

Recentemente as escalas funcionais têm sido mais aplicadas para indicar diferenças mínimas com importância clínica (KIM; LEON, 2013). As escalas *Funcional Status Scale* e *Symptom Severity Scale* juntas formam o *Boston Carpal Tunnel questionare.* Este questionário possui dois domínios: status funcional e severidade dos sintomas. Os itens desta escala vão de 1 a 5 pontos, onde 1 corresponde a sem queixas e 5 a queixa severa, onde a soma que resulta em altos índices indicam pior função auto-relatada e alta severidade dos

sintomas (DE CARVALHO LEITE *et al.,* 2006). Conforme revisão sistemática De Carvalho Leite *et al.* (2006) sobre o questionário *Boston Carpal Tunnel Questionare*, este deve ser indicado para uso em futuros ensaios clínicos de STC devido sua validade, confiabilidade e responsividade (CAMPOS *et al*.,2003) Outro instrumento auto-relatado é o DASH *Disability of the Arm, Shoulder and Hand Questionnaire* contem 30 questões, dois itens são relativos a função física, seis itens a sintomas e 3 itens função social, além destes tem 2 módulos opcionais com 4 itens dirigido para desempenho esportivo e artes ou trabalho (ORFALE *et al.,* 2005). O DASH é usado na avaliação de desordens do membro superior e possui responsividade semelhante ao *Boston Carpal Tunnel questionare* (GREENSLADE *et al.*, 2004).

2.4 TRATAMENTO

Muitas opções de tratamento, conservadores ou não, estão disponíveis para os pacientes que sofrem da STC. Os tipos de tratamento não-cirúrgicos são variados. A fisioterapia dispõe de recursos que são amplamente utilizados na redução e solução dos sintomas.

Dentre as possibilidades de tratamento conservador podemos constatar o uso indicação de medicação anti-inflamatória (HUI *et al*., 2001) e aplicação de infiltração de corticoesteróides (Peters-Veluthamaningal *et al.,* 2010), que podem ou não estar associado ao tratamento fisioterapêutico.

Os recursos e métodos fisioterapêuticos mais estudados para tratamento da STC são o ultra-som (BAYSAL *et al.*, 2006), laser de baixa intensidade (FUSAKUL *et al.*, 2014), parafina (HORNG, 2011), TENS (*transcutaneos electrical nerve stimulation),* órtese de punho à noite e durante atividades repetitivas (MULLER *et al.*, 2004, BRININGER *et al.*, 2007) acupuntura (SIM, 2011), yoga (GARFINKEL, 1998), massagens (FIELD *et al.*, 2004, MORASKA, 2008), deslizamentos tendinosos e neurais (KIM, 2015), manipulação fascial (PRATELLI *et al.*, 2015), mobilização carpal (GÜNAY; ALP, 2015), mobilização neurodinâmica (TAL-AKABI; RUSHTON, 2000, BIALOSKY *et al.*, 2009, OSKOUEI *et al.*, 2014, FERNANDEZ-DE-LAS-PEÑAS *et al.*, 2016 e 2017, WOLNY *et al.*, 2016 e 2017).

Conforme Zanette, (2010) a STC não deve ser vista somente como uma neuropatia periférica, ela representa uma complexa síndrome dolorosa que provoca sensibilização do sistema nervoso central (SNC). A terapia manual tem o pressuposto de modular os mecanismos de sensibilização integrando a fisiologia da dor a procedimentos sensibilizantes terapêuticos. Na profissão de fisioterapeuta, a terapia manual é uma abordagem clínica que inclui diagnóstico e tratamento direto a estruturas articulares e tecidos moles (WOLNY *et al*., 2017). Dentre os recursos manuais que implicam na direta mobilização do terapeuta podemos citar as técnicas abaixo.

2.4.1 Mobilização Neurodinâmica

As técnicas da mobilização neurodinâmica são formas de terapias manuais na qual as forças são direcionadas às estruturas neurais através de posicionamentos e movimentos de múltiplas articulações. Muitos casos de STC podem apresentar mobilidade limitada do nervo mediano (HOUGH, 2007). As mobilizações neurodinâmicas podem beneficiar os pacientes com STC devido ao mecanismo biomecânico como a restauração da mobilidade do nervo mediano e do edema. As mudanças neuroplásticas nos neurônios do SNC em resposta a estímulos é sugestivo de adaptação. As mobilizações neurodinâmicas estão associadas às mudanças neuroplásticas associadas a dor devido a mecanismos neurofisiológicos.

No estudo de Bialosky *et al.*, 2009 foi aplicada a técnica de mobilização neurodinâmica na qual é executada com o paciente em decúbito dorsal com 25° de flexão contralateral da cervical, depressão do ombro e abdução de 90°, rotação externa do ombro em 90° e 45°de extensão do cotovelo, antebraço supinado e movimentos do punho em flexão e extensão conforme amplitude de movimento disponível. Cada execução foi realizada pelo fisioterapeuta no período de 6 segundos levando o punho e dedos em flexão e extensão do punho e dedos. Os participantes receberam 5 séries de 10 ciclos nas 3 primeiras sessões e 7 séries de 10 ciclos nas sessões de 4 a 6. O posicionamento do paciente na intervenção de Fernandez-de-Las-Peñas *et al.* (2017a) foi o mesmo, porém além dos movimentos de punho e dedos em flexão e extensão o cotovelo também foi mobilizado em sincronia com os movimentos do punho. Enquanto o

cotovelo era mobilizado em flexão, o punho ficava em extensão alternando com o cotovelo em extensão e o punho em flexão. A velocidade e as amplitudes de movimento eram ajustadas para evitar dor durante a intervenção. Foram realizadas 3 sessões onde cada uma teve duas séries de 5 minutos cada, com intervalo de 1 minuto entre elas. Importante salientar que esta técnica de mobilização neurodinâmica aplicada pelo fisioterapeuta ao paciente é diferente dos deslizamentos tendinosos e neurais propostos por Toten e Hunter (1991) que são exercícios realizados pelo próprio paciente. Wolny *et al.* (2017) relata que é difícil comparar a eficácia de um auto-tratamento com técnica neurodinâmica. A técnica neurodinâmica é aplicada pelo fisioterapeuta, na prática são duas técnicas diferentes e devem se diferenciar no impacto causado no organismo e assim sendo nos seus efeitos terapêuticos.

2.4.2 Mobilização Carpal

O método utilizado para mobilização carpal no estudo de Tal-Akabi e Rushton (2000) foi *Maitland,* com técnicas antero-posterior e ou posterior-anterior e alongamento do retináculo dos flexores. Günay e Alp (2015) aplicaram em seu estudo deslizamentos dorsal-palmar da articulação radiocárpica e distração da mediocárpica. O Paciente apoia seu antebraço na mesa e a mão afastada da superfície, o fisioterapeuta segura o punho proximal ao estilóide ulnar para estabilizar a articulação rádio-ulnar. A mobilização envolve puxar e mover a fileira de ossos do carpo dorsal para ganho de extensão de punho e palmar para ganho de flexão de punho. A distração médio-cárpica é executada com uma mão estabilizando a rádio-ulnar distal do paciente e a outra mão sobre a fileira distal do carpo. Butler *et al*. (1991) tem a hipótese de que após mobilização carpal ocorre alteração da pressão ou até mesmo normalização da pressão na região de compressão, normalizando o suprimento sanguíneo e melhorando o sistema de transporte axonal, aumentando a condução nervosa.

2.4.3 Mobilização Fascial

A mobilização da fáscia é uma terapia manual que tem foco na fáscia muscular profunda. Essa técnica considera que a fáscia é um *continuum*

tridimensional. A fáscia é formada por fibras de colágeno onduladas e fibras de elastina organizadas em camadas distintas e alinhadas em diferentes direções. A fáscia muscular é dividida em 14 segmentos: cabeça, pescoço, tórax, lombar, pelve, escápula, ombro, cotovelo, antebraço, mão, quadril, joelho, tornozelo e pé. Cada segmento possui seis unidades miofasciais, estas consistem em fibras musculares monoarticulares ou biarticulares ao redor da fáscia profunda. Cada uma das seis unidades miofasciais de cada segmento possui localização específica na fáscia profunda chamadas de centros de coordenação. Cada centro de coordenação é localizado no ponto de convergência de forças vetoriais dos músculos envolvidas em determinado movimento.

Pratelli *et al.* (2014), aplicaram a técnica de manipulação fascial durante 45 minutos, uma vez na semana durante 3 semanas. A técnica consistia em realizar fricção profunda sobre pontos específicos, selecionados pelo exame clínico. O fisioterapeuta usou o cotovelo e os metacarpos para causar a fricção. Cada ponto com uma superfície de 2cm². A fricção era mantida por 3 minutos, como indica a técnica de Ercole *et al.* (2010). O número de pontos tratados em cada sessão foi de 4 a 8, eles eram escolhidos pelo fisioterapeuta baseado na densidade da fáscia pela palpação e nas respostas dos pacientes conforme guidelines da Fascial Manipulation®.

2.4.4 Massagem

No ensaio clínico de Field *et al.* (2004) a massagem foi aplicada da ponta dos dedos até o cotovelo por 15 minutos, uma vez por semana durante 1 mês com moderada pressão. A massagem iniciava do punho para o cotovelo e retornava em ambos os lados do antebraço, na sequência movimentos fez movimentos circulares e ao final a pele foi pinçada com o uso dos polegares e indicadores através da mão e ambos lados do antebraço.

Os possíveis mecanismos de diminuição de dor após aplicação da massagem é a liberação de neurotransmissores como a serotonina e ocitocina. Ambas obtiveram um aumento nos seus níveis tanto em síndromes como a fibromialgia como em experimentos em ratos (FIELD *et al.*, 2004). A melhora encontrada por Field *et al.* (2004) na força muscular após massagem pode estar relacionada simplesmente ao aumento da força de preensão pelo alívio da dor.

A mobilização de tecidos moles pode ser dirigida a possíveis pontos de compressão do nervo mediano como nos músculos escalenos, peitoral maior, bíceps, aponeurose bicipital, pronador redondo, flexores do punho, ligamento transverso do carpo, aponeurose palmar e músculos lumbricais (MORASKA, 2008).

2.4.5 Mobilização de Tecidos Moles

Esta técnica manual compreende a manipulação dos tecidos moles do antebraço, punho e mão. O fisioterapeuta com suas mãos rompe os tecidos cicatriciais e as restrições da fáscia. Durante esta mobilização o paciente apoia seu antebraço relaxado sobre a mesa e o clínico aplica pressões profundas com seus dedos e ambas mãos sobre o tecido cicatricial, musculatura tensa, tecido conectivo estirado e sobre as restrições miofasciais (BURKE *et al*, 2007).

3 OBJETIVOS

Em diversas situações clínicas faz-se a necessidade o uso de recursos não cirúrgicos, assim a presente proposta de estudo possui o objetivo de demonstrar os efeitos da terapia manual sobre o sintoma de dor, da sensibilidade e da força de preensão e pinça nos pacientes com síndrome do túnel do carpo idiopática de leve a moderada intensidade quando comparados com placebos ou outras intervenções.

Todos os estudos incluídos na revisão sistemática aplicaram terapia manual nos grupos intervenção. Alguns estudos utilizaram abordagem de técnica isolada e outros associada com outras intervenções, a seguir, o artigo que discute e revela os resultados desta revisão sistemática.

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5 ARTIGO

Manual Therapy for the of carpal tunnel syndrome: a systematic review

ABSTRACT

Background: Carpal tunnel syndrome (CTS), caused by compression of the median nerve at the wrist, is the most common peripheral neuropathy. Symptoms of CTS include pain, paresthesia, hypoaestesia, tingling involving the first three fingers and atrophy of the thenar eminence. This condition affects daily activities and quality-of-life. Patients with mild to moderate CTS symptoms are usually treated conservatively. The current conservative interventions prescribed for CTS consists of wrist splinting, activities modification, nonsteroidal anti-inflammatory drugs, thermotherapy, electrotherapy, exercises and manual therapies.

Objective: The purpose of this review was to assess pain, sensibility, grip and pinch strength on patients with mild and moderate idiopathic carpal tunnel syndrome (CTS) treated with manual therapy when compared with termo, electro modalities, splint and surgery.

Study design: systematic review of randomized controlled trials on CTS treatment. This review was registrated on Prospero CDR 42016053281

Method: this systematic review was planned and conducted by the PRISMA statement, three electronic databases (MEDLINE, EMBASE and PeDRO) were searched, completed in april 2017 and identified twelve randomized controlled trials that met the inclusion/exclusion criteria, which were: manual therapy treatment for individuals diagnosed with idiopathic CTS, absence of systemic diseases and no previous surgery. Appreciation of the quality of studies was done by Cochrane risk of bias tool.

Results: Twelve randomized controlled trials met the inclusion criteria for this review. Ten of twelve studies included rated pain and those studies showed significant betterment of pain after manual therapy. Grip strength had significant improvement after massage, carpal mobilization and soft tissue mobilization. Two trials evaluated sensitivity, the neurodinamic mobilization associed with massage was superior to single neurodinamic mobilization.

Conclusion: This systematic review showed that manual therapies might be the approach to reduce pain in mild and moderate idiopathic carpal tunnel syndrome when compared with termo and electro modalities, splint and surgery.

Key-words: carpal tunnel syndrome, median nerve, nerve injuries, manual therapy, rehabilitation.

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Introduction

Carpal tunnel syndrome (CTS) is the most common peripheral entrapment neuropathy.[1] It is characterized by pain that is caused by a variety of conditions which contribute to increase the pressure over the median nerve as it goes through the carpal tunnel, which is formed by the wrist bones dorsally and the retinacular ligament volarly.[2] The signs and symptoms present are pain, tingling, numbness and thenar atrophy, which may be enhanced at night. There has been many cause associated to CTS, but most cases are classified as idiopathic (no identifiable cause).[3]

CTS has the highest prevalence among the many forms of neuropathic compression. According to the American Academy of Neurology (2012)[4], different compression levels over the median nerve may affect up to 10% of the adult population. The highest incidence of the syndrome is found among the elderly, late fifties and above, and it is called of “senile carpal tunnel syndrome”.[2] The combination between ischemic changes and mechanic pressure along the time generate changes on the myelin sheath, which occasionally results in axon injury.[5]

The Prevalence rate of this syndrome is higher among women.[6] According to a Brazilian study which assed 2555 individuals, 31% was diagnosed with CTS, being the ratio of 7.4:1 (women:men).[7] Bland et al. (2003)[8] found an annual incidence of 139 new cases for each 100,000 women and 67 new cases for each 100,000 men, showing also a higher incidence among women (ratio women:men = 2:1). One explanation was proposed by Becker et al. (2002)[7] who suggested that obesity and being between 41 and 60 years old are risk factors for women develop CTS.

The high prevalence and incidence of CTS shows the need of an adequate treatment, being the options conservative and surgical. If the syndrome is classified as mild or moderate, the more conservative treatments should be indicated[9] as they may reduce the number of patients that will need a surgical intervention.[10]

There are a variety of techniques in physical therapy that offer some symptomatic relief like low level laser[11] and ultrasound[12]. Among those, the manual therapy is defined as a clinical approach that includes a physiotherapeutic diagnosis and treatment to the joint and soft tissues. The objective of the manual therapy is to diminish pain, improve the joint movement, promote stability and improve functionality.[13] The manual therapies mostly used for this pathology are joint mobilization, soft tissues mobilization and massage[14], vary from other types of nerve and tendon gliding proposed from Totten and Hunter (1991)[15].

According to what was described above, although there have been a variety of systematic reviews regarding the treatments for carpal tunnel syndrome[16,17] Page et al. (2012) Jiménez del Barrio et al. (2016), we could not find a study about the benefits of the use of manual therapies compared to the

other conservative treatments. Therefore, the objective of this study was to do a systematic review about this subject in an attempt of indicating the best course of conservative treatment for mild and moderate idiopathic CTS to relief the pain, diminish numbness and prevent the decrease in grip strength.

Methods

This paper was written in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[18]

Search methods

The search terms was carpal tunnel syndrome, median neuropathy, entrapment neuropathy, manual therapy, manipulation therapy, soft tissue therapy, neural mobilization. To reduce bias, no limits were placed upon language or location of publication. The seach was until april 2017 on three electronic databases MEDLINE (PubMed), EMBASE, and PEDro. All the studies was screened and extracted data per two review authors independently. In case of disagreement, a third reviewer search the consensus. Data extracted was age, sex, treatment type, outcomes, follow-up and results. Total search was 1338 studies, 45 studies was selected after reading title and abstract, 22 studies was screened to read full-text, 10 studies were excluded due to tendon and nerve gliding was done as active exercises instead of mobilization and 12 studies met the inclusion/exclusion criteria (see Fig1).

Eligibility criteria

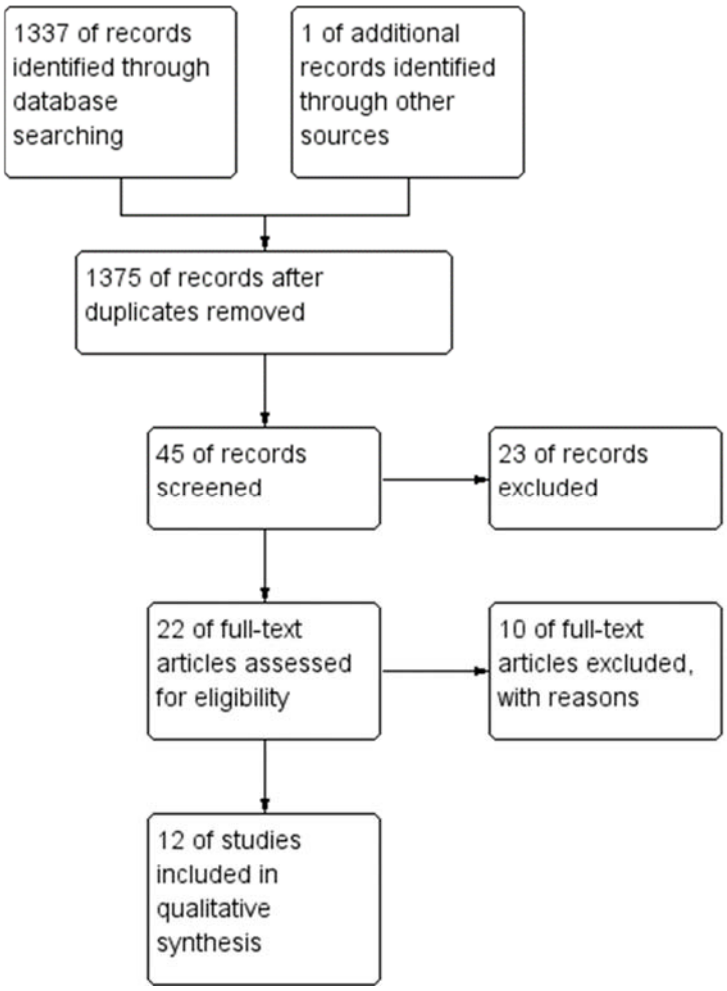
Design

The review was limited to randomized controlled trials (RCTs) and quasi-randomized controlled trials.

Participants

Only studies in which participants had a confirmed clinical and electrophysiological diagnosis of carpal tunnel syndrome were included. Diagnosis required positive Phalen test, positive Tinel sign, pain in the wrist area and additionally nerve conduction study. Patients between 18 to 80 years. The exclusion criteria of the selected studies was patients with systemic diseases, such as diabetes mellitus, rheumatoid arthritis and hypothyroidism, and individual who was pregnant, previous corticosteroid injection or surgery.

Fig. 1. PRISMA flow diagram



Assessment of methodological quality

Appreciation of the quality of studies included was done by Cochrane risk of bias tool[19], (see Fig 2.). The Cochrane risk of bias tool is a 6-item list designed to assess sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other potential sources of bias. Each item was rated as “yes”, “no” and “unclear” risk. According to Cochrane Handbook, there are 3 levels of evidence: A, B and C. The level assigned to a study gives an indication of the quality of the trial. If the study design fully met all of the 6 criteria, its level was considered to be A (low risk of bias). A study was assigned to be the B level when one or more criteria were partly met. If one or more criteria were not met, the study was assigned to be de C level, implying a high risk of bias.

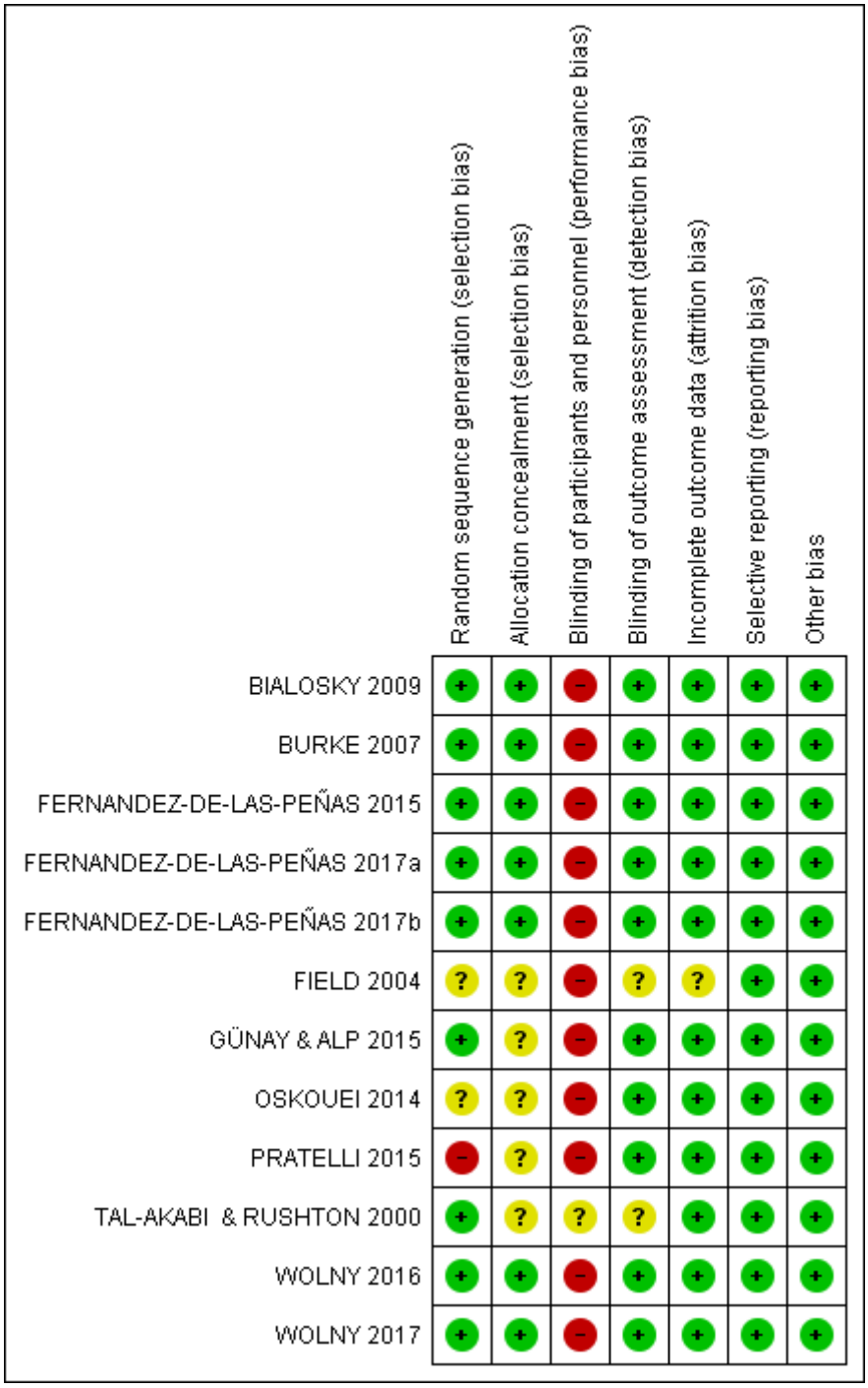


Fig 2. Risk of bias summary: this risk of bias tool incorporates the assessment of randomization (sequence generation and allocation concealment), blinding (participants and outcome assessors), incomplete outcome data, selective outcome reporting, and other risk of bias. The items were judged as “low risk,” “unclear risk,” or “high risk.” Green means “low risk,” red means “high risk,” and yellow means “unclear risk.”

Results

Characteristics of included studies

Twelve studies met the inclusion criteria. Nine of them were randomized controlled trials, and three controlled trials. They all used different types of manual therapies in the intervention group, being the most common: carpal bone mobilization[25], neuromobilization[26,27,28,29], neurodynamic mobilization associated with massage[30,31], massage[20], fascial mobilization[9], manual soft tissue mobilization[21]. None of the studies used a self-therapy program. The intervention groups were then compared to other groups where other therapies were used, such as sham techniques[32], electrophysical[26] and thermal modalities[9,30,31], splint[25], surgery[27,28,29] and soft tissue mobilization[21].

Characteristics of the Samples in the studies

The samples ranged from 16 to150 individuals diagnosed with carpal tunnel syndrome. Four RCTs were conducted with women exclusively[27,28,29,32], six included women and men[9,20,21,30,31,32] and two did not inform the sex of their patients[25,26].

Outcomes

The main outcomes used to assess the effectiveness of the treatment were: pain, grip and pinch strength, sensibility, functional status and electrophysiology evaluation (see Table 1).

Pain was the most common outcome (present in 10 of the studies), and a variety of methods to evaluate pain were used. Five studies assessed pain using the visual analogue scale[9,20,21,26,32], four used the numerical pain rating scale[25,27,28,31]and one used the pain relief scale.[33] All the studies reported significant pain relief immediately after the treatment protocols in all the patients from the intervention groups.

A significant improve in the grip strength, over time, was found in the studies that used massage, carpal bone mobilization and manual soft tissue mobilization[20,21,25]. Pinch grip strength had significant improve in soft tissue mobilization after 1 month of follow-up.[29]

The studies which evaluated the betterment of the sensory symptoms, showed that the use of neurodynamic mobilization and massage[30] present better results than the one that used neurodynamic techniques alone.[32]

Functional status was evaluated in most studies here by one of the two questionnaires: the Symptom severity and functional status[34] (Boston Carpal Tunnel Questionnaire) and the Disabilities of the arm shoulder and hand questionnaire[35] (DASH). The patients received neuromobilization[26], fascial manipulation[9], soft tissue mobilization and neural mobilization[27,28], neurodynamic techniques associated with massage and carpal bone mobilization[25], all the studies reported an improvement in the functional status of the patients.

Table 1
Characteristics of included studies

Author	Tal-Akabi and Rushton, 2000[33]	Field et al. 2004[20]	Burke et al., 2007[21]
Participants: n, gender (W/M) and number of hands (if mentioned)	21 patients (14W, 7M), 30 hands.	16 patients (15W, 1M)	22 patients (19W, 3M).
Manual therapy Interventions	G1: neurodynamic mobilization (ULTT2a) and G2: wrist mobilization (PA and AP based on Maitland´s Concept). Frequency and/or number of session not mentioned	massage therapy on symptomatic hand, once per week (4 weeks, 15 min duration)	manual soft tissue mobilization. 2 session per week/ 4weeks and 1 session per week/2weeks
Control/comparison	Control (no treatment)	Control (no treatment)	Graston technique: instrument-assisted soft tissue mobilization protocol. 2 session per week/ 4weeks and 1 session per week/2weeks
Outcome measure and timepoints	24-h symptom diary, pain (VAS), active ROM (writs extension and flexion), functional scales (functional Box Scale and Pain Relief Scale), median nerve clinical test (ULTT) and number of patients to surgery. Time points: baseline, 1th and 3rd month of follow-up.	pain (VAS), perceived Grip strenght Scale (0-10 points), State Anxiety Inventory (STAI), Profile of Mood State (POMS). Time points: baseline immediately after treatment (4 weeks).	pain (VAS), symptom severity scale, grip and pinch strength, nerve conduction test. Time points: baseline, immediate effects and 3 months follow-up.
Clinical results	Neurodynamic mobilization presented a significant reduction in pain perception and functional improvement immediately after treatment and 3 months after treatment. Wrist mobilization group showed functional improvement immediately after treatment, but not 3 months after treatment. Both groups are superior to control group. No differences in effectiveness of treatment was demonstrated Between carpal bone mobilization and median nerve mobilization.	Massage therapy group showed improved on grip strength, reduced pain levels, anxiety and depressed mood compare control group.	Both groups had slight improves nerve conduction latencies, significant improvement in functional status maintained after 3 months, statistical difference in grip strength, and wrist range of motion 3 months after treatment. No statistical difference between groups were detected.

Author	Bialosky et al. 2009[32]	Prateli et al. 2014[9]	Oskouei et al. 2014[26]
Participants: n, gender (W/M) and number of hands (if mentioned)	40 patients (40W).	42 patients (29W, 13M), 70 hands.	20 patients (gender not reported), 32 hands.
Manual therapy Interventions	neurodynamic mobilization for median nerve 4,6(+1,6) treatment session (3 weeks of treatment). Night splint.	fascial manipulation, 3 session, once a week during 3 weeks (45 minutes duration).	Neuromobilization in combination with routine physiotherapy (TENS, ultrasound and splint). 3 sessions per week, during 4 weeks.
Control/comparison	Sham neurodinamic mobilization. Night splint.	Low level laser therapy applied at the carpal level, wavelength of 780e830 nm and a power between 1000 and 3000 mW. 5 daily session lasting 10 min each.	Routine physiotherapy (TENS, ultrasound and splint). 3 sessions per week, during 4 weeks.
Outcome measure and timepoints	pain, pain pressure threshold, thermal pain (threshold and temporal summation), functional questionnaire (DASH), grip strength, tactile sensitivity (Semmes-Weinstein monofilament), nerve conduction test. Time points: baseline and immediately post-treatment (3weeks).	pain (VAS), Functional and symptomatic sub-scales of BCTQ, Timepoints: baseline, 10 days after last session and 3 months after last session.	pain (VAS), Symptoms severity and Functional status scale (BCTQ), Phalen test, median nerve tension test, median nerve conduction test. Time points: baseline, immediately after treatment (4 weeks)
Clinical results	Both groups reduce pain sensitivity and intensity immediately after treatment and both groups improve function at 3 weeks. Neurodynamic improved temporal summation ($p < 0.01$).	Fascial manipulation group showed significant reduction on pain perception and increased function at the end of the treatment and follow-up. Low level laser therapy group showed significant results at the end of the treatment, but not at the follow-up period.	Both groups presented similar improved on pain intensity, reduce severity of symptoms, median nerve test and Phalen test. Neuromobilization in combination with routine physiotherapy was superior to improved functional status scale and median nerve distal motor latency results ($p<0.05$).

Author	Fernández-de-las-Peñas et al. 2015[27]	Günay, 2015[25]	Wolny et al. 2016[30]
Participants: n, gender (W/M) and number of hands (if mentioned)	120 patients (120 W)	52 patients (gender not reported).	140 patients (122W, 18M), 180 hands
Manual therapy Interventions	Manual therapy composed by neural mobilization, nerve-tendon glide (slider mobilization) and soft tissue therapy. 3 sessions, once per week (30 min duration)	carpal bone mobilization and night splint. 10 min/day and 3 times week for 10 days.	neurodynamic techniques (median mobilization) combined with functional massage of the descending part of the trapezius and wrist. 20 therapy sessions, twice a week for 10 weeks
Control/comparison	surgical (decompressed/release of the carpal tunnel)	night splint	Laser (under transverse carpal ligament area, 658 nm of light at 50 W. 1 minute of duration and 40 seconds for a total dose of 5 J, infrared laser emitting 808 nm of light at 400mWwas used during 1 minute for a total dose of 24 J) and ultrasound (frequency,1 MHz; intensity, 1.0 W/cm; and 75% pulsed for 15 minutes) 20 therapy sessions, twice a week for 10 weeks.
Outcome measure and timepoints	pain intensity (mean pain and the worst pain), functional status and symptoms severity (BCTQ) and the self-perceived improvement. Time points: baseline and 1, 3, 6, 9 e 12 months follow-up	pain day and night (VAS), symptom severity scale, grip and pinch, nerve conduction test. Time points: baseline and 3 months after treatment.	Two-point discrimination test. Time point: baseline and after 10 weeks of treatment. Time points: baseline and immediately after treatment (10 weeks)
Clinical results	Manual therapy group exhibit higher decreased at 1 and 3 months in mean current pain and worst pain than G2 (effect size 1,1>SMD>1.8). No significant between-group differences observed at 6 and 12 months (P > 0.1). In terms of higher increases in function, G1 was superior at 1 and 3 months compared G2 (effect size large at 1 month: 1.2 SMD and moderate at 3 months: SMD 0.8). Changes in function were similar between groups at 6 and 12 months (P > .3), and both groups exhibited similar improvements in severity symptoms at all follow-up periods. Self-perceived improvement was also similar at 6 (P = 0.6) and 12 (P = 0.1) months in both groups.	Manual therapy group showed significant clinical improvements in all clinical variables compare to control group.	Both groups significantly improved the results of two-point discrimination test ($p < .001$). No difference between groups was observed.

Author	Wolny et al. 2017[31]	Fernández-de-las-Peñas et al. 2017a[28]	Fernández-de-las-Peñas et al. 2017b[29]
Participants: n, gender (W/M) and number of hands (if mentioned)	140 patients (122W, 18M), 180 hands	100 patients (100 W)	100 patients (100 W)
Manual therapy Interventions	neurodynamic techniques (median mobilization) combined with functional massage of the descending part of the trapezius and wrist. 20 therapy sessions, twice a week for 10 weeks	Soft tissue mobization directed at anatomical sites of potential entrapment of the median nerve (as scalene muscles, pectoralis minor muscle, biceps brachii muscle, bicipital aponeurosis, pronator teres, wrist flexor musculature, transverse carpal ligament, palmar aponeurosis or lumbricals muscles) and nerve- tendon glide exercise. 3 sessions, once per week (30 min duration).	Soft tissue mobization directed at anatomical sites of potential entrapment of the median nerve (as scalene muscles, pectoralis minor muscle, biceps brachii muscle, bicipital aponeurosis, pronator teres, wrist flexor musculature, transverse carpal ligament, palmar aponeurosis or lumbricals muscles) and nerve/tendon glide exercise. 3 sessions, once per week (30 min duration)
Control/comparison	Laser (under transverse carpal lig area, 658 nm of light at 50 W. 1 minute of duration and 40 seconds for a total dose of 5J, infrared laser emitting 808 nm of light at 400mW was used during 1' for a total dose of 24 J) and ultrasound (freq.,1 MHz; int., 1.0 W/cm; and 75% pulsed for 15') 20 ther. ses., tw for 10 weeks	Surgery group (endoscopic decompression and release of the carpal tunnel)	Surgery group (endoscopic decompression and release of the carpal tunnel)
Outcome measure and timepoints	pain (numerical pain rating scale) nerve conduction test, severity of symptoms and functional status (BCTQ). Time points: baseline and immediately after treatment (10 weeks)	pain pressure threshold, thermic pressure threshold (hot and cold) and pain int.. Time pts: baseline and 3, 6, 9 e 12 mths follow-up.	Symptoms and functional status (BCTQ), cervical range of motion (CRM), pinch-tip grip strength. Time points: baseline and 1, 3, 6 e 9 e 12 months follow-up
Clinical results	Only manual therapy group had increased on sensory and motor conduction velocity (P<0.01 for both). Both groups reduced pain and improve functional status (p<0.01 in all analysis in both groups). The results regarding pain reduction, subjective symptoms, and functional status were better in the manual therapy group.	Manual therapy showed increased on pain pressure threshold at 3, 6 and 9 months and significantly decreased on pain intensity at 3 months, compared with surgery group. Both groups did not promote significant change in thermal pain sensitivity at any time (p>0.05 for all time-point).	Manual therapy group exhibited a statistically greater increase in self-reported function at 1 mth (mean change, –0.8; 95% CI: –1.1, –0.5) than surgical group. The between-group effect size was large (SMD: 1.6). Changes in self-reported function were similar in both groups at 3-, 6-, and 12-mth follow-ups (*P*>0.4). Both groups exhibited similar improvements in severity of symptoms at all follow-up periods. Manual therapy exhibited higher increases in pinch-tip grip force on the symptomatic hand at 1 mth than p who received surgery. The between-group effect size was large in favour to G1 (SMD, 1.1). Changes in pinch-tip grip strength on the symptomatic hand were similar in both groups at 3, 6, and 12 mths (*P*>.2).

G1, grupo1; G2, grupo 2; ULTT2a, slight glenohumeral abduction, shoulder depression, elbow extension, lateral rotation of the whole arm, wrist, thumb, fingers extension and glenohumeral abduction; VAS, visual analogue scale; DASH, disabilities of arm, shoulger and hand questionnaire; BCTQ, Boston carpal tunnel questionnaire; TENS, transcutaneous electrical nerve stimulation; CRM, cervical range of motion.

The electro physiologic evaluation showed that there was an improvement in the distal sensory latency in patients submitted to the neuromobilization maneuver.[26]

Effectiveness of the different manual therapies

The randomized controlled trial, which compared manual therapy to electrotherapeutic modalities, supported that the manual therapy is more effective than laser and laser plus ultrasound.[9,30,31]

Finally, Fernandez-de-Las-Peñas[27] compared the efficiency of manual therapies against the surgery and concluded that better short-term outcomes were found when the manual therapy was used, as patients were able to return earlier to their daily activities and work.

Discussion

Systematic reviews have been used as a powerful tool to evaluate and synthesize the results of well designed healthcare studies and to provide evidences and guidelines regarding different healthcare interventions. Accordingly, they also allow clinicians to improve their practices and to make clinical decisions based on scientific evidence that are necessary on a daily basis.[18,36]

A variety of systematic reviews regarding the use of conservative treatments to the Carpal Tunnel Syndrome have been conducted with patients who did exercises and used medication[17],who did tendon and nerve gliding as active exercises[23] and who mixed manual therapy with tendon and nerve gliding as exercise.[37] A study conducted with steroids [10] revealed that both injected and oral steroids have a short-term benefit and are potentially harmful. Another study[23] focused mainly on active exercises for the hands' median nerve, which is classified as auto-therapy and differs from the neurodynamic techniques delivered by a physiotherapist, influencing the organism in different ways.[31]Recently a systematic review[37] compared active and passive therapies and concluded that the mechanical effects may differ because of the incomparability of the 2 types of mobilization.

Having taking into consideration the results of the studies above, the present study evaluated only the manual therapies as they, when properly performed, present no side effects and should be the first recommendation before surgery[9], as the surgery poses a failure risk rate of of 1%-25%[38]. The complications are not only regarding the risks for the patients, but we should also consider the direct medical costs of surgical interventions as well as the socioeconomic costs regarding the workers' compensation costs.[39]Besides manual therapy has low-cost and is a non-invasive method.[25]

Therefore, purpose of this review was to assess the efficacy of manual therapy for mild and moderate idiopathic CTS when compared with other treatments. Twelve RCTs met the inclusion criteria for this review and all of them showed that the conservative treatments have played an important role to treat signs and symptoms at the beginning of the carpal tunnel syndrome.

All RCTs that compared manual therapy to electrophysical modalities support that manual therapy is more effective than laser and laser plus ultrasound (pratelli, wolny 2017). This may due to the fact that the electrotherapy do not address the pathological neurodynamic of the median nerve and its surrounding structures.[22]

The main limitations found in this study was the heterogeneity of the interventions regarding the techniques used, manual therapies alone or associated with other techniques, and the follow-up time, which ranged from immediately after the treatment up to 12 months of follow-up.

Future randomized controlled trials with a standardization of the manual therapies are necessary to establish the roles of the manual therapies in treatment of the for carpal tunnel syndrome, which would allow better clinical decisions.

Conclusion

From the results complied above, we may say that the use of different manual therapies may be the best approach to treat mild and moderate idiopathic carpal tunnel syndrome when compared with thermal and electrical modalities, splint and surgery.

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6 CONCLUSÃO GERAL

A principal limitação do estudo foi a heterogeneidade das intervenções dos estudos no quesito das terapias manuais isoladas ou associadas a outras técnicas. Outra limitação é a disparidade dos estudos frente ao tempo de seguimento após a intervenção, que variou pós intervenção imediata a 12 meses, devido a estes motivos não foi factível executar uma meta-análise.

É necessário a realização de novos ensaios clínicos randomizados que utilizem técnicas padronizadas para estabelecer o papel das terapias manuais na síndrome do túnel do carpo, favorecendo a tomada de decisões frente aos tratamentos disponíveis.

Os resultados apresentados pelos doze estudos incluídos na revisão sistemática permitem concluir que o uso de terapias manuais podem ser a melhor abordagem no alívio da dor nos casos de síndrome do túnel do carpo idiopática de leve e moderado graus quando comparadas a outras técnicas como eletroterapia, termoterapia, órtese e cirurgia.

ANEXOS

ANEXO A

NORMAS DA FORMATAÇÃO DO PERIÓDICO JOURNAL OF HAND TERAPY

JOURNAL OF HAND THERAPY The Official Journal of the American Society of Hand Therapists AUTHOR INFORMATION PACK

TABLE OF CONTENTS . XXX . • Description • Impact Factor • Editorial Board • Guide for Authors p.1 p.1 p.1 p.3 ISSN: 0894-1130 DESCRIPTION . The Journal of Hand Therapy is designed for hand therapists, occupational and physical therapists, and other hand specialists involved in the rehabilitation of disabling hand problems. The Journal functions as a source of education and information by publishing scientific and clinical articles. Regular features include original reports, clinical reviews, case studies, editorials, and book reviews. Benefits to authors We also provide many author benefits, such as free PDFs, a liberal copyright policy, special discounts on Elsevier publications and much more. Please click here for more information on our author services. Please see our Guide for Authors for information on article submission. If you require any further information or help, please visit our Support Center IMPACT FACTOR . 2016: 1.159 © Thomson Reuters Journal Citation Reports 2017 EDITORIAL BOARD . Editor-in-Chief J MacDermid, McMaster University, Hamilton, Ontario, Canada Assistant Editor S Michlovitz, Cayuga Hand Therapy, Ithaca, New York, USA V Priganc, Hand Therapy Consultation Services, Richmond, Vermont, USA M. Szekeres K. Valdes, Gannon University, Ruskin, Florida, USA Editorial Board D. Aaron P. Amadio, Mayo Clinic, Rochester, Minnesota, USA J. Bear-Lehman, Pace University, New York, New York, USA D. Berger Stanton, Samuel Merritt University, Oakland, California, USA S. Blackmore C. Jansen, University of Texas Medical Branch, Galveston, Texas, USA J King AUTHOR INFORMATION PACK 9 Sep 2017 www.elsevier.com/locate/jht 2 S Kozin, Shriners Hospitals for Children, Philadelphia, Pennsylvania, USA P. McClure, Arcadia University, Glenside, Pennsylvania, USA AUTHOR INFORMATION PACK 9 Sep 2017 www.elsevier.com/locate/jht 3 GUIDE FOR AUTHORS . INTRODUCTION Authors are invited to submit manuscripts for review, in English, relating to any aspect of rehabilitation of the upper extremity. The Journal of Hand Therapy is interested in the publication of research spanning the entire spectrum of clinical, basic, and translational science, including (but not limited to): clinical practice, theory and outcomes; biomechanics, motor behavior, neuroscience, or epidemiology. A clear indication of clinical relevance is essential for publication. Manuscript categories for submission include: Clinical/Basic Research Studies, Case-Reports, Short Reports (Cross-cultural Translation, Literature Review (invited-only) Practice Forum and Letters to the Editor (published online only). Inquiries for the Editor-in-Chief should be made to: Joy MacDermid, PT, PhD at editor.macdermid@gmail.com. Submission checklist You can use this list to carry out a final check of your submission before you send it to the journal for review. Please check the relevant section in this Guide for Authors for more details. Ensure that the following items are present: One author has been designated as the corresponding author with contact details:E-mail addressFull postal address All necessary files have been uploaded: Manuscript:Include keywordsAll figures (include relevant captions)All tables (including titles, description, footnotes)Ensure all figure and table citations in the text match the files providedIndicate clearly if color should be used for any figures in printGraphical Abstracts / Highlights files (where applicable)Supplemental files (where applicable) Further considerationsManuscript has been 'spell checked' and 'grammar checked'.Insure that the abstract follows the correct format, word count and represents key findings (see below).All references mentioned in the Reference List are cited in the text, and vice versa. Check that key foundational references, methods and

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specific terminology when naming their study design in the abstract and methods. Some common study designs are listed below and should be used where applicable. We recognize that this list is not all-inclusive and that more appropriate descriptors might be suitable for some studies. Authors are encouraged to pick the most appropriate study design descriptors for their study. These suggestions are merely provided as a means of encouraging consistency, where it would be both useful and informative. The purpose of the research and the study design should be listed.Literature Synthesis: formal structured literature synthesis studies can be described in terms of the specific type: Systemic Review, Scoping Reviews, Reviews of Reviews (Overviews or Umbrella Reviews), Meta-analyses and others.Primary Clinical Studies can include a variety of designs to address research questions. The purpose of the research can be listed as: Descriptive, clinical measurement, epidemiology, etiology, natural history, prognosis, diagnosis, effectiveness, harm, economics or implementation. AUTHOR INFORMATION PACK 9 Sep 2017 www.elsevier.com/locate/jht 9 Examples of study design include:Randomized Clinical/Controlled Trial: Patients are enrolled at a relevant baseline and allocated to different intervention arms based on a random concealed process; outcomes are ascertained prospectively. Where specific variants were used please state the subtypesuch as Cross-over, Factorial, Equivalence, Non-inferiority, Expertise-based etc. Prospective Cohort: a longitudinal study where subgroups of patients are enrolled and research questions defined at a relevant baseline point (prior to when outcomes occur); patients are followed forward in time for outcomes ascertainment. For treatment studies, at least 2 groups are defined at baseline; in prognostic studies, potential predictors are collected at baseline Retrospective Cohort: a longitudinal study where subgroups of patients are involved in a prospective data collection but the research questions (and variables) were defined retrospectively; treatment groups or prognostic factors may have been defined after data collections was initiated e.g. database research Case-Control: a longitudinal study where subgroups of patients are identified/enrolled after outcomes have been ascertained and data are collected retrospectively (recall or pre-existing data) on the treatment or prognostic factors of interest. Cross-sectional: Study data are collected at a single time point. N-of-1: A single patient is enrolled at a relevant baseline and allocated to cross-over different intervention arms based on a random concealed process; outcomes are ascertained prospectively. Case Series: Data are collected on a single subgroup of patients (no comparison group). This can be cross-sectional or longitudinal. Case Report: Data are collected on a single subject. Repeated Case Study: a formal comparison of 2-5 cases, extending beyond summary data. Qualitative Study DesignsMeta-syntheses: a synthesis of the better quality qualitative studies.Grounded Theory: research that seeks to understand and identify theoretical processes; themes used to develop an understanding and theoretical explanation.Case Study: an in-depth study of an individual lived experience and perspective.Descriptive: Studies that may use qualitative and quantitative method to describe a phenomenon- without intention to develop theory or meaningEthnography: the description of the customs of groups or cultures.Interpretive Description: inductive analytic studies designed to understand clinical phenomena with a view to applications Mixed-Methods Designs include both quantitative and qualitative components that seek to address a common or complementary research questions. The components can be conducted concurrently or sequentially to expand, explain or triangulate findings of the other component. The author can explain the approaches using any of the design taxonomies described for mixed methods. A summary of the questions and design is illustrated in the figure. Basic science research. This includes mechanistic studies i.e. anatomy, biomechanics, electromyography, physiology. Where applicable the descriptors above may be used. At a minimum author must state whether data collection was observational or randomized and whether data was Longitudinal: collected at

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ANEXO B

ESTRATÉGIA DE BUSCA MEDLINE (PUBMED)

Paciente

((Carpal Tunnel Syndrome) OR (Carpal Tunnel Syndromes) OR (Syndrome, Carpal Tunnel) OR (Syndromes, Carpal Tunnel) OR (Amyotrophy, Thenar, Of Carpal Origin) OR (Median Neuropathy, Carpal Tunnel) OR (Compression Neuropathy, Carpal Tunnel) OR (Entrapment Neuropathy, Carpal Tunnel))

((Median Neuropathy) OR (Median Neuropathies) OR (Neuropathies, Median) OR (Neuropathy, Median) OR (Median Nerve Diseases) OR (Median Nerve Disease) OR (Nerve Disease, Median) OR (Nerve Diseases, Median) OR (Median Nerve Neuralgia) OR (Median Nerve Neuralgias) OR (Neuralgia, Median Nerve) OR (Neuralgias, Median Nerve) OR (Median Neuropathy, Proximal) OR (Median Neuropathies, Proximal) OR (Neuropathies, Proximal Median) OR (Neuropathy, Proximal Median) OR (Proximal Median Neuropathies) OR (Proximal Median Neuropathy) OR (Medial Neuropathy, Distal) OR (Distal Medial Neuropathies) OR (Distal Medial Neuropathy) OR (Medial Neuropathies, Distal) OR (Neuropathies, Distal Medial) OR (Neuropathy, Distal Medial))

((Median Nerve) OR (Median Nerves) OR (Nerve, Median) OR (Nerves, Median))

((Nerve Compression Syndromes) OR (Compression Syndrome, Nerve) OR (Compression Syndromes, Nerve) OR (Nerve Compression Syndrome) OR (Syndrome, Nerve Compression) OR (Syndromes, Nerve Compression) OR (Nerve Entrapments) OR (Entrapment, Nerve) OR (Entrapments, Nerve) OR (Nerve Entrapment) OR (Internal Nerve Compression Syndromes) OR (Nerve Compression Syndromes, Internal) OR (Entrapment Neuropathies) OR (Neuropathies, Entrapment) OR (Neuropathy, Entrapment) OR (External Nerve Compression Syndromes) OR (Nerve Compression Syndromes, External))

Intervenção

((Manipulations, Musculoskeletal) OR (Manual Therapies) OR (Manual Therapy) OR (Therapies, Manual) OR (Therapy, Manual) OR (Manipulation Therapy) OR (Manipulation Therapies) OR (Therapies, Manipulation) OR (Manipulative Therapies) OR (Manipulative Therapy) OR (Therapies, Manipulative) OR (Therapy, Manipulative) OR (Therapy, Manipulation))

(Soft Tissue Therapy)

(Mobili* OR Manipulat*)

(Manual Ther*)

((Massage) OR (Craniosacral Massage) OR (Massage, Craniosacral) OR (Zone Therapy) OR (Therapies, Zone) OR (Zone Therapies) OR (Therapy, Zone) OR (Reflexology) OR (Rolfing) OR (Bodywork) OR (Bodyworks) OR (Massage Therapy) OR (Massage Therapies) OR (Therapies, Massage) OR (Therapy, Massage))

((Chiropractic Manipulation) OR (Spinal Adjustment, Chiropractic) OR (Adjustment, Chiropractic Spinal) OR (Adjustments, Chiropractic Spinal) OR (Chiropractic Spinal Adjustment) OR (Chiropractic Spinal Adjustments) OR (Spinal Adjustments, Chiropractic) OR (Chiropractic Adjustment) OR (Adjustment, Chiropractic))

((Osteopathic Manipulative Treatment) OR (Osteopathic Manipulative Treatments) OR (Treatment, Osteopathic Manipulative) OR (Treatments, Osteopathic Manipulative) OR (Osteopathic Manipulation))

((Nerve Mobilization) OR (Nerve Gliding) OR (Neural Mobilization))

Design

((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials as topic[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])

TOTAL

(((Carpal Tunnel Syndrome) OR (Carpal Tunnel Syndromes) OR (Syndrome, Carpal Tunnel) OR (Syndromes, Carpal Tunnel) OR (Amyotrophy, Thenar, Of Carpal Origin) OR (Median Neuropathy, Carpal Tunnel) OR (Compression Neuropathy, Carpal Tunnel) OR (Entrapment Neuropathy, Carpal Tunnel)) OR ((Median Neuropathy) OR (Median Neuropathies) OR (Neuropathies, Median) OR (Neuropathy, Median) OR (Median Nerve Diseases) OR (Median Nerve Disease) OR (Nerve Disease, Median) OR (Nerve Diseases, Median) OR (Median Nerve Neuralgia) OR (Median Nerve Neuralgias) OR (Neuralgia, Median Nerve) OR (Neuralgias, Median Nerve) OR (Median Neuropathy, Proximal) OR (Median Neuropathies, Proximal) OR (Neuropathies, Proximal Median) OR (Neuropathy, Proximal Median) OR (Proximal Median Neuropathies) OR (Proximal Median Neuropathy) OR (Medial Neuropathy, Distal) OR (Distal Medial Neuropathies) OR (Distal Medial Neuropathy) OR (Medial Neuropathies, Distal) OR (Neuropathies, Distal Medial) OR (Neuropathy, Distal Medial)) OR ((Median Nerve) OR (Median Nerves) OR (Nerve, Median) OR (Nerves, Median)) OR ((Nerve Compression Syndromes) OR (Compression Syndrome, Nerve) OR (Compression Syndromes, Nerve) OR (Nerve Compression Syndrome) OR (Syndrome, Nerve Compression) OR (Syndromes, Nerve Compression) OR (Nerve Entrapments) OR (Entrapment, Nerve) OR (Entrapments, Nerve) OR (Nerve Entrapment) OR (Internal Nerve Compression Syndromes) OR (Nerve Compression Syndromes, Internal) OR (Entrapment Neuropathies) OR (Neuropathies, Entrapment) OR (Neuropathy, Entrapment) OR (External Nerve Compression Syndromes) OR (Nerve Compression Syndromes, External))) AND (((Manipulations, Musculoskeletal) OR (Manual Therapies) OR (Manual Therapy) OR (Therapies, Manual) OR (Therapy, Manual) OR (Manipulation Therapy) OR (Manipulation Therapies) OR (Therapies, Manipulation) OR (Manipulative Therapies) OR (Manipulative Therapy) OR (Therapies, Manipulative) OR (Therapy, Manipulative) OR (Therapy, Manipulation)) OR (Soft Tissue Therapy) OR (Mobili* OR Manipulat*) OR (Manual Ther*) OR ((Massage) OR (Craniosacral Massage) OR (Massage, Craniosacral) OR (Zone Therapy) OR (Therapies, Zone) OR (Zone Therapies) OR (Therapy, Zone) OR (Reflexology) OR (Rolfing) OR (Bodywork) OR (Bodyworks) OR (Massage Therapy) OR (Massage Therapies) OR (Therapies, Massage) OR (Therapy, Massage)) OR ((Chiropractic Manipulation)

OR (Spinal Adjustment, Chiropractic) OR (Adjustment, Chiropractic Spinal) OR (Adjustments, Chiropractic Spinal) OR (Chiropractic Spinal Adjustment) OR (Chiropractic Spinal Adjustments) OR (Spinal Adjustments, Chiropractic) OR (Chiropractic Adjustment) OR (Adjustment, Chiropractic)) OR ((Osteopathic Manipulative Treatment) OR (Osteopathic Manipulative Treatments) OR (Treatment, Osteopathic Manipulative) OR (Treatments, Osteopathic Manipulative) OR (Osteopathic Manipulation)) OR ((Nerve Mobilization) OR (Nerve Gliding) OR (Neural Mobilization))) AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials as topic[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])