UNIVERSIDADE DE BRASÍLIA – FACULDADE DE CEILÂDIA
PROGRAMA DE PÓS-GRADUAÇÃO *STRICTU-SENSU* EM CIÊNCIAS E TECNOLOGIAS EM SAÚDE

EFEITOS DO TRATAMENTO MANIPULATIVO OSTEOPÁTICO NA FUNÇÃO CARDIOVASCULAR EM INDIVÍDUOS SAUDÁVEIS E COM INSUFICIÊNCIA CARDÍACA

FELLIPE AMATUZZI TEIXEIRA

ORIENTADOR: Prof. Dr. GERSON CIPRIANO JUNIOR

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Tese apresentada à Faculdade da Ceilândia da Universidade de Brasília como requisito parcial para obtenção do título de Doutor em Ciências e Tecnologias em Saúde

ORIENTADOR: Prof. Dr. GERSON CIPRIANO JUNIOR

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“E no final, o amor que você receberá,
Será igual àquele amor que você ofereceu”
Lennon/McCartney

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3. LISTA DE ABREVIAÇÕES, NOMENCLATURAS E SÍMBOLOS

AR	Auto-Regressivo
AUC	Área Abaixo da Curva
AVBA	Alta velocidade e baixa amplitude
CP	Condutância da Pele
CTG	Grupo controle
DMF	Dilatação mediada pelo fluxo
DPGA	Área Cinzenta Dorsal Periaquedutal
ECG	Eletrocardiograma
EDV	Velocidade Diastólica Final
eNO	Óxido nítrico sintetase endotelial
eNOS	Óxido Nítrico Sintetase Endotelial
FC	Frequência cardíaca
FFT	*Fast Fourrier Transform*
HF	Espectral Absoluta de Alta Frequência
HMGB1	High mobility group protein B1
HVLA	Alta Velocidade Baixa Amplitude
IC	Insuficiência Cardíaca
IP	Índice de Pulsabilidade
IR	Índice de Resistência
LF	Espectral absoluta de Baixa Frequência
LF/HF	Balanço autonômico
MANOVA	Análise de variância múltipla
MCA	Métodos Complementares Alternativos
MHz	Mega Hertz
MIA	Mobilização intra articular
NHIS	National Health
NO	Óxido Nítrico
PA	Pressão Arterial
PCO_2	Pressão de Gás Carbônico
pH	Potencial de Hidrogênio
PO_2	Pressão de Oxigênio
PVS	Pico de Velocidade Sistólica
RMSSD	Rooth Mean Square Standard Deviation
SD1	Desvio vertical
SD2	Desvio horizontal
SDNN	Standard Deviation N-N
SHG	Grupo sham
SNA	Sistema Nervoso Autonômo
SNP	Sistema Nervoso Parassimpático
SNS	Sistema Nervoso Simpático
SUS	Sistema Único de Saúde
TART	Tensão, Assimetria, Restrição e Dor
TENS	*Transcutaneal Eletrical Neural Stimulation*

TMOG	Grupo tratamento manipulativo osteopático
ULF	Espectral Absoluta de Ultra Baixa Frequência
VDF	Velocidade diastólica final
VFC	Variabilidade da Frequência Cardíaca
VLF	Espectral Absoluta de Frequência muito baixa

4. RESUMO

Introdução: O Tratamento Manipulativo Osteopático (TMO) é dito capaz de modular o sistema vascular e o sistema nervoso autônomo (SNA). No entanto, do que é do nosso conhecimento, ainda não existe na literatura estudos associando as respostas hemodinâmicas e autonômicas pós TMO (lacuna 1). Contudo, ainda é controverso quais técnicas de TMO seriam melhores para modular o SNA (lacuna 2) e se é seguro receber o TMO sob o ponto de vista cardiovascular (lacuna 3).
Objetivo: Estudar as lacunas supracitadas.
Método: Lacuna 1: Ensaio clínico randomizado (ECR) comparando os efeitos do TMO na função vascular e autonômica – análise do dilatação fluxo mediada (DFM) e variabilidade da frequência cardíaca (VFC) – em cardiopatas. Lacuna 2: Revisão sistemática com metanálise (RSMA) acerca dos efeitos da tratamento manual da coluna vertebral (TMCV) no SNA (medidos por VFC e condutância da pele). Lacuna 3: ECR comparando a influência do TMO cervical em indivíduos saudáveis na pressão arterial (PA) e frequência cardíaca (FC) verificando a segurança de receber TMO.
Resultados: Lacuna 1: Verificou-se um aumento da DMF (pre x *time course* 14%±2,29 para 23,5% ±6,87 p=0,027), diferença absoluta (pre x *time course* 0,6mm ±0,159 para 1,07 ±0,29 p=0,03) e diâmetro de pico (pre x *time course* 4,9mm ±0,74 para 5,67 ±0,76 p=0,003 and post x *time course* 5,2mm ±0,58 para 5,67±0,76 p=0,02). Todavia, na função autonômica houve aumento dos índices vagais imediatamente após a técnica (RMSSD, SDNN e SD1) e após 10 minutos de follow-up a manutenção do aumento vagal além de aumento de índice simpático (LF). Lacuna 2: RSMA: A manipulação promove aumento da LF_{norm} e LF/HF. A mobilização intra articular aumenta a condutância da pele (durante a aplicação). Não há alteração do sistema parassimpático e FC após a manipulação. Supreendentemente, após a execução da mobilização intra articular, condutância da pele também não alterou. Lacuna 3: ECR: Sem alterações relevantes na PA e FC após TMO cervical em nenhum dos grupos imediatamente nem após 24 horas.
Conclusão: Lacuna 1: O TMO foi capaz de modular o sistema vascular e autonômico em pacientes com insuficiência cardíaca. Supreendentemente, os ajustes vasculares parecem ocorrer imediatamente após a aplicação da técnica, independente da modulação simpática. Lacuna 2: RSMA: As TMCV aumentam o SNA simpático, porém não altera o parassimpático nem a FC. Lacuna 3: ECR: O TMO cervical não produz alteração imediata e 24 horas significativas na PA e FC, mostrando ser seguro do ponto de vista cardiovascular.

Palavras-chaves: Tratamento manipulativo osteopático, variabilidade da frequência cardíaca, Sistema nervoso autônomo, insuficiência cardíaca e DMF.

5. ABSTRACT

Introduction: Osteopathic Manipulative treatment (OMT) is said to be able to modulate the vascular system and the autonomic nervous system (ANS). However, what we know, does not yet exist in the literature studies associating the hemodynamic responses and post OMT autonomic (gap 1). However, it's still controversial which OMT techniques would be best to modulate the ANS (gap 2) and if it is safe to receive the OMT cardiovascular point of view (gap 3).
Objective: Study the above-mentioned gaps.
Method: Gap 1: randomized clinical trial (RCT) comparing the effects of OMT on vascular and Autonomic function-analysis of flow mediated dilation (FMD) and heart rate variability (HRV)-in cardiac patients. 2 gap: systematic review with meta-analysis (SRMA) about the effects of manual treatment of the spine (MTS) in ANS (measured by HRV and skin conductance). Gap 3: RCT comparing the influence of cervical OMT in healthy individuals in blood pressure (BP) and heart rate (HR) checking the safety of receiving OMT.
Results: Gap 1: FMD incresead (pre x time course 14% ± 2.29 to 23.5% ± 6.87 p = 0.027), absolute difference (pre x time course 0, 6 mm ± 1.07 ± 0.29 for 0.159 p = 0.03) and diameter of peak (pre x time course 4, 9 mm ± 0.74 to 5.67 ± 0.76 p = 0.003 and post x time course 5 mm ± 0.58 to 5.67 ± 0.76 p = 0.02) also. However, vagal autonomic function indices increased immediately after the technique (RMSSD, SDNN and SD1) and after 10 minutes of follow-up increased vagal maintenance in addition to increased sympathetic (LF) index. 2 Gap: RSMA: Manipulation promotes increased LF_{norm} and LF/HF. Intra articular mobilization improves skin conductance (during the application). No change of the parasympathetic system and HR after the manipulation. Amazingly, after the execution of the intra articular mobilization, skin conductance also did not change. Gap 3: RCT: Without relevant changes in BP and HR after cervical OMT in any of the groups immediately or after 24 hours.
Conclusion: Gap 1: the OMT was able to modulate the vascular and Autonomic system in patients with heart failure. Amazingly, the vascular adjustments seem to occur immediately after the application of the technique, independent of the sympathetic modulation. 2 gap: SRMA: MTS increase sympathetic ANS, but does not change the parasympathetic or HR. Gap 3: RCT: The cervical OMT does not produce immediate change and 24 hours in BP and HR significant showing be safe on cardiovascular point of view.

Keywords: Osteopathic manipulative Treatment, heart rate variability, autonomic nervous System, heart failure and DMF.

6. INTRODUÇÃO

A Osteopatia reconhece a importância do sistema nervoso autônomo (SNA) na função corporal e suas relações com a saúde e a doença. O tratamento manipulativo osteopático foi desenvolvido em 1874 pelo médico americano Andrew Taylor Still, o qual se tornou uma medicina alternativa àquela convencional. Enquanto os médicos alopatas buscam novas medicações para tratar patógenos específicos, os osteopatas desenvolvem técnicas e estratégias manuais para tratar as causas funcionais das patologias. Várias pessoas são submetidas, todos os dias, ao tratamento manipulativo osteopático por todo o mundo. Pessoas fisicamente ativas, idosos e cardiopatas são alguns exemplos (1–4).

Existem inúmeras opções de técnicas de tratamento manipulativo osteopático. As técnicas de alta velocidade e baixa amplitude (AVBA) – manipulação da coluna, técnicas de mobilização intra articular (MIA), técnicas miofasciais, além das técnicas viscerais e cranianas estão dentro do escopo da osteopatia. Dentre elas, as técnicas miofasciais realizadas na próximas a base do crânio e na coluna vertebral parecem produzir efeitos no grau de modulação autonômica. Giles e cols demonstraram aumento do grau de modulação vagal em 23 indivíduos jovens e saudáveis na posição supina. Da mesma forma, Henley e cols também verificaram o aumento do grau de modulação vagal após a técnica para liberação miofascial cervical no *tilt test* (5,6). Ruffini e cols verificaram o mesmo resultado parassimpático após o tratamento manipulativo osteopático (7). Entretanto, as técnicas de AVBA cervical e torácica em indivíduos saudáveis parece levar a um aumento do balanço autonômico – com aumento da atividade simpática (8,9). Em contraste, as técnicas de AVBA lombares em indivíduos sem dor pode levar a um aumento da atividade parassimpática (10,11). As técnicas de MIA promovem aumento da atividade simpática durante a técnica, além de aumentar a frequência cardíaca (FC) e pressão arterial (PA), contudo a manutenção desses estímulos após o tratamento ainda é questionável (12).

A capacidade de provocar modulação autonômica após o tratamento manipulativo osteopático pode provocar secundariamente alterações vasculares. O uso de técnica AVBA na coluna lombar em sujeitos saudáveis proporcionou um aumento do fluxo sanguíneo cutâneo no dermátomo correspondente ao local da manipulação. Tal modulação vascular foi atribuída as mudanças autonômicas geradas pela técnica

AVBA (13). Em sujeitos com doença arterial periférica, tratados por 2 meses com sessões de tratamento manipulativo osteopático a cada 15 dias com técnicas de liberação miofascial, técnicas de músculo energia, técnicas de AVBA (geralmente em T10 a L1), técnicas de bombeio linfático e técnicas craniana, foi verificado que ao final do tratamento houve melhora em medidas inflamatórias vasculares, na resposta da dilatação mediada pelo fluxo (DMF) da artéria braquial mantida por 6 meses (14). Entretanto, ainda existe dúvida acerca da segurança da técnica de AVBA e MIA nas respostas cardiovasculares (FC e PA) (12). Em indivíduos com patologias vasculares e cardíacas o benefício do tratamento manipulativo osteopático ainda é questionável.

Dentre os estudos de osteopatia na área da cardiologia, em pessoas hipertensas tratadas com tratamento manipulativo osteopático e acompanhadas por 1 ano houve diminuição da PA sistólica e da camada íntima média arterial da carótida. Tais mudanças podem ser explicadas por modulação autonômica e/ou diminuição das citocinas inflamatórias locais (15). Contudo, a maioria dos estudos ainda apresentam baixa qualidade metodológica. Os trabalhos com menor risco de viés demonstraram pequenas mudanças da PA depois do tratamento manipulativo osteopático (16). Em pacientes com problemas cardíacos mais graves como a insuficiência cardíaca (IC), o tratamento manipulativo osteopático poderia ser benéfico, porém a literatura é escassa nesse assunto.

Os benefícios que o tratamento manipulativo osteopático pode promover aos pacientes com IC podem surgir por conta da gênese dessa patologia. As anormalidades do sistema hemodinâmico central e as alterações na função muscular esquelética são as principais, porém alterações reflexas no SNA também desempenham um papel importante não só na origem dos sintomas limitantes do exercício como também na progressão da IC. Tais pacientes apresentam a atividade simpática aumentada e parecem ter também a diminuição da atividade parassimpática vagal (17–19). O sistema parassimpático tem efeito anti-inflamatório mediado pela ativação do alfa7 receptor nicotínico da acetilcolina. Essa ativação inibe a liberação de citocinas e da HMGB1, mediador da inflamação dos macrófagos que, de forma persistente, pode levar a progressiva disfunção ventricular esquerda, contribuindo na sua remodelação e na apoptose de suas células (19–21).

Diversas formas de tratamento têm sido utilizadas na tentativa de regular a atividade autônoma nos pacientes com IC. Sabe-se que o aumento do grau de modulação do SNA simpático é capaz de produzir diversos efeitos fisiológicos, tais como: ajuste da frequência cardíaca, regulação do sistema renina-angiotensina-aldosterona, melhora da sensibilidade baroreflexa, supressão de citocinas pró inflamatórias, normalização da via de sinalização do óxido nítrico e supressão do *gap* de remodelação ventricular. Esses efeitos têm sido relacionados a alguns benefícios clínicos nos pacientes de IC, tais como: melhora da capacidade funcional, melhora da qualidade de vida e morbi mortalidade (19).

Encontra-se na literatura distintas formas de tratamento para a IC, entre elas modalidades clínicas e as modalidades complementares e alternativas (MCA). Destaca-se desde os anos 1970 o uso da terapia betabloqueadora com o propanolol e o aprenolol na modalidade clínica. Nos anos 1990 surgiram os estudos randomizados prospectivos demostrando os benefícios dessa terapia na morbi mortalidade para esses pacientes (22). Entretanto, o *National Health Interview Survey* listou as mais frequentes terapias de MCA para tratamento da IC: uso de óleo de peixe / ômega 3, glucosamina, equinácea e linhaça (17,7%), respiração profunda (12,7%), meditação (9,4%), quiropraxia e osteopatia (8,6%), e massagem (8,3%). O uso das MCA entre os adultos é maior entre as mulheres e os de meia-idade que são mais instruídas e têm rendimentos mais elevados. A osteopatia ainda tem sido usada para tratar as dores musculoesqueléticas associadas a condição da doença cardiovascular (23).

6.1 CONTEXTUALIZAÇÃO

A possibilidade de modulações vasculares que são atribuídas ao tratamento manipulativo osteopático e outros tratamentos manipulativos da coluna vertebral se baseiam em duas teorias: 1 – por meio de possíveis mudanças autonômicas, que por mecanismo reflexo do sistema autônomo simpático no vaso levará a alteração do diâmetro da artéria promovendo mudanças na DMF e características do fluxo e 2 – por conta das alterações intrínsecas no sistema vascular pós tratamento manipulativo osteopático, pela diminuição dos mediadores inflamatórios do vaso e aumento da oferta de óxido nítrico (NO) vascular. As alterações do grau de modulação autonômica se baseiam na proximidade anatômica dos gânglios vertebrais

autonômicos (cadeia latero vertebral simpática) com a coluna vertebral e/ou por conta da neuromodulação eferente oriundo do tronco cerebral que é estimulado pelas aferências somáticas das manipulações.

Nesta revisão serão apresentados os mecanismos de DMF e doppler assim como a anatomia e fisiologia do sistema nervoso autônomo. Incluindo a relação do SNA com o sistema cardiovascular e com a insuficiência cardíaca. Além disso, uma das suas principais formas de mensuração e a Variabilidade da Frequência Cardíaca.

6.1.1 OSTEOPATIA NO TRATAMENTO CARDIOVASCULAR

A osteopatia é um sistema de avaliação e tratamento com metodologia e filosofia própria baseado na interdependência da estrutura e função do organismo. Foi desenvolvida pelo médico americano Andrew Taylor Still em 1874. Desde então, a osteopatia baseia-se em um forte racional anatômico para justificar e tratar os sintomas e patologias. A abordagem do paciente para o osteopata é global, em uma visão holística de funcionamento corporal. Várias possibilidades de tratamento são atribuídos a osteopatia desde dores músculo esqueléticas até doenças viscerais, entre elas problemas ginecológicos, intestinais, estomacais, pulmonares e cardiovasculares e do sistema nervoso autônomo. (4,24)

A intervenção do osteopata para as doenças cardíacas e do sistema nervoso autonômico baseiam-se na estrutura e função cardiovascular e autonômica. As disfunções somáticas do sistema músculo esquelético podem gerar alteração do tônus autonômico de base e influenciar o funcionamento visceral de forma geral. Para o sistema cardiovascular, tais disfunções na região da coluna cervical e torácica, responsáveis pela inervação simpática do coração, e na base do crânio (passagem da inervação parassimpática cardíaca) podem influenciar de forma negativa o funcionamento cardiovascular. Além disso, todo o sistema arterial está em íntima relação com o sistema nervoso autônomo simpático, visto que este inerva e é uma das formas de controle do vaso. (2,24)

Para se influenciar esse mecanismo fisiológico descrito, o osteopata utiliza de técnicas que possa melhorar essa disfunção somática melhorando essa alteração de tônus autonômico. As manipulações articulares da coluna de alta velocidade e baixa amplitude (AVBA), as técnicas de mobilização intra articular (MIA), técnicas

cranianas, miofasciais, técnicas fasciais estruturais e funcionais e viscerais são algumas das possibilidades terapêuticas. As técnicas para tratamento da função cardiovascular incluem técnicas na coluna cervical e torácica, base do crânio, diafragma, ducto torácico, relação com as pleuras pulmonares e das fáscias cardíacas. De forma geral, melhorar a mecânica envolvida no movimento do diafragma, do deslizamento do coração entre as fáscias pulmonares, da relação com o esterno e seus ligamentos com o coração e da inervação autonômica são as bases do tratamento osteopático para a patologia cardíaca de forma geral. (25)

6.2.2 DILATAÇÃO MEDIADA PELO FLUXO – DMF

6.2.2.1 PERSPECTIVA HISTÓRICA

Celermjer e colaboradores (1992) desenvolveram a técnica de DMF. Um método não invasivo sendo dito capaz de medir a função do endotélio vascular realizada por meio do uso de ultrassom em resposta a hiperemia induzida por oclusão. Apresenta-se como medição fiável, e se correlaciona com a função endotelial invasiva avaliada nas artérias coronárias. Num esforço de padronização Corretti e cols em 2002 publicaram as primeiras orientações da metodologia de DMF para a artéria braquial, que até agora têm sido referenciadas mais de 1.000 vezes. Pyke e Tschakovsky sugeriram atualizar as diretrizes apresentadas por Corretti e cols, desde então essas seriam as principais referências acerca das recomendações de uso (26,27).

6.2.2.2 FISIOLOGIA DA DMF

Durante um teste de DMF, a vasodilatação ocorre em seguida de um aumento agudo no fluxo sanguíneo tipicamente induzida pela paragem circulatória do braço, com um manguito com oclusão supra-sistólica, durante um período de tempo. Tal situação aumenta a hiperemia laminar com forças de corte paralelos ao eixo longitudinal do vaso, que é traduzido via mecanorreceptores luminal da célula endotelial. Em seguida há um aumento da expressão de proteína G, de fosfoquinase A, um aumento de sinalização de óxido nítrico sintetase endotelial (eNOS), o que promove atividade catalisadora na conversão da L-arginina em NO. O NO difunde-se para a camada média ativando a guanilato ciclase solúvel que converte guanosina trifosfato em guanosina monofosfato para induzir o relaxamento do músculo liso por conta da diminuição da concentração de cálcio e vasodilatação subsequente. Na sua

forma mais tradicional, o aumento do diâmetro arterial, como consequência da hiperemia reativa, é comparado com o diâmetro basal e expresso simplesmente como percentagem deste diâmetro basal (% DMF) (27,28). A Figura 1 mostra o esquema dessa fisiologia.

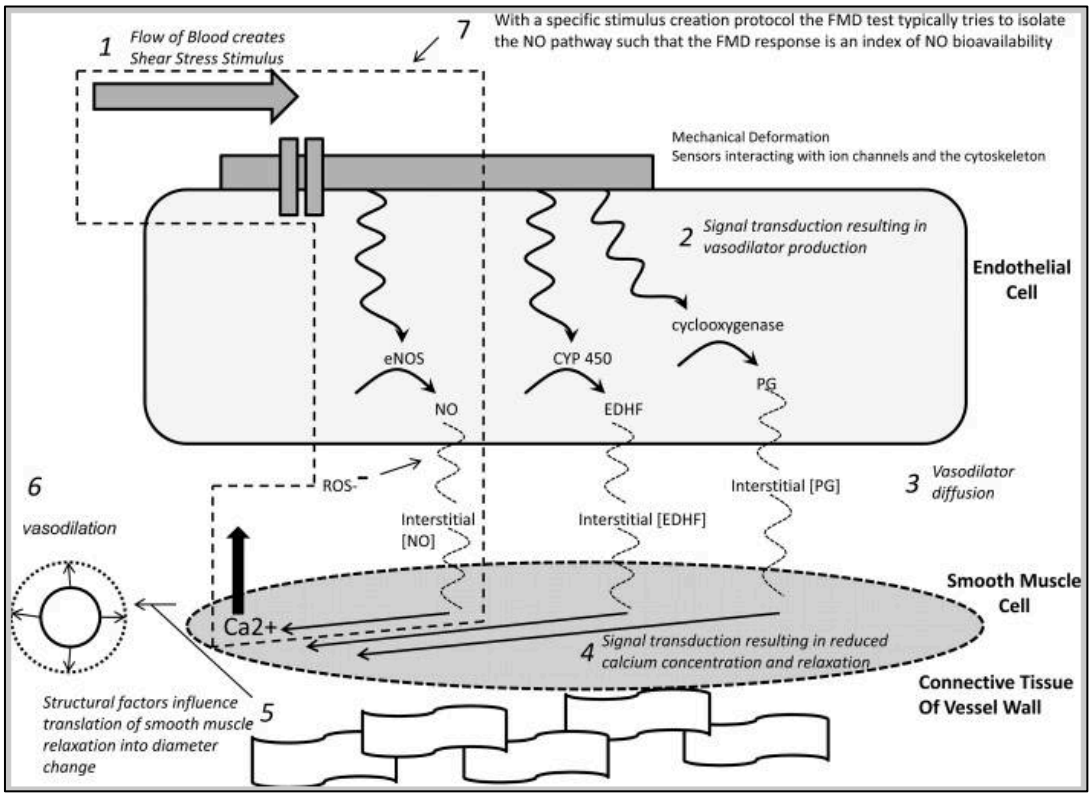

Figura 1. Esquema da fisiologia da dilatação mediada pelo fluxo.

Legenda: 1 – fluxo de sangue cria um estímulo de estresse de cisalhamento no vaso. 2 – A transdução do sinal resultando em produção de vasodilatação. 3 – Difusão vasodilatadora. 4 – O sinal de transdução resultando em redução da concentração de cálcio e relaxamento. 5 – Fatores estruturais influenciam o relaxamento muscular para a mudança do diâmetro do vaso.

Fonte: Modificado de Thijssen et al. 2011.

6.2.2.3 ELEMENTOS ESSENCIAIS NA MEDIDA DA DMF

A figura 2 demonstra os elementos primordiais para a medida da DMF de maneira esquemática.

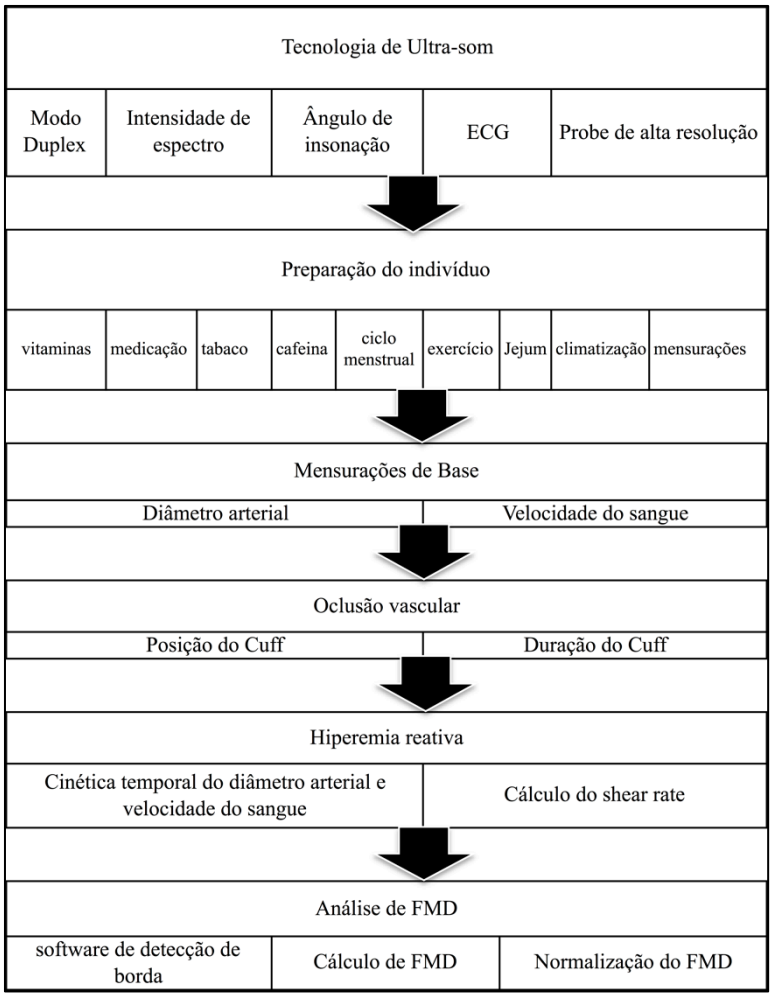

Figura 2. Elementos essenciais para análise da DMF.

Fonte: adaptado de Harris et al., 2010.

6.2.2.4 ULTRASSOM

A medição precisa da DMF é altamente dependente da identificação da parede arterial definida, o que requer imagem de ultrassom de alta resolução. Cada sonda de ultrassom é classificada de acordo com a gama de frequências em megahertz (MHz), que é inversamente proporcional à profundidade da captação da imagem. Para os vasos mais superficiais seria ideal transdutores lineares variantes de 10-14 MHz, atualmente considerada "alta resolução". O modo duplex permite a aquisição simultânea do diâmetro do vaso e velocidade do sangue, respectivamente. Isto permite o cálculo da velocidade de corte, para qualquer período de tempo determinado a partir dos quais a integral de cisalhamento ao longo do tempo, isto é, a área de taxa de cisalhamento sob a curva (AUC – *area under the curve*) pode ser calculada (29).

O ângulo de insonação para o vaso sanguíneo que corre paralelo à superfície cutânea (por exemplo, da artéria braquial) é de 90 graus, porém este é o pior cenário para a avaliação doppler da velocidade do sangue. Alguns comprometimentos da qualidade da imagem, balanço do transdutor para cima em uma extremidade mais do que o outro (conhecido como ajustes de calcanhar/dedos) fará com que o vaso pareça mover na diagonal do monitor a um ângulo inferior a 90 graus. Por vezes essa angulação não fica disponível na coleta, então verificou-se que, embora seja recomendado o ângulo de insonação de 60°, o maior ângulo normalmente aceito na literatura é de 70° (30,31).

Dependendo da rigidez do vaso e da pressão da pulsação o diâmetro arterial pode variar dentro de um único ciclo cardíaco e isso pode confundir completamente a avaliação da DMF. Os sistemas de ultrassom Doppler que possuem um eletrocardiograma (ECG) integrado facilita a avaliação do diâmetro de acordo com o ciclo cardíaco (por exemplo diástole final). Caso não esteja disponível no próprio sistema de ultrassom, um ECG externo pode ser utilizado (32).

Existem inúmeros métodos de cálculos para a velocidade do sangue. A maneira mais simples utiliza o envelope exterior do espectro Doppler para determinar a velocidade média de pico, enquanto que a abordagem um pouco mais complexa integra a área sob este envelope para calcular a velocidade média de pico. No entanto, nenhum desses cálculos reflete com precisão a gama complexa e variável de velocidades e as suas distribuições relativas dentro dos espectros de Doppler. Portanto, para avaliar com precisão a velocidade do sangue, recomenda-se que a intensidade ponderada dos cálculos do tempo médio sejam realizadas para refletir com maior acurácia a contribuição de células vermelhas que se deslocam a velocidades diferentes no interior do vaso (33).

6.2.2.5 PREPARAÇÃO DO SUJEITO

O exercício prévio ou o estado descansado pode influenciar nos resultados, portanto recomenda-se que os voluntários não realizem atividade física por pelo menos 12 horas antes da medição de DMF. Uma única sessão de exercício foi documentada para melhorar a DMF em adultos saudáveis, nos homens com excesso de peso e nas mulheres pós-menopausa (34–36). Além disso, as avaliações da DMF devem ser realizadas sob condições de jejum; no entanto, se o jejum não é possível,

uma refeição padronizada baixo teor de gordura pode ser consumida antes da medição da DMF. O consumo de uma única refeição rica em gorduras e carboidratos é capaz de atenuar a DMF em indivíduos aparentemente saudáveis e diabéticos do tipo II (37,38).

A climatização adequada também se faz importante. Recomenda-se que os indivíduos permanecem na posição em que o estudo será efetuado durante pelo menos 10 minutos em ambiente controlado silencioso com temperatura de 22 a 24° celsius). Além disso, uma visita de familiarização separada dos procedimentos é recomendada para limitar a atividade simpática induzida pelo stress no dia de medição real (39). Dentre as medidas repetidas, vários testes de DMF pode ser realizados com intervalo de 30 minutos entre cada medida. As medidas de DMF apresentam variação diurna, portanto, devem ser realizadas na mesma hora do dia (40).

A suplementação vitamínica pode ser outro fator complicador. Os indivíduos devem se abster de suplementação de vitamina para até 72 horas antes da DMF. Existe evidência direta da redução na circulação de radicais livres após a suplementação antioxidante oral (vitamina C, vitamina E entre outras) (37,38). Assim como as medicações que recomenda-se ser descontinuada de 1 e 3 dias antes de uma medição da DMF, porém essa cessão da medicação pode não ser viável, portanto devendo ser reconhecida e documentada (41).

Para aqueles indivíduos que fumam, recomenda-se que não fumem nem se exponham a fumaça do cigarro por pelo menos 12 horas antes das medições de DMF (41). A mesma recomendação vale para a cafeína, pois ela inibe a guanilato ciclase solúvel (42,43). Para as voluntárias do gênero feminino, o ciclo menstrual deve estar no mesmo período para a realização da DMF. A produção endógena de estrógeno e progesterona aumenta a atividade da eNOS e capacidade antioxidante influenciando a resposta vasodilatadora (44).

6.2.2.6 AS MEDIDAS NA OCLUSÃO E NA LIBERAÇÃO DO MANGUITO

Para a mensuração das medidas basais e prévias da DMF, a avaliação precisa de um diâmetro médio e das velocidades de sangue simultâneas, com volume de amostra adequada, por pelo menos 10 ciclos cardíacos, e é recomendada antes de

oclusão vascular. Nas medições da oclusão vascular recomenda-se que tanto os dados de diâmetro e velocidade devem ser adquiridos por pelo menos 10 segundos antes de soltar a braçadeira e continuar por pelo menos 2 minutos. Isso permitirá a documentação do diâmetro de pico, análise quantitativa das AUC de cisalhamento. Relatar o momento de pico de vasodilatação pode avaliar a função endotelial mais adequadamente ao se comparar diferentes grupos (39,45).

O software de detecção de borda foi validado, de maneira independente entre dois avaliadores, e é recomendado para a medição do diâmetro arterial. Para fins de padronização, a obtenção de diâmetros deve ser feita por meio de gravação digital de dados contínua e análise não sequencial utilizando software de detecção de bordas. O cálculo de resposta a DMF, com o diâmetro "verdadeiro" de pico, é obtido e expresso como um aumento na vasodilatação acima de valores de referência. A normalização da DMF pelo cisalhamento (AUC) ainda é incerta. Além disso, o tempo para se obter o pico de vasodilatação pode ser um indicador importante (46). Se o software de detecção de borda não está disponível, recomenda-se que os dados (diâmetro e velocidade) sejam coletados a cada 4 segundos para os primeiros 20 segundos após liberação do manguito, seguido por cada 10 segundos para o período de coleta de dados dois minutos restantes (47,48).

O cálculo da DMF como variação percentual utiliza a seguinte fórmula:

$$\text{DMF}(\%) = \frac{\text{(Diâmetro de pico – Diâmetro de base)}}{\text{Diâmetro de base}} \times 100$$

6.2.3 DOPPLER

6.2.3.1 INTRODUÇÃO A ULTRASSONOGRAFIA VASCULAR

O fluxo de sangue através de um vaso é aferido pela diferença de pressão entre as extremidades do vaso e pela resistência apresentada pela parede do vaso. Cada vaso normal no corpo humano tem padrão de fluxo característico representável em formas de onda espectrais obtidos com a ultrassonografia doppler (49). Os sinais de ultrassom refletidos em superfícies fixas tendem a manter a mesma frequência com que foram transmitidos, porém a ultrassonografia com *doppler* reflete sinais de objetos em movimento tais como os glóbulos vermelhos e suas mudanças de velocidade. A saída de uma ultrassonografia *Doppler* é por uma onda contínua e, normalmente, apresenta um sinal sonoro sempre que se tenha circulação na artéria examinada (39,45).

O *scanner duplex* faz análise espectral, delimita a gama de frequências, que são as velocidades do fluxo sanguíneo encontradas na forma de onda arterial durante um ciclo cardíaco. A forma de onda normal de velocidade doppler é composta de três componentes que correspondem a diferentes fases do fluxo arterial: fluxo anterógrado rápido, atingindo um pico durante a sístole, uma reversão transitória do fluxo durante a diástole precoce, e fluxo anterógrado mais lento durante o final de diástole (29).

O feixe de som dirigido perpendicularmente à superfície alvo de interesse para a obtenção da eco imagem, aparece mais brilhante com escalas cinzentas. Com angulação perpendicular, as imagens são mais facilmente obtidas porque as artérias são, geralmente, paralelas ao transdutor. Para o componente *doppler duplex*, um ângulo de 60 graus entre o feixe de insonação e a parede do vaso deve ser mantida. Isto torna o ângulo de Doppler de importante consideração, pois os dados de velocidade podem também ser utilizados para classificar doenças e ângulos acima de 60 graus pode resultar em medidas superestimadas da velocidade e, por isso, devem ser evitados conforme mostrado na figura 3 (50).

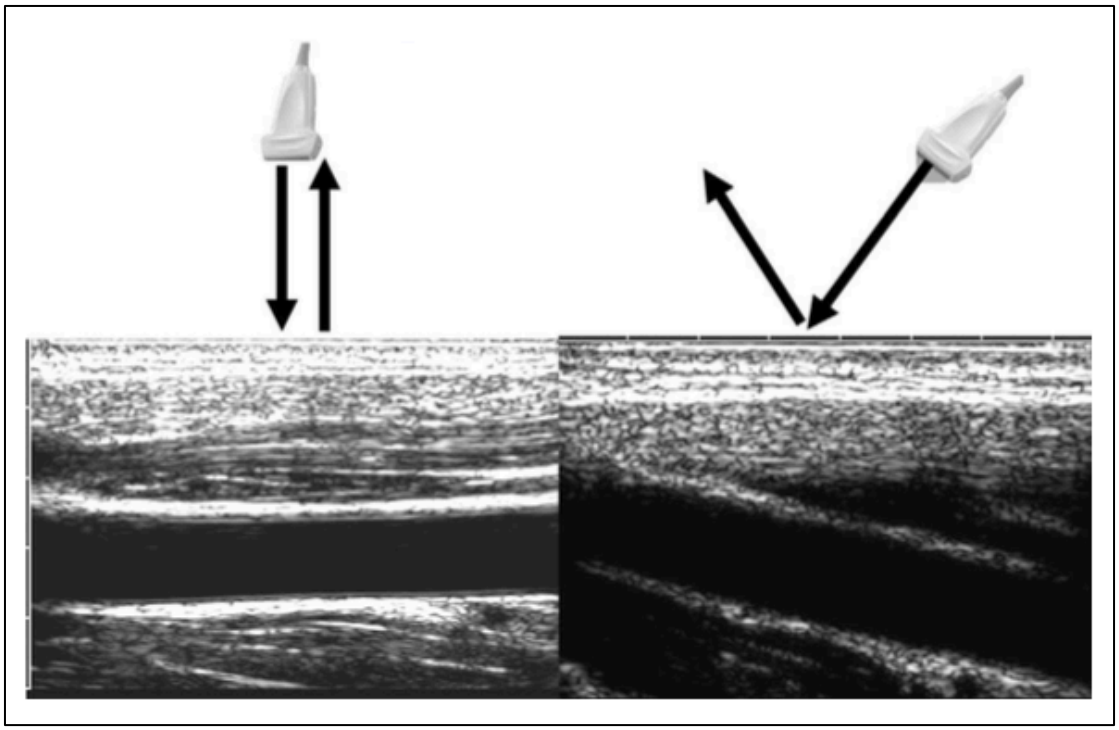

Figura 3. Ultrassom perpendicular e não perpendicular.

Fonte: modificado de Gerhard-Herman et al. 2006

6.2.3.2 CÁLCULO DOS ÍNDICES DE FLUXO ARTERIAL

O índice de resistência (IR) pode ser calculada a partir de medições espectrais usando a equação IR = (PVS - VDF) / PVS, sendo que PVS é o pico de velocidade sistólica e VDF é a velocidade diastólica final. O índice de pulsatilidade (IP) pode ser calculada usando a equação IP = (PVS - VDF) / VM, onde VM é a velocidade média de fluxo durante o ciclo cardíaco (33). Figura 4 ilustra a onda espectral.

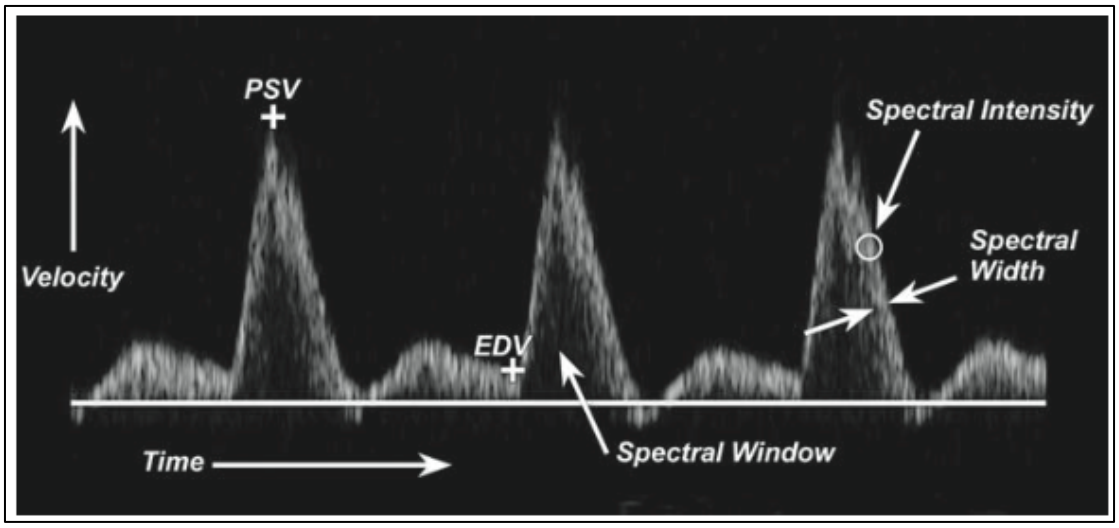

Figura 4. Diagrama da análise espectral do ultrassom com doppler. PVS – pico de velocidade sistólica, VDF – velocidade diastólica final. *Spectral intensity* – Intensidade escpectral, *Spectral window* – janela espectral, *Spectral width*, largura espectral, *velocity* – velocidade e *time* – tempo.

Fonte: modificado de Chavhan et al., 2008.

O IR e o IP fornecem informações sobre o fluxo de sangue e resistência vascular que não pode ser obtida a partir de medições de velocidade absoluta. Os efeitos da variação e angulação do vaso são anulados nos cálculos desses índices. Várias formas de ondas anormais podem ser comparados por meio do cálculo do IR e do IP. Eventos fisiológicos que alteram a resistência vascular incluem: exercício físico, mudanças de orientação gravidade e nível de estresse, digestão entre outros (51).

6.2.3.3 PADRÕES DE FLUXO DOPPLER NORMAIS

Em fluxo de tomada, todas as células vermelhas do sangue se movem com a mesma velocidade, produzindo uma frente de onda plana. O espectro de Doppler a partir deste padrão de fluxo é caracterizado pela linha espectral estreita e uma janela espectral transparente, o qual representa a ausência de velocidades mais baixas. Esta forma de onda é tipicamente vista em grandes artérias, tais como a aorta (26,51,52).

As células vermelhas do sangue periférico movem com velocidade mais lenta do que os glóbulos vermelhos centrais devido o atrito oferecido pela parede do vaso. Essa diferença de velocidades produz a frente de onda parabólica. No espectros de doppler, ocorrerá o alargamento da linha espectral e enchimento da janela espectral de forma de onda. Este padrão geralmente é visto em vasos com um diâmetro inferior a 5 mm (26,51,52).

O fluxo turbulento consiste em ampla gama de velocidades. Inclui componentes de fluxo invertido e é facilmente apreciado como várias cores nas imagens por doppler colorido. É visível como alargamento espectral com componentes abaixo do fluxo basal. A turbulência perto das bifurcações é considerada normal, porém longe delas é sugestivo de alguma anormalidade (26,51,52). A tabela 1 contém os valores de normalidade da velocidade vascular arterial em algumas artérias da cabeça e pescoço, membros superiores e membros inferiores.

Artéria	PVS (cm/s)	VDF (cm/s)	IR
Carótida externa	57 a 87	11 a 21	0,72 a 0,84
Carótida interna	62 a 90	23 a 37	0,54 a 0,66
Carótida comum	78 a 118	20 a 32	0,72 a 0,84
Femoral comum	100	-	1,37
Femoral superficial	80 a 90	-	1,38
Poplítea	70	-	1,41
Subclávia	105	-	-
Axilar	80	-	-
Braquial	60	-	-

Tabela 1. Valores de normalidade da velocidade vascular.
Legendas: PVS – pico de velocidade sistólica, VDF – velocidade diastólica final, IR – índice de resistência. - Dados não fornecidos pela literatura.
Fonte: modificado de Gerhard-Herman et. al, 2006 (50) e Holland et. al, 1998.(53)

6.2.4 SISTEMA NERVOSO AUTÔNOMO

O SNA é composto pelos nervos e centros nervosos que comandam a vida vegetativa. O termo sistema nervoso autonômico foi descrito por John Newport Langley, em 1898, que considerava este sistema como independente das regiões não vegetativas do sistema nervoso central (54). Ainda é descrito classicamente como sistema motor visceral, inervando a musculatura lisa, o músculo cardíaco modificado (o tecido cardíaco intrínseco encarregado de estimulação e condução dos impulsos nervosos) e das glândulas. As fibras eferentes viscerais se acompanham das aferentes viscerais. Os ramos aferentes são condutores dos impulsos nervosos do sistema doloroso visceral, portanto estas fibras tem papel fundamental na regulação da função visceral. (55,56).

Os ramos eferentes e os gânglios do SNA se organizam dentro de dois sistemas ou divisões denominados sistema nervoso simpático (SNS) e sistema nervoso parassimpático (SNP). A condução dos impulsos nervosos desde o SNC até o órgão efetor dependerá de uma série de neurônios dentro desse sistema. Existem dois neurônios para transmitir a informação pelo SNA. O corpo celular do primeiro neurônio (pré-sináptica ou pré-ganglionar) se encontra dentro da substância cinzenta

na medula espinhal. Seu axônio somente estabelecerá sinapses com corpos celulares de neurônios (pós-sinápticos ou pós-ganglionares), que seriam os segundos neurônios do sistema. O segundo neurônio sempre estará fora do SNC, sendo em um gânglio laterovertebral, no caso do SNS ou no órgão efetor, incluindo músculo liso, cardíaco especializado e as glândulas, que fazem parte do SNP (57,58).

Essa diferenciação leva a um entendimento sobre a diferença entre as fibras pré-ganglionares e pós-ganglionares. No SNS as fibras pré-ganglionares são curtas, enquanto que as fibras pós-ganglionares são longas para poder atingir o órgão alvo do nervo. Já no SNP as fibras pré-ganglionares são fibras longas enquanto que as pós-ganglionares são fibras curtas, pois estão próximas ou no órgão alvo do sistema. Além disso, a divisão simpática e a parassimpática tem uma diferença em relação aos neurotransmissores. O SNS utiliza a noradrenalina como neurotransmissor (exceto as glândulas sudoríparas) e o SNP, a acetilcolina (56,58).

O SNS e o SNP têm funções antagônicas em relação ao funcionamento visceral torácico, abdominal e craniano. De forma geral, o SNS atua aumentando o funcionamento das vísceras supra diafragmáticas (torácicas) e diminuindo as vísceras infradiafragmáticas (abdominal), sendo que o SNP atua de forma oposta. Em relação ao crânio, o SNP estimula o funcionamento das glândulas e o SNS diminui o seu funcionamento (59). A figura 8 mostra a divisão do SNS e SNP.

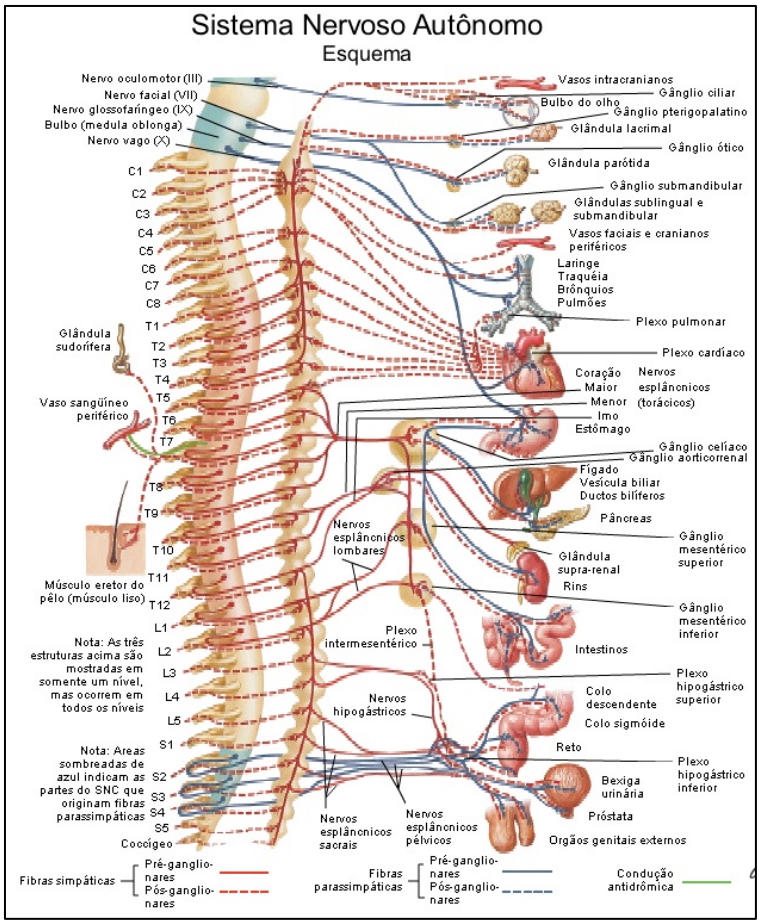

Figura 5. Esquema representativo do sistema nervoso autônomo simpático e parassimpático.

Fonte: Netter, 2011.

6.2.4.1 SISTEMA NERVOSO SIMPÁTICO (SNS)

Foi descrito pela primeira vez por Jacob B Winslow, da sua obra exposição anatômica da estrutura do corpo humano, publicado em 1732, o termo simpático foi baseado de uma palavra grega denominada *simpatein*, que significa “sofrer com”, visto que esse anatomista entendia que as doenças eram levadas de um órgão a outro por meio desse sistema. O SNS foi descrito antes mesmo do entendimento do SNS como parte do SNA (60).

O SNS está anatomicamente localizado no segmento tóraco lombar. Entre os níveis de T1 e L2(3) estão localizados os núcleos intermédios laterais, localizados bilateralmente na substância cinzenta da medula. Tais núcleos são compostos de neurônios pré-sinápticos do SNS e parecem hastes laterais da substância cinzenta, que

adota forma em H nos cortes horizontais. Nesses núcleos estão localizados o corpo celular do primeiro neurônio do SNS. O corpo celular do segundo neurônio encontra-se em dois lugares, os gânglios para vertebrais e os gânglios pré-vertebrais (54).

Os gânglios para vertebrais se unem para formar as cadeias latero vertebrais simpáticas direita e esquerda de cada lado da coluna vertebral se localizando em toda a extensão da coluna. Cada nível da coluna apresentará um par de gânglio correspondente. Entretanto, na coluna cervical, estes gânglios têm diferenciações, sendo chamados de gânglios cervicais superior, médio e inferior. Para alguns autores o gânglio cervical inferior e o primeiro gânglio torácico se unem formando o gânglio estrelado. O gânglio ímpar se forma na parte inferior quando se unem os troncos a altura do cóccix (61).

Os gânglios pré-vertebrais se unem em plexos que acompanham os principais ramos da aorta abdominal. Os principais são o gânglio celíaco, mesentérico superior, aórtico renal, mesentérico inferior e Inter mesentérico que farão a inervação das vísceras subdiafragmáticas incluindo estômago, pâncreas, duodeno, fígado, intestino delgado, porção cólon ascendente e 2/3 proximais do cólon transverso e baço – celíaco; 1/3 distal do cólon transverso, cólon descendente, sigmóide, reto e ânus – mesentérico superior; útero/próstata, bexiga, 1/3 distal do ureter, uretra, ovários/testículos (mesentérico inferior); rins e 2/3 proximais do ureter (aórtico renal) (61).

A partir dessas ramificações, formam-se os plexos autonômicos, que serão denominados, celíaco, mesentérico superior, aórtico renal e mesentérico inferior, sendo que os 3 primeiros com o nervo vago fazendo a porção parassimpática e o último sendo o parassimpático sacral com o nervo esplânico pélvico, respeitando as inervações já mencionadas em relação aos seus órgãos alvo (62).

6.2.4.2 SISTEMA NERVOSO PARASSIMPÁTICO (SNP)

A divisão parassimpática do SNA foi descrita pelo anatomista inglês John Newport Langley, o mesmo que descreveu o SNA, e nomeou o parassimpático por este termo representar “ao lado” do sistema simpático, visto que este sistema se localiza, anatomicamente, no crânio e no sacro (61). Dividido em parassimpático sacral, cranial e visceral, é o antagônico natural do simpático e possui

anatomia diferenciada. A sua porção cranial é composta pelos pares cranianos III, VII e IX sendo responsável pela porção parassimpática da pupila, secreção lacrimal, secreção nasal e secreção bucal (61).

O nervo vago (X) possui o trajeto mais longo e a distribuição mais extensa de todos os pares cranianos. Seu nome é originado do latim *vagari*, que significa errante, devido a sua extenso comprimento. Origina-se por uma série de radículas da face lateral do bulbo, núcleo dorsal do vago e núcleo do trato solitário de cada lado do bulbo, que se fundem e deixa o crânio através do forame jugular entre os pares IX e XI (55,61,62). Antes da saída do X do crânio existe um gânglio (Gânglio superior) que está relacionado com o seu componente sensitivo geral do nervo, inferiormente ao forame, há um gânglio inferior (nodoso) relacionado com os componentes sensitivos viscerais do nervo. Continua seu trajeto inferiormente na bainha carotídea até a base do pescoço onde enviará ramos para o palato, a faringe e a laringe (55,61,62).

Em sua porção craniana o X apresenta um ramo meníngeo para a duramater e um ramo auricular, na região cervical ramos faríngeos para o plexo faríngeo (motor) ramos cardíacos cervicais (aferentes viscerais), nervo laríngeo superior, ramos internos e nervo laríngeo recorrente direito. Na porção torácica o nervo laríngeo recorrente do lado esquerdo, ramos cardíacos torácicos ramos pulmonares e plexo esofágico. Na região abdominal ramos esofágicos, gástricos, hepáticos, celíacos, pilóricos, renais e intestinais para flexura esquerda do cólon. O nervo esplânico pélvico é o responsável parassimpático dos órgãos da pelve baixa no homem e na mulher originários de S2 a S4 (55,61,62).

Existe uma descrição anatomo-fisiológica que propõe que existe uma porção parassimpática localizada na medula espinhal ignorada pela maioria dos autores. Essa existência é discutida e foi estudada por Hashimoto, Kuré e Okinaka em estudo publicado em 1933 que verificou a presença de fibras vasodilatadoras da língua em segmentos da coluna cervical alta. Seus axônios saem pela raiz posterior para se articular ou no gânglio espinal ou no gânglio laterovertebral com um segundo neurônio homólogo ao neurônio pós ganglionar clássico. Esse sistema parassimpático axial é negado pela maioria dos autores. Atribuiria-se a este sistema parassimpático axial a vasodilatação ativa dos vasos do tronco e dos membros (63).

6.2.4.3 FISIOLOGIA DO SISTEMA NERVOSO AUTÔNOMO CARDIOVASCULAR

O SNA controla tônica e reflexamente o sistema cardiovascular, por meio dos neurotransmissores adrenalina e acetilcolina liberadas no coração que modificam o débito cardíaco por alterar a força de contração das fibras miocárdicas e a sua frequência cardíaca. Nos vasos, a liberação de noradrenalina modifica o estado contrátil do músculo liso vascular e a sua resistência vascular periférica. Contudo, o simpático pode exercer efeito nas células musculares lisas e miocárdicas gerando um efeito trófico (20).

As respostas reflexas do SNS e do SNP permitem ajustes do débito cardíaco e da resistência vascular periférica, contribuindo para a estabilização e manutenção da pressão arterial sistêmica durante diferentes situações fisiológicas. Nesse contexto, sabe-se de pelos menos três arcos reflexos que estão envolvidos na modulação da atividade parassimpática para o coração e simpática para coração e vasos, ligados aos baroceptores arteriais (alta pressão), aos receptores cardiopulmonares (baixa pressão) e aos quimoceptores arteriais (64,65).

Os baroceptores arteriais são sensíveis às deformações da parede vascular e, devido ao seu alto ganho, constituem-se na forma mais importante de controle da pressão arterial em curto prazo, ou seja, momento a momento. Além do controle reflexo da atividade autonômica, exercem também um controle tônico inibindo a atividade simpática e, por consequência, estimulando a parassimpática. Assim, o comprometimento de sua função, por não modular a atividade simpática e parassimpática de modo adequado, pode atuar como elemento permissivo ao estabelecimento de alterações primárias de controle da função cardiovascular (66,67).

Os receptores cardiopulmonares são distribuídos em três grupos de receptores que são ativados por mudanças na pressão das câmaras cardíacas, induzindo respostas reflexas autonômicas que modulam principalmente a frequência cardíaca, a dilatação da vasculatura muscular esquelética, a resistência renal e seu débito urinário. Os quimiorreceptores arteriais respondem a aumentos ou quedas de PO_2, PCO_2 e/ou pH desencadeando respostas homeostásticas do sistema cardiorrespiratório para corrigir essas variações; quedas na PO_2 e aumentos da PCO_2 e no pH, elicitam respostas autonômicas reflexas de aumento da resistência periférica (68,69).

O controle reflexo da circulação comandado pelos baroceptores é um importante preditor de risco após evento cardiovascular. Existem evidências clínicas do valor prognóstico da sensibilidade do barorreflexo e da variabilidade da frequência cardíaca (VFC) na mortalidade cardíaca pós infarto do miocárdio, independente da fração de ejeção do ventrículo esquerdo e de arritmias ventriculares. Dessa forma, intervenções no sentido de melhorar a sensibilidade do barorreflexo, inibir a simpaticotonia e aumentar ou melhorar a participação do *imput* vagal cardíaco no controle da PA e da FC são estratégias não prioritárias no manejo das doenças cardiovasculares (70).

6.2.4.4 DISFUNÇÃO AUTÔNOMA NA INSUFICIÊNCIA CARDÍACA

A ativação dos sistemas neuro-humorais, especialmente o sistema nervoso simpático, está envolvida na progressão e aumento da mortalidade na IC. No início da lesão miocárdica há a ativação aguda desse sistema como resposta adaptativa e tem por finalidade manter ou restaurar os níveis de débito cardíaco e PA. Em modelos experimentais de IC, a atividade nervosa simpática está presente no início da disfunção ventricular esquerda. Além disto, existem evidências de que alterações precoces do barorreflexo estão relacionadas ao estresse oxidativo, em um modelo experimental de IC (65,71).

Em pacientes com insuficiência cardíaca, Grassi e cols. observaram por meio da técnica de microneurografia, que a atividade nervosa simpática muscular encontrava-se significativamente maior quando comparada aos indivíduos saudáveis, e que ela aumentava com a gravidade da doença. Pacientes com IC de diferentes etiologias sem sobrecarga de volume ou pressão, também demonstraram simpaticotonia importante (72).

Entretanto, o mecanismo essencial responsável pela hiperatividade simpática na IC permanece desconhecido e pode estar relacionado a diversos sistemas, tais como: atenuação da sensibilidade dos mecanorreceptores arteriais e cardíacos; alteração pressórica na artéria e no capilar pulmonar; exacerbação do quimiorreflexo periférico e central; ativação das aferências simpáticas cardíacas que estão relacionadas à sensação de dor cardíaca durante a isquemia coronariana; ativação dos aferentes renais sensíveis a estímulos mecânicos ou químicos e ativação do sistema renina-angiotensina, entre outros tal como a hiperatividade medular simpática

responsável pelas disfunções osteopáticas. Como a atividade simpática está envolvida na adaptação circulatória da IC desde a instalação e durante a sua progressão e tem valor prognóstico, atualmente são estudadas várias estratégias para reverter o remodelamento miocárdico estrutural e hipertrófico que em geral são divididas em terapias farmacológicas e não farmacológicas (68,73).

Com o tratamento clínico ou cirúrgico adequado na IC, ocorre redução dos níveis circulantes de catecolaminas e da atividade simpática. Em estudo realizado a reversão da disfunção sistólica na miocardiopatia hipertensiva, por tratamento medicamentoso, leva a redução da atividade simpática para o coração e melhora do reflexo cardiopulmonar e do barorreflexo. Estímulos elétricos podem levar a diminuição da simpaticotonia como demonstrado por Vieira e cols com a aplicação de TENS no gânglio estrelado levando a melhora da FC, diminuição da atividade simpática e melhora da PA (74–76).

Existe consenso de que a função vagal preservada é benéfica na manutenção da variabilidade da pressão arterial com consequente proteção de lesão de órgãos-alvo, em especial na isquemia do miocárdio. Além disso, existem evidências experimentais de atenuação de resposta da freqüência cardíaca durante a estimulação do nervo vago em cães com insuficiência cardíaca, que podem resultar de alterações na liberação, degradação e ligação da acetilcolina ou na atividade da enzima acetilcolinesterase no coração (77).

A administração de algumas drogas parassimpatomiméticas e beta-bloqueadoras após infarto do miocárdio e na insuficiência cardíaca tem demonstrado aumento da VFC, indicando efeito protetor sobre o sistema cardiovascular. A busca por terapias com ação cardioprotetora devem ser capazes de inibir a ocorrência de eventos cardíacos em situações de estresse ou esforço físico. A terapia medicamentosa e a atividade física hoje são as terapias de maior relevância clínica para esses pacientes (78–80).

6.2.5 VARIABILIDADE DA FREQUÊNCIA CARDÍACA (VFC)

A variabilidade da frequência cardíaca (VFC) demonstra as oscilações entre os batimentos cardíacos consecutivos entre os picos R-R que tem influência do SNA sobre o nódulo sinusal do coração. Descrita e estudada há vários anos, seu interesse

clínico surgiu quando pode monitorar o sofrimento fetal. Em seguida vieram os estudos associando a VFC diminuída a maior risco de mortalidade pós infarto do miocárdio, sendo assim um preditor de mortalidade. O estudo de Cole et al., do *new england journal of medicine* demonstrou de vez a associação entre a baixa frequência cardíaca de recuperação pós exercício e a mortalidade. (75,81,82).

6.2.5.1 FISIOLOGIA DA VARIABILIDADE DA FREQUÊNCIA CARDÍACA

A excitação cardíaca inicia-se com um impulso gerado no nódulo sinusal, o qual é distribuído pelos átrios, resultando na despolarização atrial, que é representada no ECG pela onda P. Este impulso é conduzido aos ventrículos por meio do nódulo atrioventricular e distribuído pelas fibras de Purkinje, resultando na despolarização dos ventrículos, a qual no ECG é representada pelas ondas Q, R e S, formando o complexo QRS. A repolarização ventricular é representada pela onda T. Os índices de VFC são obtidos pela análise dos intervalos entre as ondas R, as quais podem ser captadas por instrumentos como eletrocardiógrafos, conversores analógicos digitais e os cardiofrequencímetros, a partir de sensores externos colocados em pontos específicos do tórax.

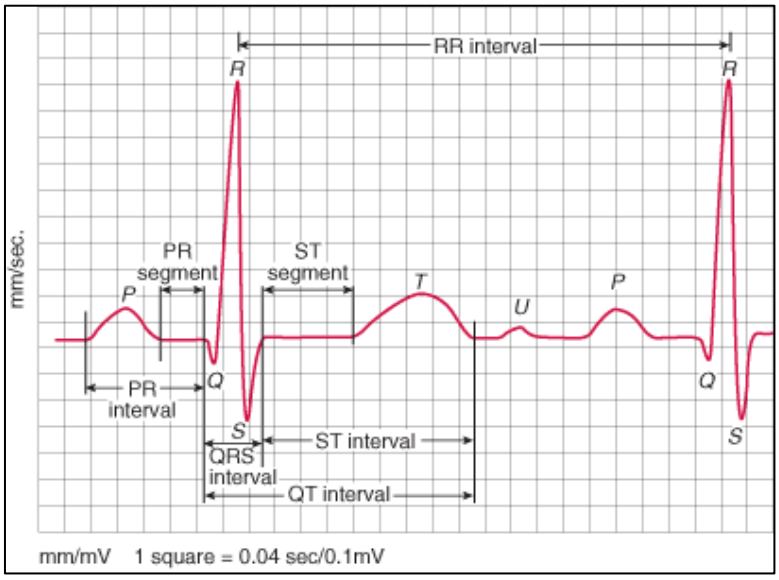

Figura 6. Traçado do eletrocardiograma e o intervalo R-R.

Fonte: Site da internet: http://www.medicine.mcgill.ca/physio/vlab/cardio/introecg.htm. Acessado em 10/07/2015.

6.2.5.2 DISPOSITIVOS DE MENSURAÇÃO E ÍNDICES DA VARIABILIDADE DA FREQUÊNCIA CARDÍACA

O padrão ouro para a mensuração da VFC é o ECG. Contudo, apresentam dificuldades de serem aplicados em situações externas ao ambiente de laboratório (atividade física, hospital, clínicas etc). Além disso, apresentam um alto custo, portanto os cardio frequencímetros surgiram para solucionar tais dificuldades. O frequencímetro Polar S810 apresentou boa acurácia em situações de repouso e de exercício quando comparados com o ECG (83–85). Contudo, o polar não registra possíveis erros de medidas, sendo necessário um ECG prévio para identificar possíveis arritmias. Além disso, é dito que o polar possa superestimar os valores de VFC (86).

A VFC pode ser obtida por meio de vários métodos. Dentre eles, existem os lineares e não lineares. Os métodos lineares são divididos em temporal (realizado por meio de índices estatísticos e geométricos) e frequencial. As unidades temporais são em milissegundos medidos a cada intervalo RR. Em seguida, pode-se obter média, desvio padrão e índices derivados do histograma e mesmo mapa de coordenada cartesianas desse intervalo. A transformação dos valores temporais em frequenciais do intervalo RR determina a análise frequencial (87).

Dentre inúmeras formas de mensurar as medidas temporais, os principais índices são apresentados: Intervalo RR – intervalo entre as medidas R e R do eletrocardiograma, expresso em ms; SDNN – Desvio padrão de todos os intervalos RR normais gravados em um intervalo de tempo, expresso em ms; RMSSD – É a raiz quadrada da média do quadrado das diferenças entre intervalos RR normais adjacentes, em um intervalo de tempo, expresso em ms. O índice SDNN representa atividades simpática e parassimpática sem distinguir as alterações. Entretanto, o índices RMSSD representa a atividade parassimpática (88–90).

As medidas de Poincaré apresentam um método geométrico para análise da dinâmica da VFC. Esta medida representa uma série temporal dentro de um plano

cartesiano no qual cada intervalo RR é correlacionado com o intervalo antecedente. Com essa definição em um ponto, isso é plotado em um gráfico. Contudo, as mensurações podem ser feitas de forma qualitativa (visual), ou por meio da avaliação da figura formada pelo seu atrator. No ajuste da elipse obtêm-se os índices SD1 e SD2. O SD1 representa a dispersão dos pontos perpendiculares à linha de identidade e parece ser um índice de registro instantâneo da variabilidade batimento a batimento e o SD2 representa a dispersão dos pontos ao longo da linha de identidade e representa a VFC em registros de longa duração (91,92).

Outro método linear muito utilizado é o domínio da frequência. O tacograma contém um sinal aparentemente periódico que oscila no tempo e que é processado por algoritmos matemáticos, como a transformada rápida de *Fourier* (FFT) ou modelos auto-regressivos (AR). Esta análise decompõe a VFC em componentes oscilatórios fundamentais, sendo que os principais são: Componente de alta frequência (*High Frequency* - HF), com variação de 0,15 a 0,4Hz, que corresponde à modulação respiratória e é um indicador da atuação do nervo vago sobre o coração; Componente de baixa frequência (*Low Frequency* - LF), com variação entre 0,04 e 0,15Hz, que é decorrente da ação conjunta dos componentes vagal e simpático sobre o coração, com predominância do simpático e suas respectivas medidas normalizadas. A relação LF/HF caracteriza o balanço simpato-vagal sobre o coração. O poder total (*total power*) representa a área do gráfico do tacógrafo. Outras medidas como a VLF e ULF (*very low frequency* e *ultra low frequency* respectivamente) são questionadas quanto a sua função (87,88,91,93,94). A tabela 1 resume as principais variáveis da VFC.

Variáveis Temporais	Variáveis Frequenciais	Análise de Poincarré
Média do Intervalo RR – valor dado em Milissegundos (ms). Indicador vagal	TP – *Total Power*. Área espectral total (PT) – indicador global do sistema	SD1 Desvio vertical (ms) – indicador vagal
SDNN – *Standard Deviation* N-N (ms). Desvio Padrão dos intervalos N-N. Indicador vagal	LF – *Low Frequency*. Baixa frequência (BF) (ms2), espectral absoluta de BF – indicador simpatovagal	SD2 Desvio horizontal (ms) – indicador global simpatovagal
RMSSD – *Rooth Mean Square Standard Deviation* (ms). Desvio padrão da Raíz quadrada da média. Indicador vagal	LFnorm. - Baixa freqüência normalizada (BFnorm) (%), espectral normatizada de BF – percentual de simpático	
	HF – *High Frequency*. Alta freqüência (AF) (ms2), espectral absoluta de AF – indicador vagal	
	HFnorm. – Alta freqüência normalizada (AFnorm), espectral normatizada de AF (%) – percentual vagal	
	LF/HF – Balanço autonômico (BF/AF) (ms2/ ms2) – índice entre simpático e vago, sendo que os valores >1 indicam simpaticotonia relativa, =1 anfotônico, <1 vagotonia relativa.	

Tabela 2. Variáveis desfechos da VFC e suas explicações.

Fonte: modificado de Vanderlei, 2009.

6.3 JUSTIFICATIVA

Portanto, ainda há escassez de estudos avaliando os efeitos do tratamento manipulativo osteopático na função vascular e autonômica ao mesmo tempo em pacientes com IC (lacuna 1). Soma-se a isso as controversas respostas autonômicas pós técnicas de manipulação (AVBA) ou técnicas de mobilização intra articular (MIA) da coluna vertebral em indivíduos saudáveis (lacuna 2). E por último, dúvida acerca das respostas cardiovasculares da pressão arterial e frequência cardíaca pós tratamento manipulativo osteopático cervical do tipo manipulação de AVBA (lacuna 3).

Nesta tese são apresentados 3 estudos desenvolvidos para se preencher as lacunas descritas. Realizou-se um ensaio clínico randomizado e aleatorizado [manuscrito 1] com o objetivo de verificar as modulações vasculares e autonômicas após o tratamento manipulativo osteopático em cardiopatas (lacuna 1). Uma revisão sistemática com metanálise [manuscrito 2] para tentar entender os feitos da manipulação da coluna no SNA (lacuna 2), além de outro ensaio clínico randomizado e aleatorizado [manuscrito 3] acerca dos efeitos do tratamento manipulativo osteopático cervical nas variáveis cardiovasculares em saudáveis checando a segurança dos pacientes que recebem as técnicas de AVBA (lacuna 3).

6.4 OBJETIVOS PROPOSTOS

A presente tese possui como objetivo principal: verificar os efeitos do tratamento manipulativo osteopático na função vascular e autonômica de pacientes cardiopatas por meio de um ensaio clínico randomizado (lacuna 1). Como segundo objetivo verificar o estado da arte da literatura em relação as manipulações de alta velocidade e baixa amplitude (AVBA) e a mobilização intra articular (MIA) ambas na coluna vertebral e as modulações do SNA e, ainda comparar os resultados dos trabalhos encontrados dentro deste tema por meio de uma revisão sistemática com metanálise (lacuna 2). E por último, demonstrar quais seriam as respostas do tratamento manipulativo osteopático cervical na PA e FC em indivíduos saudáveis por meio de um segundo ensaio clínico randomizado, (lacuna 3).

6.4.1 ORGANIZAÇÃO DO TRABALHO

A organização da presente tese é apresentada da seguinte maneira:

1 – introdução e contextualização dos temas que apresentam relação com a tese, justificativa e objetivos propostos da tese.

2 – apresentação de 3 resumos dos manuscritos que envolvem os trabalhos durante o doutorado.

3 – discussão geral e conclusões integrando as partes do projeto e detalhes extras da execução da tese que não puderam ser apresentados nos manuscritos.

4 – como anexo, uma lista de outros estudos feitos durante o programa de doutorado, que foram apresentados em congressos e auxiliou a um racional mais completo para essa escrita deste tese.

7. ARTIGOS

Foram executados três manuscritos para constar o corpo da presente tese. o primeiro intitulado: efeitos do tratamento manipulativo osteopático na função vascular e autonômica em cardiopatas: um ensaio clínico randomizado é denominado manuscrito 1. o segundo foi chamado de: Efeitos da manipulação e mobilização da coluna vertebral no sistema nervoso autônomo: uma revisão sistemática com metanálise. E por fim, o último manuscrito denomina-se: O tratamento manipulativo osteopático cervical tem efeito imediato e tardio nas variáveis cardiovasculares em indivíduos saudáveis?

7.1 MANUSCRITO 1

O manuscrito 1 será submetido para a revista *Journal of Physioterapy* e foi redigido de acordo com suas normas. Entretanto, com a finalidade de evitar o autoplágio, é apresentado o resumo desse manuscrito.

RESUMO

Objetivo: Verificar o efeito agudo e *time course* do tratamento manipulativo osteopático (TMO) na função vascular e autonômica.

Desenho: Ensaio clinico randomizado. Pacientes foram divididos em grupo TMO e Sham.

Parâmetros: Reabilitação Cardiorrespiratória e Tecnologias Assistivas em Fisioterapia

Participantes: Pacientes com insuficiência cardíaca (n=20, idade 59,5 ±11,82, Weber *Class* C).

Intervenções: Uma sessão de TMO e Sham com um aparelho chamado ativador quiroprático sem carga.

Mensuração da medida principal: Medimos a função vascular por meio da dilatação medida pelo fluxo da artéria braquial (DMF) e a função autonômica por meio da variabilidade da frequência cardíaca. As medidas foram realizadas Pre

intervenção, Pós e *time course* de 10 minutos. Para fins de comparação foi utilizada a análise entre grupos multivariada (MANOVA).

Resultados: Verificamos um aumento da DMF (pre x time course 14%±2,29 para 23,5% ±6,87 p=0,027), absolute difference (pre x time course 0,6mm ±0,159 para 1,07 ±0,29 p=0,03) e peak diammeter (pre x time course 4,9mm ±0,74 para 5,67 ±0,76 p=0,003 and post x time course 5,2mm ±0,58 para 5,67±0,76 p=0,02). Todavia, na função autonômica houve aumento dos índices vagais imediatamente após a técnica (RMSSD, SDNN e SD1) e após 10 minutos de *follow-up* uma manutenção do aumento vagal além de aumento de índice simpático (LF).

Conclusão: A informação mais importante do nosso estudo foi que o TMO é capaz de modular o sistema vascular e autonômico em pacientes com insuficiência cardíaca. Adicionalmente os ajustes vasculares parecem ja ocorrer mesmo antes da modulação autonômica simpática.

Palavras-chave: tratamento manipulativo osteopático, osteopatia, cardiopata, DMF, doppler, variabilidade de frequência cardíaca, sistema nervosa autonômico.

7.2 MANUSCRITO 2

O manuscrito 2 será submetido para a revista *Archives of Physical medicine and Rehabilitation* e foi redigido de acordo com suas normas. Seu resumo é apresentado a seguir:

Resumo

O tratamento manual da coluna vertebral (TMCV) atribui como uma de seus principais embasamentos fisiológicos, os efeitos secundários as modulações autonômicas que este é capaz de causar, todavia essas respostas ainda são controversas na literatura. O objetivo desta revisão sistemática com metanálise foi avaliar a influencia de duas técnicas distintas de TMCV na modulação do sistema nervoso autonômico (SNA). Nós procuramos em três base de dados, MEDLINE (Fev 1965 – Novembro 2015), PEDro (Physiotherapy evidence database) e na Chochrane

library (2015) até Novembro de 2015. Verficamos a qualidade metodológica dos estudos pela escala PEDro. Incluimos os ensaios clínicos que utilizaram mensuração do SNA com variabilidade de frequência cardíaca (VFC), frequência cardíaca (FC) ou a condutância da pele (CP) e que utilizaram a técnica de manipulação de alta velocidade de baixa amplitude (AVBA) ou de mobilização intra articular (MIA) como TMCV. Dois avaliadores independentes selecionaram seis estudos que tiveram pontuação na escala PEDro acima de 6 em todas as variáveis estudadas de VFC, FC e CP. As técnicas de AVBA promovem aumento da LF_{norm} (5,82 ms^2 [95% CI: 2,26 to 9,38 I^2=0% p=0,001])e LF/HF(0,38 [95% CI: 0,10 to 0,66 I^2=0% p= 0,008]), enquanto que, durante a aplicação de MIA, há um aumento da CP(6,66 [95% CI: 1,28 to 12,04 I^2=0% p=0,02]). O local de aplicação da técnica não influenciou o resultado obtido. Em nossos resultados, as técnicas de AVBA não alteraram o sistema nervoso parassimpático e a FC. Supreendentemente, após a execução da MIA, condutância da pele também não alterou. Esta metanálise indica que a TMCV, em especial as manobras de AVBA e de MIA, independente da região da coluna, provocam uma excitação no SNA simpático em sujeitos sadios. Entretanto a mudança provocada pela MIA ocorre apenas durante a execução da técnica, mas parece não se manter após a aplicação.

7.3 MANUSCRITO 3

O manuscrito 3 foi submetido para a revista *Journal of manipulative and physiological therapeutics* e o resumo é apresentado a seguir:

RESUMO

OBJETIVO: avaliar os efeitos do tratamento manipulativo osteopático (TMO) cervical sobre a pressão arterial (PA) e freqüência cardíaca (FC) de maneiras imediatas e *time course* em indivíduos jovens saudáveis.

MÉTODOS: Um único ensaio clínico randomizado duplo cego foi realizado. A amostra do estudo incluiu 77 voluntários aleatoriamente randomizados em 3 grupos: grupo tratamento manipulativo osteopático (TMOG) com estimulação sob a região da coluna C1 e C2 bilateralmente, o grupo Sham (SHG) com dispositivo denominado

ativador quiroprático sem carga e grupo controle (CTG) sem estimulação. Foi avaliada a PA e FC no início e após 1 e 10 minutos e 24 horas posteriores. Para comparar a PA e FC entre os grupos de análise multivariada de variância (MANOVA) foi utilizado.

RESULTADOS: Não foi encontrada qualquer alteração relevante na PA e FC após TMO cervical em nenhum dos grupos imediatamente. Além disso, os resultados não demonstram alterações significativas em 24 horas de *time course*.

CONCLUSÃO: Apesar da proximidade do gânglio cervical com C1 e C2 vértebras, este estudo mostra que o TMO cervical não induz uma alteração imediata e 24 horas significativa na PA e FC. De acordo com estes resultados, os pacientes jovens saudáveis não apresentam efeitos colaterais cardiovasculares com manipulação cervical.

Palavras-chave: tratamento manipulativo osteopático; manipulação Osteopática; manipulação vertebral; manipulação da coluna vertebral; frequência cardíaca; pressão sanguínea

8. DISCUSSÃO GERAL E CONCLUSÕES

8.1 INTEGRAÇÃO DAS PARTES DO PROJETO

Para o manuscrito 1, foi demonstrado por meio deste ensaio clínico randomizado que o tratamento manipulativo osteopático é capaz de promover a modulação vascular aumentando a DMF braquial, e suas medidas adjacentes como a medida basal e o diâmetro de pico. Contudo, tal resposta parece não ser modulada agudamente pelo SNA simpático visto que esta foi após a mudança vascular. Do que é do nosso conhecimento, esse é o primeiro estudo que avaliou as respostas vasculares e autônomas ao mesmo tempo após o tratamento manipulativo osteopático. Esse resposta nos leva a entender que as alterações do SNA simpático promovidas pelo tratamento manipulativo osteopático pode ocorrer em resposta à alteração arterial prévia.

O manuscrito 2 demonstra que a compilação dos resultados da presente meta-analise demonstrou que as técnicas manuais da coluna vertebral são capazes de modular de forma aguda o SNA em sujeitos saudáveis em comparação com o sham. As técnicas de alta velocidade e baixa amplitude (AVBA), promovem aumento de 2 variáveis da variabilidade da frequência cardíaca (LF_{norm} e LF/HF), enquanto que, durante a aplicação da mobilização intra articular (MIA), há um aumento da condutância da pele (CP). O local de aplicação da técnica não influenciou o resultado obtido. Em nossos resultados, as técnicas de AVBA não alteraram o sistema nervoso parassimpático e a frequência cardíaca. Supreendentemente, após a execução da MIA a CP também não alterou. Do que é do nosso conhecimento, esse é o primeiro estudo que avalia essas respostas por meio da metanálise.

O manuscrito 3 demonstra que os resultados do tratamento manipulativo osteopático cervical não alterou o sistema cardiovascular em jovens saudáveis. Devido à proximidade dos gânglios cervicais simpático na coluna cervical, era esperado que o pudesse modular a FC e PA. Foram avaliados os efeitos imediatos e após 10 minutos porque talvez as respostas cardiovasculares poderiam levar mais tempo para ocorrer. Além disso, esperamos 24 horas para avaliar novamente, no entanto, sem mudanças. Com isso, pode-se concluir que essas técnicas apresentam

segurança do ponto de vista cardiovascular, visto que não leva a alterações significativas.

Para os dados do manuscrito 1, além das medidas de vasculares de DMF e autonômicas de VFC, foi mensurado o fluxo arterial durante a desoclusão. Considerando a limitação da formatação, este dado não foi incluído no manuscrito 1, porém é demonstrado nesta seção. O fluxo foi mensurado pré, pos imediato e 10 minutos de prosseguimento. A cada liberação de oclusão foram mensuradas 10 medidas de velocidade média e índice de resistência. A figura 16 mostra o comportamento do fluxo sanguíneo por meio das medidas de velocidade média e índice de resistência do vaso. Há diminuição da velocidade e da resistência, indo de acordo com os achados prévios do manuscrito 1.

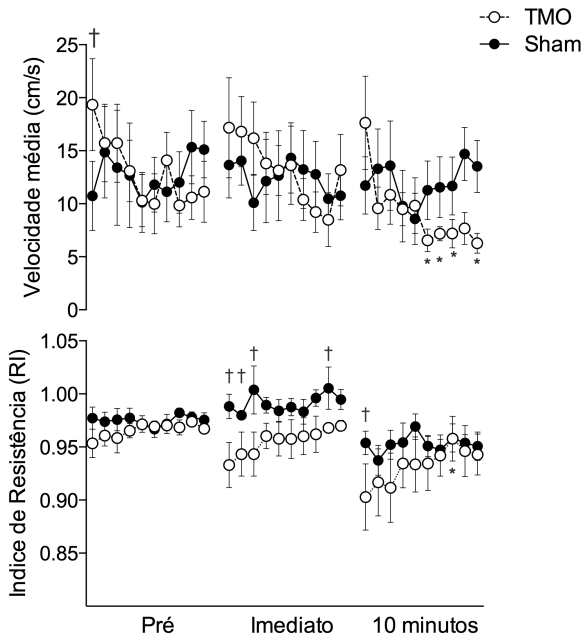

Figura 7. Comportamento da velocidade média do vaso e índice de resistência pré, pós imediato e 10 minutos de prosseguimento. TMO – tratamento manipulativo osteopático

Fonte: próprio autor, 2015.

O tratamento manipulativo osteopático parece de fato modular o sistema vascular e autonômico em cardiopatas. Contudo, o fato que chama mais atenção nesse primeiro estudo é que as respostas autonômicas simpáticas parecem vir depois das

respostas vasculares. Houve um incremento parassimpático e a modulação vascular ao mesmo tempo, gerando um aumento da resposta da DMF. Dentre as respostas autonômicas que seriam esperadas, a diminuição do SNA simpático justificaria o aumento do diâmetro do vaso, porém isso não ocorreu. Portanto, tal padrão parece nos levar a um entendimento que, nesse caso, as respostas autonômicas simpáticas podem ser moduladas pelo comportamento vascular e/ou central do sistema nervoso.

Em relação ao manuscrito 2, o resultado mostram duas respostas distintas, primeiramente demonstrando que as técnicas de AVBA ativam o SNA simpático. Ainda foi verificado que não altera variáveis cardiovasculares tais como a FC. Entretanto, quando a técncia de MIA é realizada, durante a execução da mesma há a ativação autonômica simpatico, porém quando se deixa de dar o estímulo, a ativação cessa. Tal mecanismo é explicado pela ativação da área cinzenta dorsal periaquedural (DPAG) e, através de vias descendentes neurais, ativando o centro cardioacelerador localizado de T1 a T4 na medula espinhal. Com isso, a mobilização, que tem um estímulo por maior tempo no indivíduo, poderia ativar todo esse trajeto levando não apenas a um aumento do SNA simpático, porém em nossa metanálise, vimos que isso não é duradouro, ao contrário das técnicas de AVBA. Ainda se tem dúvidas em relação a quantidade de tempo em que o estímulo perdura.

Em relação ao manuscrito 3, a resposta do estudo que demonstrou que a PA e FC não alteram frente a tratamento manipulativo osteopático cervical nos indivíduos saudáveis mostra segurança sob o ponto de vista cardiovascular. Na presente tese, verificou-se que, ao mesmo tempo que as técnicas de AVBA promovem a modulação simpatica, elas não alteram as variáveis cardiovasculares. Essa informação merece destaque porque se ativar o sistema simpático sem provocar um aumento da PA ou da FC pode ser mais benéfico às pessoas a dependar da sua condição de saúde.

Quando se relaciona a resposta dos 3 estudos, verifica-se a necessidade de se elucidar melhor os mecanismos da função vascular e autonômica pós tratamento manipulativo osteopático. Encontramos nos estudos respostas que nos leva adiante no sentido de entender que as respostas vasculares parecem ser mais independentes do SNA. O SNA simpático, pode ser influenciado pelas respostas vasculares, além de verificarmos as diferenças entre se realizer a técnica de AVBA e de MIA. Contudo, alguns questionamentos ainda ficam para futuras pesquisas e teses: As respostas em

pessoas saudáveis ao tratamento manipulativo osteopático seria da mesma forma como o encontrado em cardiopatas? O estímulo mecânico poderia levar a respostas específicas para os receptores autonômicos cardíacos? Em longo prazo, quais seriam as respostas? Ainda a ciência busca essas respostas.

8.2 DETALHES DA EXECUÇÃO DO PROJETO

Em termos metodológicos, alguns detalhamentos acerca das técnicas não puderam ser colocados no manuscrito final 1. Além disso, foram realizadas uma série de procedimentos de avaliação de dados que poderiam também ser melhor explicados, além de alguns dados que foram deixados para possíveis discussões posteriores. Esta parte é um complemento dessas informações.

8.2.1 TRATAMENTO OSTEOPÁTICO

As manipulações osteopáticas foram realizadas utilizando uma sequência de tratamento baseada na avaliação TART (tensão, assimetria, restrição e dor), conforme descrito no manuscrito 1, porém cabe aqui um maior aprofundamento. Foram verificadas as tensões, assimetrias, restrições de movimento e dor nos pacientes nas regiões relacionadas ao coração e sua inervação autonômica. A base do crânio, coluna cervical e torácica, primeira costela, caixa torácica, diafrágma e a mobilidade cardíaca foram avaliadas sob o ponto de vista osteopático. A maioria das disfunções foram encontradas na cervical média, base do crânio a direita no osso occiptal, primeira costela e na transição C7-T1. Foram corrigidas tais disfunções, associada a um tratamento mais hemodinâmico que incluíram técnicas de bombeio do ducto torácico (*thoracic pump*) e de descompressão cardíaca. Nenhum paciente relatou efeito adverso durante a terapia. O grupo sham recebeu simulação de terapia por meio do ativador quiroprático que foi realizado nos mesmos locais onde foram encontradas as disfunções. As figuras de 8 a 12 mostram as técnicas empregadas durante o tratamento osteopático de acordo com a avaliação.

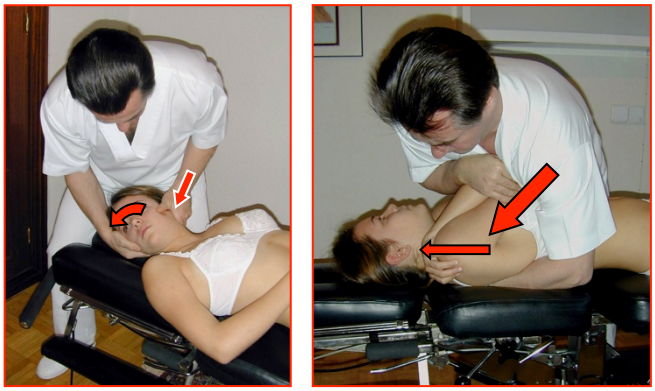

Figura 8. Técnica de manipulação cervical em rotação para a esquerda e manipulação da primeira costela em posterioridade.

Fonte: Ricard, 1993

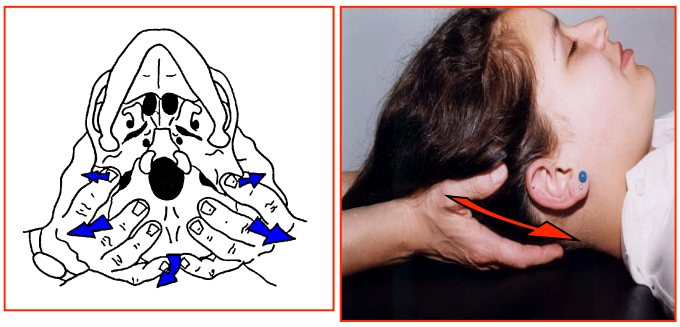

Figura 9. Técnica de descompressão da base do crânio segundo Magoun.

Fonte: Ricard, 2002.

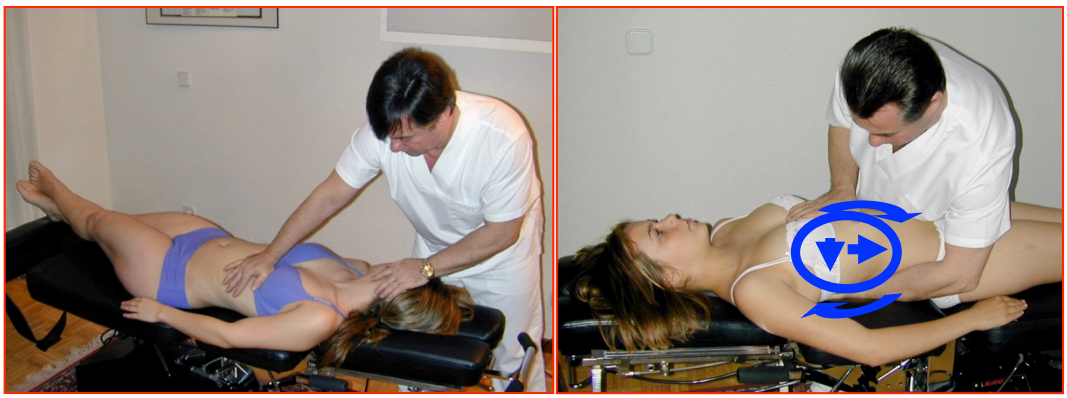

Figura 10. Técnica de estiramento da pleura a esquerda e técnica funcional para o diafragma

Fonte: Ricard, 2015 (25)

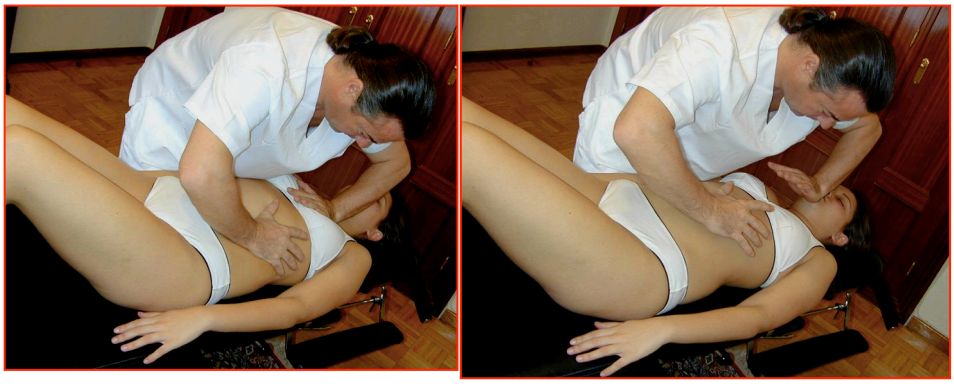

Figura 11. Técnica de descompressão cardíaca. Primeira fase de compressão e segunda fase de descompressão.

Fonte: Ricard, 2015

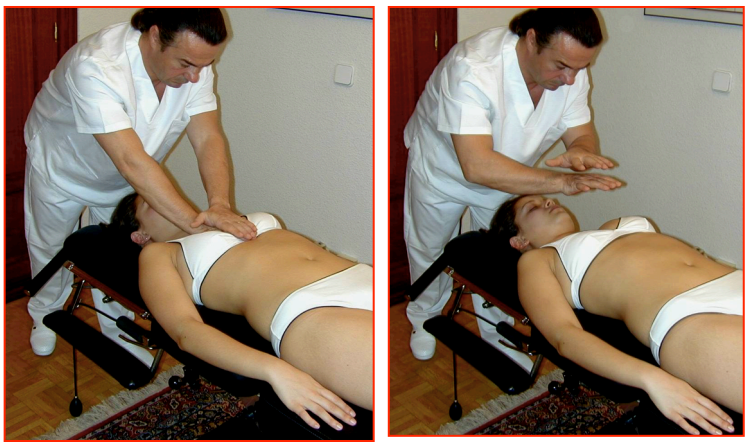

Figura 12. Técnica de bombeio do ducto torácico.

Fonte: Ricard, 2015

8.2.2 AVALIAÇÃO DOS PACIENTES – COLETA DE DADOS

As avaliações foram realizadas ao mesmo tempo, porém foram coletadas outras medidas, tais como a VFC antes, durante e logo após o tratamento manipulativo osteopático. Também medidas de algometria pré e pós tratamento manipulativo osteopático, além dos dados de doppler pré, pós imediato e 10 minutos depois nas artérias braquial, carótida comum e femoral. Tais medidas não entraram no estudo principal pois são medidas que nos ajudam a entender outros aspectos fisiológicas das manipulações. De forma geral, o tratamento manipulativo osteopático provocou um aumento das medidas simpáticas e quase nenhuma alteração nos fluxos,

a não ser da velocidade média do sangue na artéria braquial e uma pequena diferença na femoral.

As figuras em sequência demonstram o protocolo realizado para fins de ilustração. Na figura 13 demonstra o aparelho de ultrassom duplex ao qual foram realizadas as coletas. Em seguida na figura 14 um dos voluntários durante a coleta de dados. As figuras 15, 16 e 17 demonstram os dados já trabalhados de DMF, doppler e VFC.

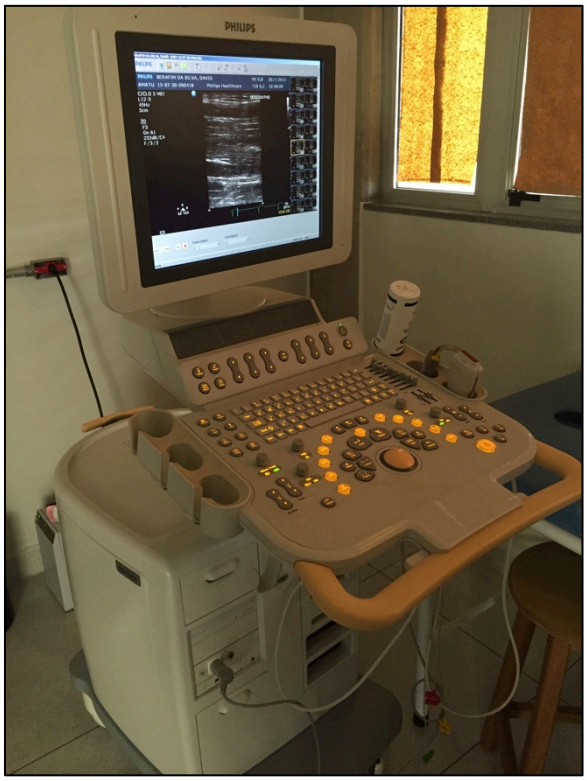

Figura 13. Aparelho de ultrassom utilizado no estudo.

Fonte: próprio autor, 2015.

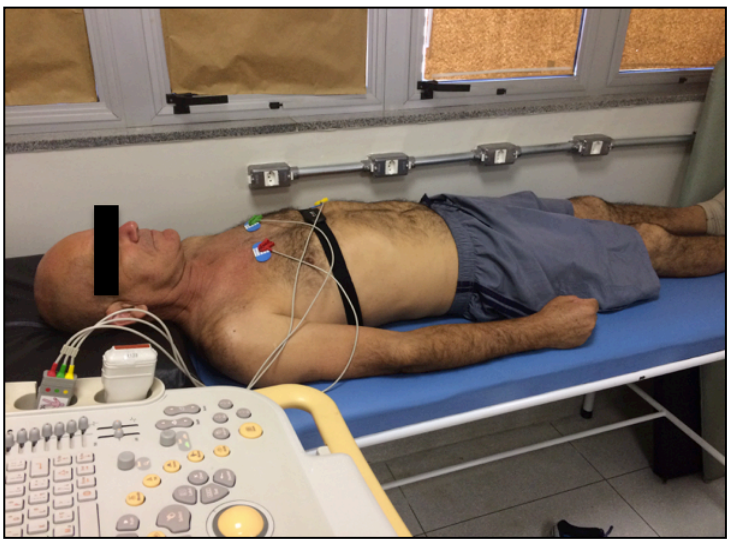

Figura 14. Exemplo de coleta de dados em voluntário

Fonte: próprio autor, 2015.

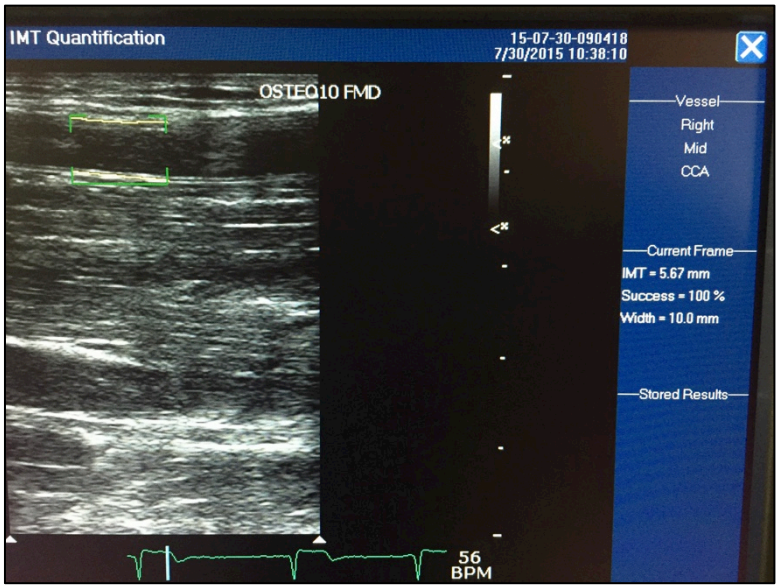

Figura 15. Exemplo de análise com software de detector de borda para a DMF.

Fonte: próprio autor, 2015

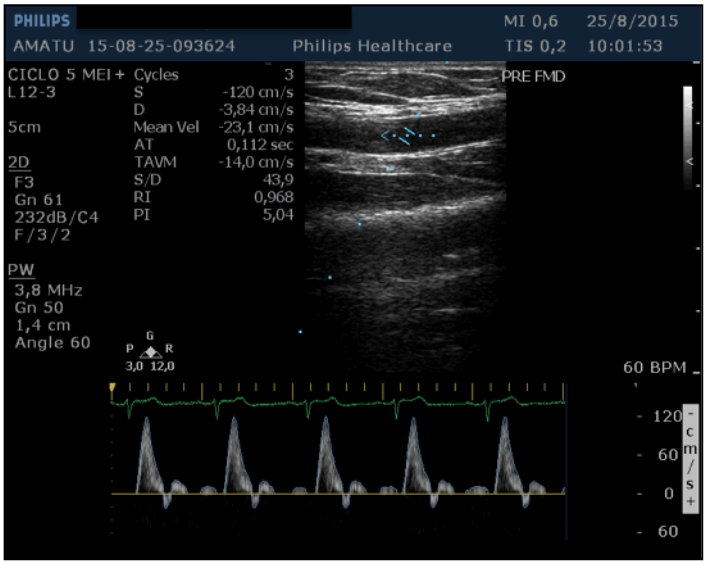

Figura 16. Exemplo de análise de doppler.

Fonte: próprio autor, 2015

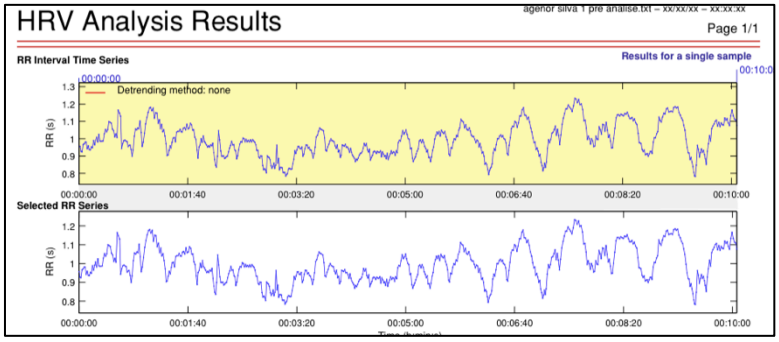

Figura 17. Exemplo de tacograma de variabilidade de frequência cardíaca

Fonte: próprio autor, 2015

8.3 CONCLUSÕES

Portanto, segue a nossa conclusão para a lacuna 1: A informação mais importante do nosso estudo foi que o tratamento manipulativo osteopático é capaz de modular o sistema vascular e autonômico em pacientes com insuficiência cardíaca. Adicionalmente os ajustes vasculares parecem já ocorrer mesmo antes da modulação autonômica simpática. Para a lacuna 2: Revisão sistemática com metanálise: Surpreendentemente, os estudos que mensuraram o SNA com a VFC utilizaram a AVBA como TMCV e aqueles que usaram a CP a técnica empregada foi a MIA. Verificamos a ativação simpática com um aumento na LF normalizada (5,82 ms^2 [95% CI: 2,26 to 9,38 I^2=0% p=0,001]), e LF/HF (0,38 [95% CI: 0,10 to 0,66 I^2=0% p= 0,008]) e aumento da CP (6,66 [95% CI: 1,28 to 12,04 I^2=0% p=0,02]) durante a aplicação da MIA. Contudo, não foram evidenciadas mudanças na FC, no sistema nervoso parassimpático e nem na CP pós MIA. Portanto, o TMCV promove modulação do SNA, e essa alteração é um aumento do sistema nervoso simpático. A lacuna 3: Ensaio clínico randomizado: Apesar da proximidade do gânglio cervical com C1 e C2 vértebras, este estudo mostra que tratamento manipulativo osteopático cervical não produz alteração imediata e 24 horas significativas na PA e FC.

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ANEXO 1 – PRODUÇÕES DURANTE O DOUTORADO

RESUMOS EXPANDIDOS PUBLICADOS EM ANAIS DE CONGRESSOS

1.

AMATUZZI TEIXEIRA; QUINTANILHA, H. L. R. M. ; BRANCO, A. C. ; THOMAZ, S. R.; NAKATA, C. H. ; SILVA, M. ; CIPRIANO JUNIOR, G. . A manipulação Osteopática cevical gera efeitos imediatos na variáveis cardiovasculares em indivíduos saudáveis?. In: congresso da SOCESP, 2015, SÃO PAULO. cardiologia interdisciplinar integrando o humano pelo coração. sao paulo: farol editora, 2015. v. 25. p. 227.

2.

SILVA, V. M. ; LIMA, A. ; AMATUZZI TEIXEIRA ; NEVES, L. ; SILVA, M. ; BOTTARO, M. ; ARENA, R. ; GURNEY, B. ; CIPRIANO JUNIOR, G. ; CIPRIANO, G. . Non-Invasive Ventilation Improves Cardiovascular Adjustments And Fatigability In Patients With Heart Failure. 2013. ATS International Conference, Philadelphia.

APRESENTAÇÕES DE TRABALHO

1.

AMATUZZI TEIXEIRA, F. ; QUINTANILHA, H. L. ; DUARTE, A. C. B. ; THOMAZ, S. ; NAKATA, C. H. ; SILVA, M. L. ; CIPRIANO JUNIOR, G. . A MANIPULAÇÃO OSTEOPÁTICA CERVICAL GERA EFEITOS IMEDIATOS NAS VARIÁVEIS CARDIOVASCULARES EM INDIVÍDUOS SAUDÁVEIS? 2015. (Apresentação de Trabalho/Congresso). Congresso da SOCESP, São Paulo.

2.

AMATUZZI TEIXEIRA, F. ; XAVIER, A. P. ; GOMES, E. ; NAKATA, C. H. ; THOMAZ, S. ; SILVA, M. L. ; CIPRIANO JUNIOR, G. . EFEITOS AGUDOS DO TRATAMENTO MANIPULATIVO OSTEOPÁTICO NA FUNÇÃO AUTONÔMICA EM IDOSOS. 2015. (Apresentação de Trabalho/Congresso). Congresso da SOCESP, São Paulo.

3.

NAKATA, C. H. ; AMATUZZI TEIXEIRA, F. ; Urache LVT ; SILVA, M. L. ; THOMAZ, S. ; LIMA, A. C. G. B. ; SANTOS, F. V. ; BORGES, R. F. ; CIPRIANO JUNIOR, G. . ACUTE EFFECTS OF INTERFERENTIAL ELECTRICAL STIMULATION ON HEART RATE VARIABILITY IN HEALTHY WOMEN. 2015. (Apresentação de Trabalho/Congresso). AACVPR 30th Annual Meeting, Washington.

4.

AMATUZZI TEIXEIRA; CIPRIANO JUNIOR, G. . 1 workshop de redação de artigos científicos. 2015. (Apresentação de Trabalho/Outra). Universidade de Brasília – UnB.

5.

AMATUZZI TEIXEIRA, QUEIROZ, BARREIRA, LISSA, OLIVEIRA, CASTELO BRANCO, MALDANER, JÁCOMO, CIPRIANO JÚNIOR. ACUTE EFFECTS OF OSTEOPATHIC MANIPULATIVE TREATMENT IN HEART RATE VARIABILITY IN PATIENTS WITH HEART FAILURE: A CROSS-OVER STUDY. 2014. (Congresso). Heart Failure Congress, Athenas.

6. SILVA, V. M. ; LIMA, A. ; NEVES, L. ; AMATUZZI TEIXEIRA ; SILVA, M. ; BOTTARO, M. ; ARENA, R. ; GURNEY, B. ; CIPRIANO JUNIOR, G. ; CIPRIANO, G. . Non-Invasive Ventilation Improves Cardiovascular Adjustments And Fatigability In Patients With Heart Failure. 2013. (Apresentação de Trabalho/Congresso). ATS International Conference, Philadelphia

7.

AMATUZZI TEIXEIRA ; Osteopatia e Sistema Nervoso Autonômico: Novas Perspectivas. 2013. (Apresentação de Trabalho/Congresso).CIOST – Congresso internacional de Osteopatia, Foz do Iguaçu.

INICIAÇÃO CIENTÍFICA

1.

ISABELLE BARREIRA. INFLUÊNCIA AGUDA DO TRATAMENTO MANIPULATIVO OSTEOPÁTICO (TMO) NO SISTEMA NERVOSO AUTONOMICO (SNA) EM INDIVÍDUOS JOVENS. 2013. Iniciação Científica. (Graduando em Fisioterapia) -Universidade de Brasília. Orientador: Fellipe Amatuzzi Teixeira.

2.

EMILLY KAROLINE DE SOUZA GOMES. EFEITOS DO TRATAMENTO MANIPULATIVO OSTEOPÁTICO NA PRIMEIRA COSTELA NA PRESSÃO ARTERIAL DE JOVENS SAUDÁVEIS. Início: 2014. Iniciação científica (Graduando em Fisioterapia) - Universidade de Brasília, Conselho Nacional de

Desenvolvimento Científico e Tecnológico. (Orientador).

TRABALHO DE CONCLUSÃO DE CURSO DE GRADUAÇÃO

1.

HANNA LISSA RIBEIRO MIRANDA QUINTANILHA E AMANDA CASTELO BRANCO DUARTE. EFEITOS IMEDIATOS DA MANIPULAÇÃO OSTEOPÁTICA CERVICAL NAS VARIÁVEIS CARDIOVASCULARES EM INDIVÍDUOS SAUDÁVEIS. 2014. Trabalho de Conclusão de Curso. (Graduação em Fisioterapia) - Universidade de Brasília. Orientador: Fellipe Amatuzzi Teixeira.

2.

ANA PAULA PEREIRA XAVIER. EFEITOS IMEDIATOS DA MANIPULAÇÃO OSTEOPÁTICA CERVICAL NAS VARIÁVEIS CARDIOVASCULARES EM INDIVÍDUOS IDOSOS. 2014. Trabalho de Conclusão de Curso. (Graduação em Fisioterapia) - Universidade de Brasília. Orientador: Fellipe Amatuzzi Teixeira.

3.

LUCAS CERATTI SILVELLO DE MELLO LIMA. EFEITO DO TRATAMENTO MANIPULATIVO OSTEOPÁTICO SOBRE O FLUXO SANGUÍNEO E A PRESSÃO ARTERIAL EM INDVÍDUOS SAUDÁVEIS. 2015. Trabalho de Conclusão de Curso (Graduação em Fisioterapia) - Universidade de Brasília. Orientador: Sérgio Ricardo Thomaz, Co-orientador: Fellipe Amatuzzi Teixeira.ANEXO 2 – PARECER DO COMITÊ DE ÉTICA E PESQUISA.

FACULDADE DE CIÊNCIAS DA SAÚDE DA UNIVERSIDADE DE BRASÍLIA - CEP/FS-UNB

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: EFEITOS DO TRATAMENTO MANIPULATIVO OSTEOPÁTICO (TMO) NA FUNCIONALIDADE DE PACIENTES COM INSUFICIÊNCIA CARDÍACA CONGESTIVA: UM ENSAIO CLINICO RANDOMIZADO

Pesquisador: FELLIPE AMATUZZI TEIXEIRA

Área Temática:

Versão: 2

CAAE: 10146913.2.0000.0030

Instituição Proponente: PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS E TECNOLOGIAS EM

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 378.381

Data da Relatoria: 24/07/2013

Apresentação do Projeto:

Vide parecer anterior

Objetivo da Pesquisa:

Vide parecer anterior

Avaliação dos Riscos e Benefícios:

Vide parecer anterior

Comentários e Considerações sobre a Pesquisa:

Vide parecer anterior

Considerações sobre os Termos de apresentação obrigatória:

Vide parecer anterior

Recomendações:

Vide parecer anterior

Conclusões ou Pendências e Lista de Inadequações:

As pendências sobre o TCLE foram atendidas. Ressalva-se a importância de adicionar o logo da UnB no mesmo.

Endereço: Faculdade de Ciências da Saúde - Campus Darcy Ribeiro
Bairro: Asa Norte **CEP:** 70.910-900
UF: DF **Município:** BRASILIA
Telefone: (61)3107-1947 **Fax:** (61)3307-3799 **E-mail:** cepfs@unb.br

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

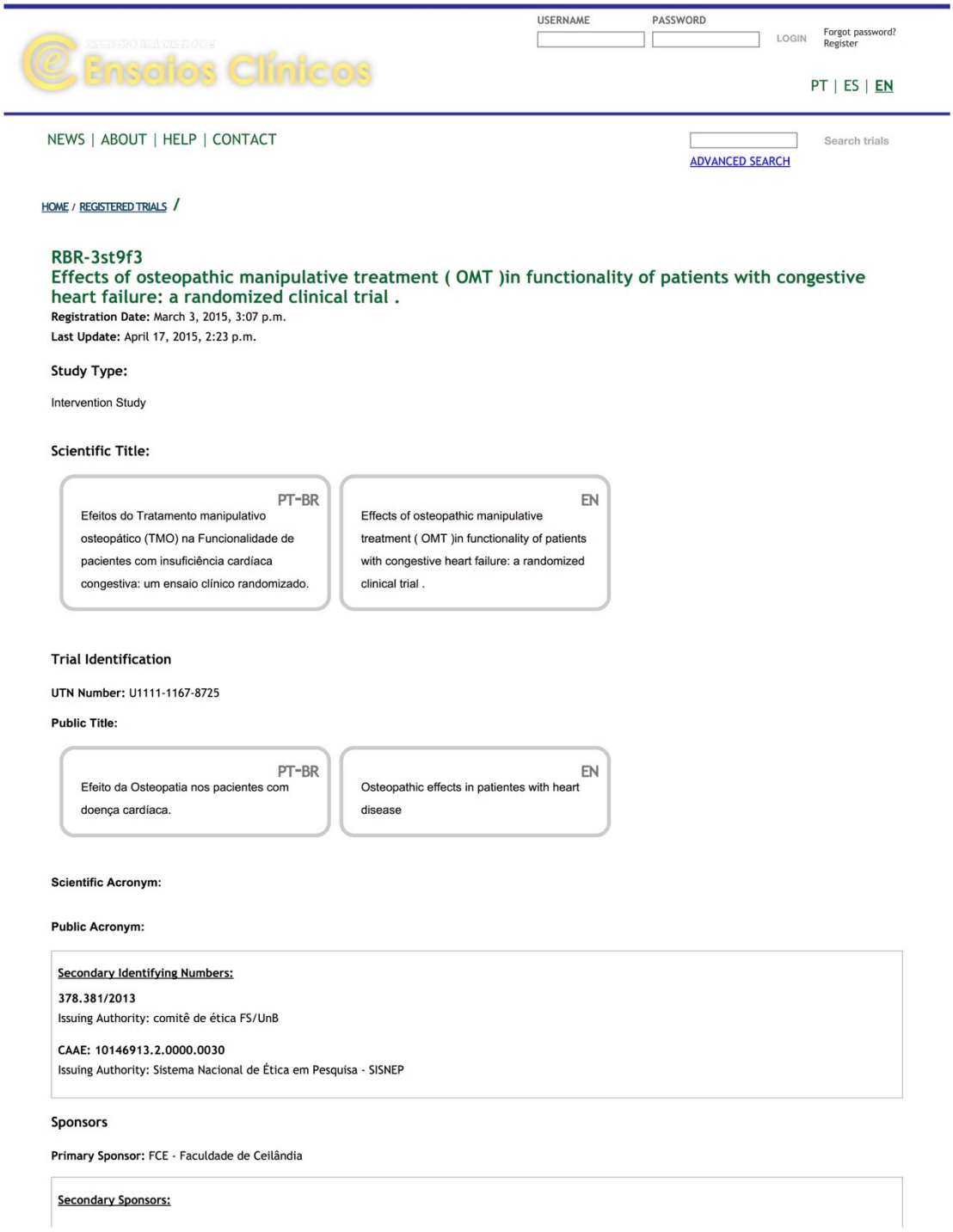
Considerações Finais a critério do CEP:

BRASILIA, 30 de Agosto de 2013

Assinador por:
Natan Monsores de Sá
(Coordenador)

Endereço: Faculdade de Ciências da Saúde - Campus Darcy Ribeiro
Bairro: Asa Norte **CEP:** 70.910-900
UF: DF **Município:** BRASILIA
Telefone: (61)3107-1947 **Fax:** (61)3307-3799 **E-mail:** cepfs@unb.br

ANEXO 3 – REGISTRO BRASILEIRO DE ENSAIOS CLÍNICOS



USERNAME PASSWORD LOGIN Forgot password? Register

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RBR-3st9f3

Effects of osteopathic manipulative treatment (OMT)in functionality of patients with congestive heart failure: a randomized clinical trial .

Registration Date: March 3, 2015, 3:07 p.m.

Last Update: April 17, 2015, 2:23 p.m.

Study Type:

Intervention Study

Scientific Title:

PT-BR	EN
Efeitos do Tratamento manipulativo osteopático (TMO) na Funcionalidade de pacientes com insuficiência cardíaca congestiva: um ensaio clínico randomizado.	Effects of osteopathic manipulative treatment (OMT)in functionality of patients with congestive heart failure: a randomized clinical trial .

Trial Identification

UTN Number: U1111-1167-8725

Public Title:

PT-BR	EN
Efeito da Osteopatia nos pacientes com doença cardíaca.	Osteopathic effects in patientes with heart disease

Scientific Acronym:

Public Acronym:

Secondary Identifying Numbers:

378.381/2013
Issuing Authority: comitê de ética FS/UnB

CAAE: 10146913.2.0000.0030
Issuing Authority: Sistema Nacional de Ética em Pesquisa - SISNEP

Sponsors

Primary Sponsor: FCE - Faculdade de Ceilândia

Secondary Sponsors:

Institution: FCE - Faculdade de Ceilândia

Source(s) of Monetary or Material Support:

Institution: FCE - Faculdade de Ceilândia

Health Conditions

Health Condition(s) or Problem(s):

PT-BR
doença cardiovascular, insuficiência cardíaca congestiva, doença arterial periférica, rastreamento do sistema nervoso autonômico em jovens e em pessoas idosas.

EN
congestive heart failure, peripheral artery disease , tracking the autonomic nervous system in young and elderly.

General Descriptors for Health Condition(s):

PT-BR
C14: Doenças cardiovasculares

ES
C14: Enfermedades cardiovasculares

EN
C14: Cardiovascular diseases

Specific Descriptors for Health Condition(s):

PT-BR
I51.6: Doença cardiovascular não especificada

ES
I51.6: Enfermedad cardiovascular, no especificada

EN
I51.6: Cardiovascular disease, unspecified

PT-BR
I25.0: Doença cardiovascular aterosclerótica, descrita desta maneira

ES
I25.0: Enfermedad cardiovascular aterosclerótica, así descrita

EN
I25.0: Atherosclerotic cardiovascular disease, so described

PT-BR
I25: Doença isquêmica crônica do coração

ES
I25: Enfermedad isquémica crónica del corazón

EN
I25: Chronic ischaemic heart disease

PT-BR
G09.330.190: Processos Fisiológicos Cardiovasculares

ES
G09.330.190: Procesos Fisiológicos Cardiovasculares

EN
G09.330.190: Cardiovascular Physiological Processes

Interventions

Intervention Code(s)

Dietary supplement

Other

Interventions:

PT-BR

Grupo experimental (GE): 30 pacientes cardiopatas serão tratados por meio de tratamento manipulativo osteopático que consiste em manipulações da coluna vertebral, tecidos moles, vísceras e fáscias por 2 meses, 1 vez por semana. Grupo sham (GS): Os mesmos 30 pacientes cardiopatas que receberão tratamento também participarão do grupo sham que será feito por meio de simulação do tratamento osteopático por meio de toque na pele leve sem intenção de tratamento por mais 2 meses, 1 vez por semana. Grupo Controle (GC): 30 indivíduos sem doença cardíaca não receberão nenhum tipo de intervenção de tratamento, fará apenas as avaliações iniciais e finais.

EN

Experimental group (EG): 30 cardiac patients will be treated by manipulative osteopathic treatment consisting of spinal manipulations , soft tissue , fascia and viscera for 2 months, 1 time per week. Sham group (SG) : The same 30 patients with heart disease who receive treatment also participate in the sham group that will be done by simulation of osteopathic treatment through touch the light skin unintentionally treatment for over 2 months , 1 time per week. Control Group (CG): 30 patients without heart disease will not receive any treatment intervention , will only the initial and final evaluations .

Descriptor for Intervention(s):

PT-BR

E02.190.599.280: Manipulação Osteopática

ES

E02.190.599.280: Manipulación Osteopática

PT-BR

E02.190.599: Manipulações Musculoesqueléticas

ES

E02.190.599: Manipulaciones Musculoesqueléticas

PT-BR

E02.190.599.233: Manipulação Quiroprática

ES

E02.190.599.233: Manipulación Quiropráctica

Recruitment

Recruitment Status: Recruiting

Recruitment Country

Brazil

Planned Date of First Enrollment: 2015-04-06

Planned Date of Last Enrollment: 2015-10-06

Target Sample Size:	Gender (inclusion sex):	Inclusion Minimum Age:	Inclusion Maximum Age:
50	-	18 Y	90 Y

Inclusion Criteria:

PT-BR

Para o grupo experimental: Insuficiência

EN

For the experimental group : Congestive

PT-BR	EN
cardíaca congestiva, doença cardiovascular, doença de chagas Para o grupo controle: não ter doença cardiovascular e ser maior de 18 anos.	heart failure , cardiovascular disease, Chagas disease For the control group : not having cardiovascular disease and be over 18 years.

Exclusion Criteria:

PT-BR	EN
Para o grupo experimental: New York Heart Association classe I, paciente descompensado hemodinamicamente, sinais ou sintomas de piora cardiovascular nos últimos 3 meses. Para o grupo controle: Doença cardiovascular, hipertensão, cirurgias, fibromioalgia, disautonomia.	For the experimental group : New York Heart Association class I, hemodynamically decompensated patient , signs or symptoms of cardiovascular worsening in the last 3 months. For the control group : cardiovascular disease , hypertension, surgeries , fibromioalgia , dysautonomia.

Study Type

Study Design:

PT-BR	EN
Ensaio clínico de tratamento, randomizado, controlado, cruzado, duplo-cego, com três braços	Clinical trial of treatment , randomized , controlled, crossover , double -blind, three-arm

Expanded access program	Study Purpose	Intervention Assignment	Number of arms	Masking type	Allocation type	Study Phase
False	Treatment	Cross-over	3	Double-blind	Randomized-controlled	N/A

Outcomes

Primary Outcomes:

PT-BR	EN
Melhora da capacidade física do cardiopata, mediante o teste de esforço cardiopulmonar com pelo menos 20% do aumento dos valores iniciais no grupo experimental.	improvement in physical function in cardiac by cardiopulmonary exercise test with at least 20 % of the increase from baseline in the experimental group .

Secondary Outcomes:

PT-BR	EN
Aumento da variabilidade da frequência cardíaca, verificadas pela variabilidade da frequência cardíaca em pelo menos 20% do valor inicial no grupo experimental; aumento do fluxo sanguíneo na artéria braquial, verificado por meio da avaliação	Increased heart rate variability , verified by heart rate variability by at least 20 % of the initial value in the experimental group ; increased blood flow in the brachial artery verified by evaluating flow -mediated vasodilatation measured as a percentage ,

de fluxo mediado por vasodilatação mensurado em percentual, com pelo menos 20% de aumento do valor inicial no grupo experimental; diminuição dos marcadores bioquímicos de sangue, verificados por meio de exame sanguíneo de pelo menos 20% de diminuição do valor inicial no grupo experimental;

at least 20% of its initial value increased in the experimental group ;
decrease of blood biochemical markers, the blood verified by examining at least 20 % decrease from baseline in experimental group ;

Contacts

Contacts for Public Queries

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Affiliation: Universidade de Brasília

Contacts for Scientific Queries

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Contact(s) for Site Queries

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Zip Code: 72220-900

Telephone: +556199667264

E-mail: famatuzzi@gmail.com

Affiliation: Universidade de Brasília

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ANEXO 4 – NORMAS DA REVISTA E QUALIS – MANUSCRITO 1.

JOURNAL OF PHYSIOTHERAPY – FATOR DE IMPACTO 3,1

Journal of Physiotherapy (JoP) is the first Open Access core physiotherapy journal; it welcomes contributions that are relevant to the science or practice of physiotherapy.

CONTENT Original Research

The Editorial Board is committed to publishing excellent research and will consider the following types of papers:

• Systematic reviewsSystematic reviews are strongly preferred over narrative (non-systematic) reviews. High quality systematic reviews with firm conclusions are a publication priority. However, systematic reviews are unlikely to be published if they find there is not enough good quality evidence to review or if the literature is inconclusive. Note that this journal gives priority to systematic reviews that are prospectively registered in a publicly available register (e.g., PROSPERO at http://www.crd.york.ac.uk/PROSPERO). Authors should submit evidence of registration when submitting a manuscript for consideration. There are specific guidelines available for this type of study at the end of the Presentation section of these Author Guidelines.• Clinical trialsAll clinical trials submitted to JoP must have been registered in a publicly-accessible trials register. We will accept any register that satisfies the International Committee of Medical Journal Editors requirements (such as The Australian New Zealand Clinical Trial Registry at http://www.anzctr.org.au). Authors must provide the name and website address of the register and the trial registration number on submission. The journal will only accept trials that have been registered prospectively unless data collection began before 2006, in which case retrospective registration is acceptable. There are specific guidelines available for this type of study at the end of the Presentation section.• Economic analyses• Experimental studies• Qualitative studiesQualitative research refers to research where the analysis of data involves qualitative judgements. Commonly qualitative research explores aspects of the human, social world. Qualitative research methodologies include narrative inquiry, case studies, naturalistic inquiry, ethnography, hermeneutics, phenomenology, and survey research using open-ended questions. There are specific guidelines available for this type of study at the end of the Presentation section.• Epidemiological studies• Observational studies• Narrative reviewsNarrative reviews critically appraise and summarise literature on a common topic area but do not set specific criteria for selecting literature to be included or a specific review protocol. A narrative review draws together major arguments in a field of discourse or provides a significant historical review of an important aspect of physiotherapy. Narrative reviews should be on topics that do not lend themselves to systematic reviews, e.g., examination of the mechanisms underlying a clinical phenomenon. Narrative reviews will almost always be invited and will be considered only if they are written by authors with

extensive research experience in the field, usually reflected in multiple significant publications. Authors considering submission of a narrative review should first consult the Journal Editor regarding potential suitability of the review for publication. Narrative reviews of intervention, diagnosis, and prognosis will generally not be accepted.

The following types of studies are a low priority:• Studies of the reliability or validity of clinical measurement procedures • Surveys of physiotherapy students• Surveys of physiotherapy practice• Any survey with a low response rate (less than 70%)

Submission of these types of studies should be accompanied by a short (less than 100 words) explanation of why the study would be of particular interest to readers of JoP. The Editorial Board will decide, on the basis of this explanation and the abstract, whether the manuscript should be considered for publication. If accepted, such studies will be published as papers of less than 2000 words with no more than one table or figure.

The following types of studies are not accepted:

• Clinical practice guidelinesAlthough the journal is particularly interested in presenting the recommendations of clinical practice guidelines to its readers, clinical practice guidelines are often developed by consensus and may be endorsed by a professional body. This can make it difficult to apply the Journal's normal process of peer review. Therefore, particularly relevant guidelines that have been developed using a rigorous process and endorsed by a high quality professional body, such as NHMRC, will be summarised in the Appraisal section of the journal, but will not be republished. Details of the location where hard or electronic copies of the full guidelines are available will be given in the summary.• Pilot studiesPilot clinical trials are those that are not designed to have adequate statistical power. Their purpose is to test the feasibility of an intervention in terms of recruitment and delivery of the intervention, as well as to examine the rate of dropouts. They usually provide information to power a future trial and do not therefore reach firm conclusions.

Manuscript length (not including title page, abstract, references, tables or figure legends) depends on the type of study: • Systematic reviews: up to 5000 words• Clinical trials, experimental and qualitative studies: up to 3500 words• Observational studies: up to 2500 words

Authors may be invited, or in some cases required, to place important supplementary material as electronic addenda (eAddenda) on the JoP web site.

MANUSCRIPT PRESENTATION

Research manuscripts should consist of a title page, abstract, text, references, tables, and figures. Manuscripts should be prepared with 2.5 cm margins and a footer containing an abbreviated title, the first author's family name, page number and date. The abstract, introduction, method, results, and discussion should be 1.5 line-spaced, but all other text should be single-spaced. Put a double return between paragraphs. Download the journal's manuscript template.

Title Page

The title of the manuscript should not be more than 25 words and should be in two parts. Give the main results of the study followed by a colon and the method used, e.g., 'A resource-efficient exercise program after discharge from rehabilitation improves standing ability in people after stroke: a randomised trial'. Download example titles for different research designs.

Then, list all authors and their degrees, positions, institutions, country, and email address. Nominate a corresponding author for the review who is authorised to negotiate and approve editorial revisions, provide his/her title (Professor, Dr, etc.), and give contact details (email address). You may nominate a different corresponding author for publication; provide his/her title (Professor, Dr, etc.) and short

contact details (department/institution, postal address and email address).

Provide a running head of up to six words. Next, for indexing purposes, select up to five key words from the Index Medicus Medical Subject Headings (MeSH). MeSH Headings can be found on the PubMed MeSH browser at http://www.nlm.nih.gov/mesh/meshhome.html.

List the word count for the abstract and the body of the text, as well as the number of references, tables, and figures.

Finally, list the Ethics Committee(s) that approved the study and the procedures for gaining consent, source(s) of support, acknowledgements, and any competing interests. The statements regarding ethics and consent do not need to be re-stated in the body of the manuscript. Acknowledgments should include statements of important contributions that do not justify authorship. The nature of the contribution should be specified. It is customary to seek permission of people named in the acknowledgments. Download the journal's Title Page template.

Abstract

An abstract of no more than 250 words is required for all submissions using the headings: Question, Design, Participants, Intervention, Outcome measures, Results, Conclusion, and Trial registration (if appropriate). The results should include estimates of effect sizes and their confidence intervals rather than *p* values. Abstracts should not contain references. Download examples of abstracts for different research designs

Introduction

The introduction should justify the aims of the research. Only references essential to understanding these aims should be included. Introductions rarely need to be longer than five paragraphs. At the end of the introduction, list the research questions as given in the Abstract again. Download Research question examples for different research designs

Method

Use the subheadings: Design; Participants, therapists, centres; Intervention; Outcome measures; and Data analysis, as appropriate to the design of the study. Restrict headings to no more than two levels of importance (i.e., avoid sub-subheadings). Where aspects of the method have been described in other widely-available publications a reference to those publications may suffice, whereas newly-developed procedures should be described in more detail.

In the **Design** section, describe the overall design, especially the timing of intervention and measurement, and any randomisation or blinding procedures.

In the **Participants, therapists, centres** section, outline the recruitment procedures and the inclusion and exclusion criteria for eligibility of participants, therapists, and centres.

In the **Intervention** section, give as much detail as necessary so that the intervention could be faithfully replicated by a reader. If this requires extensive material, consider placing some in an Appendix, which can be an electronic-only addendum to the paper.

In the **Outcome measures** section, state the impairment/activity limitation/participation restriction being collected (e.g., walking) and its measurement with units (e.g., velocity during 10 m Walk Test in m/s). Other examples are: strength measured as peak isometric elbow extensor torque using hand-held dynamometry in Nm, or pain measured as intensity at rest on a 10 cm VAS in cm. It can be useful to divide outcome measures into those examining impairments vs activity limitations vs participation restrictions. It is only necessary to refer to manufacturers' information for equipment when the precise specifications could be important to interpretation of the study. Information should be placed in a footnote at the end of the text, coded using consecutive, superscripted lower case letters.

In the **Data analysis** section, outline any *a priori* power analysis carried out to determine the number of participants needed for the study. Outline any conversions or calculations made with the data. Explain how the research questions are answered by the interpretive tests but do not name the statistical package used if it is widely available.

Results

The first subheading should be **Flow of participants, therapists, and centres through the study** where the numbers at each point in the study are presented as well as baseline characteristics. The remainder of the results should report only the data that answer the research questions and should be organised under subheadings that reflect those questions. Pertinent results should be reported using text and/or tables and/or figures; tables are more useful than figures because exact values are given. Avoid repeating in the text data presented in tables or figures. Do not duplicate data in tables and figures.

When reporting data, be conscious of the precision of the data and only report a meaningful number of decimal places. Usually, report numbers between 0 and 1 to 2 decimal places, between 1 and 10 to 1 decimal place, and above 10 with no decimal place.

All data reported as numbers should also be given as a percentage of the sample (in brackets) rounded off, e.g., 17 (34%) participants were men. All data reported as means should also be accompanied by the standard deviation (in brackets), e.g., the mean height of participants was 1.53 m (SD 0.23).

When reporting the results of interpretive tests, report the size of the effect rather than its statistical significance, e.g., 'People with arthritis were twice as likely to sprain their ankle (OR 0.50, 95% CI 0.25 to 0.75)' or 'People after stroke walked 0.65 m/s (95% CI 0.60 to 0.70) slower than their age-matched healthy counterparts', but not 'People with asthma were significantly more breathless after exercise (p = 0.02)'.

Discussion

New and important findings should be emphasised but, as a rule, data already presented in the Method and Results sections should not be repeated. Implications and limitations of the findings and their clinical application should be discussed. The length of the Discussion should be commensurate with the number of important findings; usually it will be less than 750 words. Do not include a separate conclusion at the end of the Discussion.

References

Only essential references should be cited. Most research will require fewer than 30 references. If the research requires considerably more (e.g., systematic reviews of areas with many clinical trials), references may be provided as supplementary material or eAddenda.

The referencing style used by the journal is the JAMA style, which can be found as a standard referencing style in EndNote, RefWorks, Mendeley, and Zotero. If you use reference management software such as these, please convert your paper to the JAMA style before submission. Journal titles should be abbreviated according to the journals list in PubMed (). Please ensure that all references are complete and presented using numbered style.

Tables

Tables should appear after the references and each table should start on a separate page. They should be numbered consecutively in the order to which they are referred in the text. A short caption should be given above each table (e.g., 'Table 1. Characteristics of participants.'). Within the table, give the units of outcome measures in brackets and italics, e.g., *(m/s)*. When reporting counts (frequencies), give percentages in brackets. Use abbreviations for time (i.e., *s, min, hr*, etc.) and amount (i.e., *kg, deg, Nm*, etc.) without a legend explaining them. Where abbreviations for physiotherapy-specific terms are used (e.g., ROM, MCP, etc.), provide a legend below the table. Tables should be presented with a minimum of horizontal lines and no vertical lines. Download examples of tables.

Figures

Figures should start on a separate page after the tables. They should be displayed at the proposed publication size and numbered consecutively in the order to which they are referred in the text. A short caption should be given below each figure, e.g., 'Figure 1. Mean (SD) effect of posture on forced expiratory volume for the experimental group (closed circles) and the control group (open circles)'. Do not place boxes around figures. Do not put axes on the top and right sides of graphs. Use symbols and/or line types rather than colour to differentiate data. Where several graphs refer to closely-related

material, present them as separate panels of a single figure labelled A, B, C, etc., and provide one caption explaining what is in each panel. Photographs should be in sharp focus, have simple backgrounds, and be in black and white unless colour is essential to illustrate the point (e.g., MRI).

For publication, photographs should be supplied as digital images saved at a minimum of 300 dpi in .jpg format. Graphs and line drawings generated by commonly-used graphing programs (such as Microsoft Excel) are acceptable. Written permission should be obtained for use of previously published Figures and Tables, and for publication of photographs of recognisable subjects. These documents should be uploaded with the final manuscript once it has been accepted.

Boxes

When information needs to be listed but is not a table (contains numbers) or a figure (photograph, graph, or flow diagram), then it should be called a Box. Boxes should be numbered consecutively in the order to which they are referred in the text. A short caption should be given above each box (e.g., 'Box 1. Elements of a viable patient education program.') Download examples of boxes formatted to these specifications.

Style

Manuscripts should be written in simple, direct, and grammatically-correct English. Use Australian/English spelling. Use gender neutral and non-labelling language (e.g., 'People with back pain' rather than 'back pain patients'). When people are enrolled in a trial, use 'participant' rather than 'subjects'. Use capitals (upper case letters) sparingly but capitalise proper nouns. Divisions of the data set are also capitalised (e.g., 'Group 1' or 'Stage 2'). See previous issues for other specific aspects of JoP style.

Click below for the guidelines and examples available for the following types of studies: • Systematic Review guidelines• Systematic Review examples• Clinical Trial guidelines

• Clinical Trials examples• Qualitative Study guidelines• Papers reporting the results of questionnaires guidelines

MANUSCRIPT SUBMISSION

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PEER REVIEW

Research manuscripts are subject to peer review. If the Journal Editor considers that the manuscript is likely to be of interest to readers and is potentially publishable, the manuscript is sent to two reviewers. Reviewers will usually have specific expertise in the field and a record of recent publication in peer-reviewed journals. Reviewers are asked to advise the Journal Editor if the manuscript is credible and of importance to the physiotherapy profession; they are also asked to comment on the manuscript's validity, relevance, clarity, and conciseness. They are asked to provide their reports within four weeks of receipt of the manuscript.

Reviewers are asked to consult checklists where appropriate. Specifically, reviewers of randomised controlled trials are asked to consult the CONSORT e-checklist, reviewers of systematic reviews are asked to consult the PRISMA statement, and reviewers of studies of the accuracy of diagnostic tests are asked to consult the STARD checklist. These checklists can be found at http://www.consort-statement.org/resources/downloads

The Journal Editor considers the reviewers' comments and decides if the manuscript is to be accepted in its current form, accepted subject to minor revisions, potentially publishable but requiring significant revision, or not suited to publication in JoP. Authors are provided with the reviewers' comments, sometimes with additional comments made by the Scientific Editor, and are informed of the decision. Authors of manuscripts requiring revision are invited to consider and respond to the comments made by the reviewers and the Journal Editor, revise the manuscript accordingly, and re-submit. Usually the revised manuscript is returned to the original reviewers for further comment. Some manuscripts undergo several rounds of review before a final decision (accept or reject) is made.

Usually authors hear within 7-10 days if the journal Editor decides that the submission is not suitable for publication in JoP. Time to first decision after review (accept, revise with guarantee, revise without guarantee, or reject) is generally no more than 2 months from submission. Once accepted, manuscripts will go into production and be made available online as an article in press. They undergo extensive editing to improve clarity and comply with JoP style. Author(s) are given the opportunity to review the accuracy of the edited manuscript at proof stage prior to publication. Authors are provided with a .PDF of the final version.

TRIAL PROTOCOLS

Journal of Physiotherapy accepts research protocols for major prospective studies. An abstract of the protocol will be published in the journal, supported by the full version of the protocol available as Appraisal content from the journal website.

To be eligible for consideration the study must have received nationally competitive funding. Submissions will be reviewed by the Protocol Section Editor, and by members of the journal's Editorial Board. The protocols we select for publication need to meet several high standards including that the trial will be likely to directly influence how physiotherapists practice, and/or the trial will significantly enhance understanding of conditions treated by physiotherapists.

Protocols must be submitted via the Elsevier electronic manuscript submission system (EES) including upload of the

full study protocol and an abstract prepared according to the *Journal of Physiotherapy* Protocol template; and upload of a completed Authorship statement.

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Journal of Physiotherapy publishes one or two editorials on scientific or professional issues of physiotherapy practice in each issue. Editorials are usually commissioned; however, anyone wishing to write an editorial should contact the Journal Editor at ScientificEditorJoP@physiotherapy.asn.au for discussion about the topic. Editorials should be no more than 2000 words with a maximum of three authors (unless agreed with the Journal Editor before the work begins) and 20 references. Commissioned editorials are not formally peer reviewed, but may be subject to informal review. Non-commissioned editorials will be formally peer reviewed.

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Correspondence to *Journal of Physiotherapy* should be uploaded via the Elsevier Editorial System. Correspondence is reviewed by the Journal Editor and may be edited. Generally, correspondence falls into two categories: letters challenging physiotherapy assumptions about practice, and letters commenting on papers published in the journal (particularly welcome). In general, such letters should be submitted soon after publication of the paper they refer to. Authors of the papers will usually be invited to reply.

All letters should be no more than 500 words and should contain no more than five references.

QUALIS

Periódicos

ISSN	Título	Área de Avaliação	Classificação
1836-9553	Journal of Physiotherapy	EDUCAÇÃO FÍSICA	A1
2240-4929	Italian Journal of Physiotherapy	ENGENHARIAS IV	B5
1836-9553	Journal of Physiotherapy	MEDICINA II	B1
0004-9514	Australian Journal of Physiotherapy	PSICOLOGIA	B3

ANEXO 5 – NORMAS DA REVISTA E QUALIS – MANUSCRITO 2

Archives of Physical Medicine and Rehabilitation – fator de impacto 2,69

Archives of
Physical Medicine and Rehabilitation

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Archives of Physical Medicine and Rehabilitation publishes original articles that report on important trends and developments in physical medicine and rehabilitation and in the wider interdisciplinary field of rehabilitation. *Archives of Physical Medicine and Rehabilitation* brings readers authoritative information on the therapeutic utilization of physical and pharmaceutical agents in providing comprehensive care for persons with disabilities and for chronically ill individuals. *Archives* began publication in 1920, publishes monthly, and is the official journal of the ACRM | American Congress of Rehabilitation Medicine. Its content is cited more often than any other rehabilitation journal.

Types of papers

Original Research: Present new and important basic and clinical information, extend existing studies, or provide a new approach to a traditional subject. Manuscripts should be limited to 3000 words of text (Introduction through Conclusions). Figures, tables, and references should be limited to the number needed to clarify, amplify, or document the text.

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Authors are invited to submit Information/Education Page manuscripts or proposals to the *Archives*' Editorial Office

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Ethics in Publishing

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Original Article level 1 headings are: Methods, Results, Discussion, and Conclusions. Articles should include the level 2 subsection heading Study Limitations at the end of the Discussion section. Longer articles may need other level 2 and/or level 3 subsection headings to clarify their content, especially the Results and Discussion sections.Other types of articles such as Commentaries and Special Communications do not require this format.

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Abstract

For articles reporting original data (Original Articles, Brief Reports) and Review Articles (including Meta-Analyses), a structured abstract is required (see the Instructions for Structured Abstracts). For other manuscripts (e.g., Commentaries, Editorials and Special Communications), include a conventional, unstructured abstract of no more than 250 words.

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Main Manuscript

Introduction

State the purpose of the article. Summarize the rationale for the study or observation. Give only pertinent references, and do not review the subject extensively. Do not include data or conclusions from the work being reported. Do not include a heading for this section.

Methods

Describe the selection of the observational or experimental subjects (patients or experimental animals, including controls) clearly. Discuss eligibility of experimental subjects. Give details about randomization. Describe the methods for any blinding of observations. Identify the methods, equipment and materials, and procedures in sufficient detail to allow others to reproduce the results.Reference established methods, including statistical methods (see below); provide very brief descriptions for methods that have been published but are not well known; describe new or substantially modified methods, give reasons for using them, and evaluate their limitations. Identify precisely all drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration.

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Discussion

Emphasize the new and important aspects of the study and the conclusions that follow from them. Do not repeat in detail data or other material given in the introduction or the Results section. Include in the Discussion section the implications of the findings and their limitations, including implications for future research. Authors should address the issue of effect magnitude, in terms of both the statistics reported and the implications of the research. Relate the observations to other relevant studies.

Study Limitations

Include the subsection (Level 2 heading), "Study Limitations" to discuss the limitations of the study.

Conclusions

Link the conclusions with the study's goals but avoid unqualified statements not supported by the

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Acknowledgments

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Journal of Manipulative and Physiological Therapeutics – fator de impacto 1,72

JOURNAL OF MANIPULATIVE AND PHYSIOLOGICAL THERAPEUTICS

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Title Page Form CopyrightConflict of Interest Case/Case Series

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Funding sources

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EDITORIAL PROCESS

Pre-peer review, and internal review by editors

To insure that only relevant and appropriate papers are sent to peer review, submitted manuscripts are pre-reviewed for relevance, appropriate submission format, and basic quality before sending out to peer review. Reasons for early rejection may include: the submission does not meet the requirements as stated in the instructions for authors, the work is of poor quality, and/or the topic is not relevant to the mission of journal.

The editorial staff reads each manuscript and then decides whether to send the paper to outside reviewers. If a submission is rejected without external review, the author will typically be notified electronically within 2 to 3 weeks of receipt. Over 80% of submitted papers are sent to external peer review, which is usually made up of at least 2 reviewers, but may be more.

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Revised manuscripts should be accompanied by an additional Word file with responses to all editor requests and reviewers' comments. This file should contain an itemized list addressing each of the revision requests and demonstrate how these have been addressed in the manuscript. The preferred order of files is as follows: cover letter, response to reviews (revised manuscripts only), manuscript file(s), figure(s).

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4. Figures(separateJPEGfilesnobiggerthan2MB)5. Signedassignmentofcopyrightformsforeachauthor6. Completedconflictofinterestformforeachauthor7. Permissionstopublish,consentforms,permissionsforms,forhumanoranimalstudies,evidenceofboardapproval.

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Please fill in title page form from the *JMPT* submission website.

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Manuscripts must be prepared in accordance with the Declaration of Vancouver "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" (available from the *JMPT* Editorial Office or from www.icmje.org). The manuscript should be in double-spaced format. Do not break any words (hyphenate) at the end of any line and do not insert hard page breaks. The journal follows American Medical Association Manual of Style (10th ed. Oxford University Press, NY, 2007).

Structured abstract

The structured abstract should be no more than 250 words. The abstract should consist of 4 paragraphs, labeled: Objectives, Methods (include relevant information such as design, subjects/population, setting, statistical methods, etc), Results, and Conclusions.

Manuscript organization

The text of observational and experimental articles is usually divided into sections with the headings Introduction, Methods, Results, and Discussion. Longer articles may need subheadings within some sections to clarify or break up content. Other types of articles such as case reports, reviews, editorials, and commentaries may need other formats. Studies with designed that have guidelines should follow published guidelines. (eg, CONSORT, MOOSE, QUOROM, STARD, TREND, etc.) Any questions about format should be directed to the editor.

Introduction

Clearly state the purpose of the article. Summarize the rationale for the study or observation. Give only pertinent references and do not review the subject extensively; the introduction should serve only to introduce what was done and why it was done. State the specific purpose, research objective, or hypothesis tested by the study (typically found at the end of the introduction section).

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The selection and description of participants, technical information, and statistics used should be reported in this section. Describe the selection of the observational or experimental subjects (patients or experimental animals, including controls). Papers of a specific study design should follow current and relevant guidelines (e.g., CONSORT, MOOSE, QUOROM, STARD, TREND, etc.) and include appropriate materials in the text. Identify the methods, apparatus (manufacturer's name and address in parentheses) and procedures in sufficient detail to allow others to reproduce the work for comparison of results. Give references to establish methods, provide references and brief descriptions for methods that have been published but may not be well known, describe new or substantially modified methods and give reasons for using them and evaluate their limitations.

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Present your results in logical sequence within the text, tables, and figures. Do not repeat findings in multiple places (eg, do not include the same data in both text and tables). Emphasize or summarize only important observations, do not discuss findings in this section.

Discussion

The discussion should emphasize the important aspects of the study and include conclusions that follow from these observations. Do not repeat data presented in the Results section and do not include information or work that is not directly relevant to the study. State new hypotheses when indicated, but clearly label them as such. Statements that are unsupported, that generalize, or that over extrapolate the findings should not be included.

Conclusions that may be drawn from the study may be included in the discussion; however, they may be more appropriately presented in a separate section. The principal conclusions should be directly linked to the goals of the study. Unqualified statements and conclusions not supported by your data should not be included. Avoid claiming priority or referring to work that has not been completed or published. State new hypotheses when warranted but clearly label them as such. Recommendations (for further study, etc), when appropriate, may be included.

Limitations subsection

Place limitation subsection at the end of the Discussion section. List and discuss the limitations of the study, possible sources of bias, and any reasonable alternate explanations for the findings and interpretation for the study.

Acknowledgments

Acknowledge only those who have made substantive contributions to the study itself; this includes support personnel such as statistical or manuscript review consultants, but not subjects used in the study or clerical staff. Clearly state what each contributor has provided. Authors are responsible for obtaining the written permission (to be included at time of submission) that is required from persons, institutions, or businesses being acknowledged by name because readers may infer their endorsement of the data and conclusions.

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2. Titleofarticlewithfirstwordcapitalizedandallotherwordsinlowercase,exceptnamesofpersons,places,etc .

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Tables should be placed at the end of the blinded manuscript file at the time of submission. If the paper is accepted, tables will be placed appropriately in the final publication. Tables should be numbered as they appear in the text (e.g., Table 1). Identify statistical measures of variation, such as standard deviation and standard error of mean. If data are used from another source, the author should acknowledge the original source in the text and include the written permission from the copyright holder to reproduce the material with the submission.

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Do not submit tables as photographs. Avoid the use of too many tables in relation to length of the text, as this may produce difficulties in layout of the pages. Avoid the use of tables that do not fit in the 'portrait' layout. Table contents and number of tables may be subject to editing.

Type legends for tables above each table. Include expanded version of all acronyms and symbol meanings in the legend. Identify each legend with Arabic numerals in the same manner and sequence as they were indicated in the text in parentheses (eg, Table 1). Include in the manuscript text where the table should be placed. For example "call out" where the table should be located using (Table 1) in the text.

Terminology

Standard spelling and terminology should be used whenever possible. Avoid creating new terms or acronyms for entities that already exist. Technical terms that are used in statistics should not be used as non-technical terms, such as "random" (which implies a randomizing device), "normal," "significant" (which implies statistical significance), and "sample."

Units of Measurement

In most countries the International System of Units (SI) is standard, or is becoming so, and bioscientific journals in general are in the process of requiring the reporting of data in these metric units. However, insofar as this practice is not yet universal, particularly in the United States, it is permissible for the time being to report data in the units in which calculations were originally made, followed by the opposite unit equivalents in parentheses; ie, English units (SI units) or SI units (English units). Nevertheless, researchers and authors considering submission of manuscripts to the *JMPT* should begin to adopt SI as their primary system of measurement as quickly as it is feasible.

Abbreviations and symbols

Use only standard abbreviations for units of measurement, statistical terms, biological references, journal names, etc. Avoid abbreviations in titles and abstracts. The full term should precede its abbreviation for the first use in the manuscript, unless it is a standard unit of measurement. For standard abbreviations, consult the following: 1) Uniform requirements for manuscripts submitted to biomedical journals (Ann Intern Med 1997;126:36-47); 2) American Medical Association manual of style. 10th ed. Baltimore: Williams & Wilkins; 2007; 3) Scientific style and format, the CBE manual for authors, editors, and publishers. 6th ed. Cambridge (UK): Cambridge University Press; 1994.

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0161-4754	Journal of Manipulative and Physiological Therapeutics	SAÚDE COLETIVA	B1

ANEXO 8 – COMPROVANTE DE SUBMISSÃO DO MANUSCRITO 3

fellipe amatuzzi Teixeira <famatuzzi@gmail.com>

Submission Confirmation **Journal of Manipulative and Physiological Therapeutics** <cjohnson@nuhs.edu> 10 de novembro de 2015 01:14

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