

**UNIVERSIDADE FEDERAL DE SANTA MARIA
CENTRO DE CIÊNCIAS DA SAÚDE
PROGRAMA DE PÓS GRADUAÇÃO EM REABILITAÇÃO
FUNCIONAL**

Murilo Rezende Oliveira

**EFEITOS DA CORRENTE INTERFERENCIAL SOBRE VARIÁVEIS
CARDIOVASCULARES EM VOLUNTÁRIOS NORMOTENSOS**

PPGREF/UFSM, RS

OLIVEIRA, Murilo Rezende Mestre 2018

Santa Maria, RS
2018

Murilo Rezende Oliveira

**EFEITOS DA CORRENTE INTERFERENCIAL SOBRE VARIÁVEIS
CARDIOVASCULARES EM VOLUNTÁRIOS NORMOTENSOS**

Dissertação apresentada ao Programa de Pós-Graduação em Reabilitação Funcional, da Universidade Federal de Santa Maria (UFSM, RS), como requisito parcial para obtenção do título de **Mestre em Reabilitação Funcional**.

Orientador: Prof. Dr. Luis Ulisses Signori

Santa Maria, RS
2018

OLIVEIRA, MURILO

EEFEITOS DA CORRENTE INTERFERENCIAL SOBRE VARIÁVEIS
CARDIOVASCULARES EM VOLUNTÁRIOS NORMOTENSOS / MURILO
OLIVEIRA. 2018.

75 p.; 30 cm

Orientador: Luis Ulisses Signori

Dissertação (mestrado) - Universidade Federal de Santa
Maria, Centro de Ciências da Saúde, Programa de Pós Graduação
em Reabilitação Funcional, RS, 2018

1. Eletroterapia 2. Sistema Nervoso Autônomo 3. Frequência
Cardíaca 4. Pressão Arterial I. Signori, Luis Ulisses II.
Título.

Murilo Rezende Oliveira

**EFEITOS DA CORRENTE INTERFERENCIAL SOBRE VARIÁVEIS
CARDIOVASCULARES EM VOLUNTÁRIOS NORMOTENSOS**

Dissertação apresentada ao Programa de Pós-Graduação em Reabilitação Funcional, da Universidade Federal de Santa Maria (UFSM, RS), como requisito parcial para obtenção do título de **Mestre em Reabilitação Funcional**.

Aprovado em 19 de julho de 2018:

Luis Ulisses Signori, Dr. (UFSM)
(Presidente/Orientador)

Rodrigo Della Méa Plentz, Dr. (UFCSPA)

Carine Callegaro, Dr. (UFSM)

Santa Maria, RS

2018

DEDICATÓRIA

Dedico esta dissertação e o mestrado à todas as pessoas que apostaram e confiaram no meu potencial. Principalmente à família, amigos, colegas, professores e a todos os pacientes que serão beneficiados com está e futuras pesquisas que possam auxiliar e melhorar suas condições de saúde.

AGRADECIMENTO

Agradeço primeiramente a Deus pela grande oportunidade de cursar este mestrado e a minha família, por todo apoio, confiança, paciência e por entender nos momentos em que não pude comparecer. Assim como os amigos que fizeram parte desta caminhada.

Ao professor Dr. Luis Ulisses Signori por todos ensinamentos, pela sua dedicação neste trabalho e pela paciência a cada reunião. Foi imprescindível no meu amadurecimento.

Aos colegas que ajudaram nas coletas de dados, Natiele Righi, Geovana Righi, Bruno Arbiza, Juliana Almeida e colegas do mestrado como Edineia Brito, Tainara Tolves, Gustavo Urbanetto e Barbara, nos quais se tornaram grandes amigos ao longo dessa caminhada.

Aos voluntários por participarem da pesquisa, auxiliando na elucidação desta pesquisa.

Ao grupo de pesquisa em Fisiopatologia e Reabilitação pelas diversas reuniões científicas, práticas e debates sobre artigos e oratórias para meu aprimoramento.

Agradeço também a todos envolvidos no Programa de Pós-Graduação em Reabilitação Funcional (PPGRF), em especial à secretária Taís pela sua atenção e dedicação na resolução de cada dúvida e ao Professor Dr. Marcos Antônio, coordenador deste PPG.

RESUMO

EFEITOS DA CORRENTE INTERFERENCIAL SOBRE VARIÁVEIS CARDIOVASCULARES EM VOLUNTÁRIOS NORMOTENSOS

AUTOR: Murilo Rezende Oliveira
ORIENTADOR: Luis Ulisses Signori

O sistema nervoso autônomo (SNA) atua na modulação do sistema cardiovascular e da pressão arterial (PA). Os efeitos da eletroterapia sobre o sistema cardiovascular vêm sendo amplamente estudada. Dentre as correntes de eletroestimulação sensorial, a estimulação elétrica nervosa transcutânea (TENS) tem apresentado resultados favoráveis quando aplicada sobre os gânglios paravertebrais, pois altera o balanço autonômico e, dependendo dos parâmetros de aplicação, reduz a pressão arterial (PA) em voluntários normotensos e hipertensos. Outra forma de estimulação sensorial é a corrente interferencial (CI), mas seus efeitos sobre o sistema cardiovascular foram pouco estudados. Esta corrente elétrica apresenta características especiais, em relação a TENS, pois devido a sua menor impedância, pode gerar efeitos mais profundos nos tecidos, o que poderia apresentar resultados mais pronunciados sobre sistema cardiovascular. O objetivo da presente pesquisa foi avaliar os efeitos da aplicação da CI com diferentes AMF (100Hz e 10Hz) sobre o balanço autonômico e a PA de voluntários saudáveis. Neste sentido, se realizou um ensaio clínico randomizado, duplo cego e crossover. A amostra foi composta por 30 voluntários saudáveis, de ambos os性os (21 mulheres) com idade média de 23.7 ± 2.7 anos e índice de massa corporal (IMC) de 23.2 ± 2.7 kg/m². Os voluntários foram submetidos à intervenção placebo, CI com AMF 100Hz e CI com AMF 10Hz aplicadas na região paravertebral ganglionar por 30 minutos. Todas as intervenções e as avaliações foram realizadas no intervalo de uma semana. O balanço autonômico foi avaliado pela técnica da variabilidade da frequência cardíaca (VFC) e os sinais capturados por frequencímetro (Polar 810i). As medidas de PA foram mensuradas através do monitor multiparamétrico (Dixtal, modelo 2021). As avaliações foram realizadas antes e imediatamente após as intervenções. A pesquisa demonstrou que a CI modificou o balanço autonômico, onde a AMF 10Hz diminuiu a atividade simpática e aumentou atividade parassimpática, enquanto que a AMF 100Hz apresentou resultados opostos. A PA não se modificou ao longo do estudo. Esses resultados sugerem que CI com AMF 10Hz apresenta um potencial terapêutico no manejo não farmacológico da hipertensão.

Palavras-chaves: Sistema Nervoso Autônomo. Sistema Nervoso Simpático. Sistema Nervoso Parassimpático. Frequência Cardíaca. Pressão Arterial. Eletroestimulação.

ABSTRACT

EFFECTS OF INTERFERENTIAL CURRENT ON CARDIOVASCULAR VARIABLES IN NORMOTENS VOLUNTEERS

AUTOR: Murilo Rezende Oliveira
ORIENTADOR: Luis Ulisses Signori

The autonomic nervous system (ANS) acts on modulation of the cardiovascular system and blood pressure (BP). The effects of electrotherapy on the cardiovascular system have been widely studied. Among the currents of sensorial electrical stimulation, Transcutaneous electrical nerve stimulation (TENS) has presented favorable results when applied to the starred ganglia, since it alters the autonomic balance and depending of the parameters, favoring the reduction of BP in normotensive and hypertensive volunteers. Another form of sensory stimulation is the interferential current (IC), but its effects on the cardiovascular system have been little studied. This electrical current presents special characteristics in relation to TENS, because due to its lower impedance, it can generate deeper effects in the tissues, which could present more pronounced results on cardiovascular system. The aim of the present study is to evaluate the effects of the application of IC with different amplitude-modulated frequency (AMF) (100Hz and 10Hz) on the autonomic balance and BP of healthy volunteers. A randomized, double-blind, crossover clinical trial was performed. The sample consisted of 30 healthy volunteers of both sexes (21 women) with a mean age of 23.7 ± 2.7 years and a body mass index (BMI) of 23.2 ± 2.7 kg/m². The volunteers were submitted to the placebo intervention, IC with AMF 100Hz and CI with AMF 10Hz applied in the paravertebral ganglion region for 30 minutes. All interventions and evaluations were performed with interval of one week. The autonomic balance was evaluated by the technique of heart rate variability (HRV) and the signals captured by frequency meter (Polar 810i). The BP measurements were measured using a multiparameter monitor (Dixtal, model 2021). Evaluations were performed before and immediately after the interventions. The research showed that IC modified the autonomic balance, where AMF 10Hz decreased sympathetic activity and increased parasympathetic activity, while the AMF 100Hz presented opposite results. BP did not change over the course of the study. These results suggest that AMF 10Hz presents a therapeutic potential in the nonpharmacological management of hypertension.

Keywords: Autonomic nervous system. Sympathetic nervous system. Parasympathetic nervous system. Heart Rate. Blood Pressure. Electric Stimulation.

LISTA DE FIGURA

Figura 1 - Características descritivas de formas de onda.....	24
Figura 2 – Amplitude de modulação da frequência (AMF).....	26
Figura 3 - Exemplo de aplicação da CI nos métodos tetrapolar (A) e bipolar (B) na região anterior da coxa.....	27

Artigo

Figura 1 - Flow Diagram of study.....	48
Figura 2 - Local of electrodes (paravertebral ganglionar region - C7 and T4).....	49
Figure3 - The sympathetic-vagal balance.....	50

LISTA DE TABELAS

Tabela 1 - Classificação da Pressão Arterial.....	21
Tabela 2 – Revisão das variáveis dos estudos.....	32

Artigo

Table 1 - Results of heart rate variability data.....	51
Table 2 - Results of Blood Pressure.....	53

LISTA DE ABREVIATURAS E SIGLAS

AMF	Amplitude de Modulação da Frequência
CI	Corrente Interferencial
HA	Hipertensão Arterial
HF	<i>High Frequency</i>
Hz	Hertz
LF	<i>Low Frequency</i>
LF/HF	Razão simpatovaga
PA	Pressão Arterial
PAD	Pressão Arterial Diastólica
PAS	Pressão Arterial Sistólica
SNA	Sistema Nervoso Autônomo
TENS	Estimulação Elétrica Nervosa Transcutânea
UFSM	Universidade federal de santa maria
VFC	Variabilidade da Frequência Cardíaca
VLF	<i>Very Low Frequency</i>
WHA	<i>World Health Association</i>

SUMÁRIO

1 INTRODUÇÃO	13
2 REFERENCIAL TEÓRICO	15
2.1 SISTEMA NERVOSO AUTÔNOMO (SNA)	15
2.2 BALANÇO AUTONÔMICO.....	16
2.3 VARIABILIDADE DA FREQUÊNCIA CARDÍACA (VFC)	17
2.4 HIPERTENSÃO ARTERIAL (HA).....	20
2.5 TRATAMENTOS	22
2.6 ELETROTERAPIA	22
2.6.1 Classificação das correntes elétricas.....	23
2.6.2 Formas de ondas elétricas.....	23
2.6.3 Frequência.....	24
2.6.4 Largura ou duração de pulso	25
2.6.5 Amplitude ou intensidade da corrente	25
2.6.6 Tempo <i>on/off</i>	25
2.6.7 Rampa de subida e rampa de descida	25
2.7 CORRENTE INTERFERENCIAL (CI).....	25
2.8 EFEITOS DA CORRENTE INTERFERENCIAL (CI) NO BALANÇO AUTONÔMICO E PRESSÃO ARTERIAL (PA).....	28
2.9 JUSTIFICATIVA/OBJETIVO	33
3 ARTIGO	34
ABSTRACT	35
INTRODUCTION	37
METHODS	38
Design overview and Settings	38
Participants	38
Interventions	38

Outcomes and follow-up	39
Heart Rate Variability	39
Blood pressure	40
Statistical analysis.....	40
Sample size	41
RESULTS	41
DISCUSSION	42
CONCLUSION	44
References	45
4 CONCLUSÃO	54
REFERÊNCIAS	55
ANEXOS	62
ANEXO 1: Normas da revista <i>Physiotherapy</i>	62

1 INTRODUÇÃO

A hipertensão arterial (HA) é o principal fator de risco para doenças cardiovasculares, sendo considerada um grave problema de saúde pública responsável por cerca de 7,1 milhões de mortes ao ano no mundo e 50% das mortes por doença cardiovascular, atingindo 32,5% dos brasileiros adultos e mais de 60% dos idosos (WHA, 2013). A HA é caracterizada como uma doença crônica não transmissível, de causas multifatoriais associada a alterações funcionais, estruturais e metabólicas (MALACHIAS et al., 2016).

O sistema cardiovascular sofre efeitos diretos do sistema nervoso através da ação do sistema nervoso autônomo (SNA). O SNA divide-se em vias simpática e parassimpática, estabelecendo um papel importante na regulação da pressão arterial (PA) e na frequência cardíaca (ERDOGAN et al., 2011). Neste sentido, o desequilíbrio neste sistema, através da maior ativação simpática e a redução da atividade parassimpática, leva a disfunção no balanço autonômico e pode ser considerada um importante fator fisiopatológico no desenvolvimento da HA (MONTANO et al., 2009), gerando redução da variabilidade da frequência cardíaca (VFC) (LUCINI et al., 2002).

O manejo não farmacológico desta doença é um importante recurso, em especial em pacientes com hipertensão resistente (DUDENBOSTEL et al., 2016) ou refratária (MODOLO et al., 2015) que não evoluem bem com o manejo farmacológico. As principais medidas não medicamentosas são as modificações no estilo de vida, que compreendem as mudanças na dieta alimentar (SALES et al., 2012), a prática de exercícios físicos e/ou atividades físicas (GKALIAGKOUSI; GAVRIILAKI; DOUMA, 2015) e exercícios respiratórios (BERNARDI et al., 2001; HERING et al., 2013).

Dentre os recursos terapêuticos não farmacológicos, a eletroterapia vem se destacando através da aplicação da eletroestimulação sensorial, como a Corrente Interferencial (CI) e a Estimulação Elétrica Nervosa Transcutânea (TENS). A TENS, corrente de baixa frequência (<1000 Hz) (ROBINSON; SNYDER-MACKLER, 2008) mostrou ser capaz de modificar as variáveis cardiovasculares, como a PA e frequência cardíaca, de voluntários saudáveis e pacientes hipertensos (STEIN et al., 2011; TOMASI et al., 2015; VIEIRA et al., 2012; VILELA-MARTIN et al., 2016; WONG; JETTE, 1984). Por outro lado, correntes de média frequência, como a CI, devido à impedância mais baixa da pele, penetram mais profundamente nos tecidos (DOHNERT; BAUER; PAVÃO, 2015; SANTOS et al., 2013), o que poderia apresentar melhores efeitos que a TENS. Entretanto, ainda pouco se sabe os efeitos da CI sobre

este sistema em voluntários normotensos e hipertensos (JIN; HWANG; CHO, 2017; NOBLE et al., 2000; SANTOS et al., 2013).

Neste sentido, estudar as alterações da CI sobre o balanço autonômico e a PA, apresentam potencial terapêutico e consequentemente relevância clínica. Este recurso eletroterápico pode ser uma ferramenta não farmacológica coadjuvante no manejo da hipertensão. Diante do exposto, a seguir será apresentado uma revisão de literatura referente ao tema e posteriormente os resultados do ensaio clínico randomizado desenvolvido para avaliar os efeitos da CI com AMF em 100Hz e AMF em 10Hz sobre variáveis cardiovasculares em voluntários saudáveis.

2 REFERENCIAL TEÓRICO

2.1 SISTEMA NERVOSO AUTÔNOMO (SNA)

O sistema nervoso autônomo (SNA) representa uma interface entre o sistema nervoso central (SNC) e o corpo (MONTANO et al., 2009). Este sistema é considerado é o principal mecanismo de defesa endógena projetado para manter a homeostase (SHAFI et al., 2017), atuando na regulação e função do corpo após eventos cotidianos, como as emoções, o estresse físico e mental, o sono, a ansiedade, e as interações sociais (MONTANO et al., 2009).

O SNA cardíaco, mais especificamente, pode ser dividido em componentes extrínsecos e intrínsecos. O componente extrínseco pode ser subdividido em componentes simpáticos e parassimpáticos (SHEN; ZIPES, 2014). As fibras simpáticas formam-se, em sua maioria, dos gânglios autonômicos, localizados ao longo da medula espinhal cervical e torácica. Estes gânglios autonômicos incluem gânglios cervicais superiores, que se comunicam com C1-3; os gânglios estreitos, que se comunicam com C7-8 a T1-2; e os gânglios torácicos. Os corpos celulares dos neurônios simpáticos pós-ganglionares são armazenados nesses gânglios, dos quais os axônios formam nervos cardíacos superiores, médios e inferiores e terminam na superfície do coração (SHEN; ZIPES, 2014).

A ativação da atividade simpática causa a constrição arterial, no qual resulta no aumento da resistência vascular periférica, vasoconstrição, aumentando o retorno venoso ao coração e aumento da frequência cardíaca. Além disso, a ativação desta atividade resulta no aumento da contratilidade cardíaca através de efeitos, como o efeito cronotrópico (regularidade e frequência do ritmo cardíaco), o dromotrópico (velocidade de condução no nódulo atrioventricular) e os efeitos inotrópicos (capacidade de contração da musculatura cardíaca) positivos. O resultado é o aumento da pressão arterial (PA), mediada pela liberação de norepinefrina das terminações nervosas e pelos seus efeitos sobre receptores α adrenérgicos nos vasos sanguíneos e receptores β_1 adrenérgicos no coração (SHAFI et al., 2017).

A inervação parassimpática se origina predominantemente no núcleo ambíguo da medula oblonga. As fibras pré-ganglionares parassimpáticas são localizadas no nervo vago e são divididas em ramos superior, médio e inferior. A maioria das fibras do nervo vago estão entre a veia cava superior e a aorta, no caminho para os túneis atrioventriculares (SHEN; ZIPES, 2014). A ativação da atividade parassimpática provoca resultados opostos da atividade simpática, reduzindo a frequência cardíaca e a contratilidade cardíaca, exercendo seus efeitos

nos receptores muscarínicos através dos nervos parassimpáticos, no qual secretam acetilcolina (SHAFI et al., 2017).

Desta forma, o equilíbrio entre as porções simpáticas e parassimpáticas é um importante regulador do sistema cardiovascular e consequentemente da PA de sujeitos normotensos e hipertensos (BRUNO et al., 2011).

Mecanismos do SNA aferente, no sistema cardiovascular, também são explicados por barorreceptores e quimiorreceptores, localizados no Sistema Nervoso Periférico (SNP). Os barorreceptores são localizados no seio carotídeo, acima da bifurcação da artéria carótida e na parede do arco aórtico. Estes receptores se estendem em resposta a aumentos na pressão arterial (PA), transmitindo sinais através do nervo vago (barorreceptores aórticos) e nervo glossofaríngeo (barorreceptores carotídeos) ao núcleo traqueal solitário na região medular do tronco encefálico. A função dos barorreceptores é manter a PA estável, dentro de uma faixa estreita de variação, esteja o indivíduo em repouso ou desenvolvendo diferentes atividades comportamentais, através do aumento na estimulação vagal do coração e inibição da atividade nervosa simpática. Os efeitos dos barorreceptores são a dilatação arteriolar, vasodilatação, bradicardia, diminuição do débito cardíaco e diminuição da PA (SHAFI et al., 2017; SHEN; ZIPES, 2014).

Já os quimiorreceptores estão localizados em pequenos órgãos nos corpos aórticos e carotídeos (na bifurcação da artéria carótida). Esses receptores são sensíveis alto teor de dióxido de carbono (CO_2), aos baixos níveis de oxigênio (O_2), um pH baixo e as mudanças que podem ocorrer na PA. Os sinais desses receptores são transmitidos através do nervo vago para o centro do tronco encefálico. A ativação dos quimiorreceptores é inibido pela ativação dos barorreceptores em situações de aumento da PA e a desativação dos barorreceptores potencializa a resposta ventilatória e vasoconstritora dos quimiorreceptores. Assim, os barorreceptores ajudam a manter a PA, enquanto os quimiorreceptores influenciam o controle respiratório, sendo fundamentais para manter a PA (SHAFI et al., 2017).

2.2 BALANÇO AUTONÔMICO

Normalmente, quando a atividade dessas fibras simpáticas e parassimpáticas está em equilíbrio dinâmico, é chamado de balanço autonômico. No entanto, a atividade das duas podem ser moduladas rapidamente em resposta a mudanças ambientais, ocorrendo um desequilíbrio e/ou disfunção autonômica, onde uma das atividades do SNA domina sobre a outra (MCCRATY; SHAFFER, 2015; THAYER; YAMAMOTO; BROSSCHOT, 2010).

Há evidências que sugerem que o desequilíbrio autonômico, em que tipicamente o sistema simpático é hiperativo e o sistema parassimpático é hipoativo, está associado a várias condições patológicas, incluindo doenças cardiovasculares, como arritmias cardíacas, hipertensão arterial (HA), paradas cardíacas e mortalidade (MONTANO et al., 2009; SHIELDS, 2009; THAYER; YAMAMOTO; BROSSCHOT, 2010). Sendo que a HA é caracterizada fisiopatologicamente por uma alteração na regulação do sistema autonômico, indicado pela redução da variabilidade da frequência cardíaca, hiperatividade simpática e a redução da sensibilidade parassimpática (LUCINI et al., 2002). Logo, a correção terapêutica do desequilíbrio autonômico está associada à redução substancial da mortalidade cardiovascular (LA ROVERE et al., 1998; MANCIA et al., 2013).

Portanto, a avaliação do balanço autonômico é considerada de extrema importância na compreensão da fisiopatologia das doenças cardiovasculares. Durante anos, os níveis de catecolaminas de plasma e urinário proporcionaram a única maneira de avaliar a atividade simpática (MONTANO et al., 2009). Entretanto, novas técnicas para avaliação da atividade simpática e parassimpática foram incorporadas ao longo dos tempos, dentre essas a variabilidade da frequência cardíaca (VFC).

2.3 VARIABILIDADE DA FREQUÊNCIA CARDÍACA (VFC)

A avaliação do SNA é considerado de extrema importância na compreensão da fisiopatologia das doenças cardiovasculares (MONTANO et al., 2009). E dentre as técnicas utilizadas para avaliar tal sistema, uma das mais comuns é através da variabilidade da frequência cardíaca (VFC) (TARVAINEN et al., 2014).

VFC está sendo estudada desde 1965, a partir da monitorização do sofrimento fetal, até em 1987, ser associada ao risco de mortalidade após infarto agudo do miocárdio (IAM). A partir disto, passou a ser considerado como um preditor de mortalidade pós IAM (ANIS JUNIOR, 2000). Esta técnica relata oscilações dos intervalos entre batimentos cardíacos consecutivos (intervalos R-R), que estão relacionadas às influências do SNA sobre o nódulo sinusal. É uma medida não-invasiva, que pode ser utilizada para identificar fenômenos relacionados ao SNA em indivíduos saudáveis, atletas e portadores de doenças cardiovasculares (VANDERLEI et al., 2009).

Um indivíduo saudável com mecanismos autonômicos eficientes é representado através da alta VFC, caracterizando um sinal de boa adaptação. Já a baixa VFC pode indicar uma adaptação anormal e insuficiente do SNA, que pode significar uma presença de mau funcionamento fisiológico no indivíduo. A partir disso, é possível estudar a modulação

autonômica do coração, sendo que a baixa VFC reflete um tônus simpático excessivo ou um tônus parassimpático inadequado (PUMPRLA et al., 2002).

Os índices de VFC são obtidos por instrumentos como eletrocardiógrafos, conversores analógicos digitais e cardiofrequencímetros (VANDERLEI et al., 2009) e sua análise pode ser feita por meio de métodos lineares e não-lineares (MCCRATY; SHAFFER, 2015).

Os métodos lineares são divididos em domínios do tempo e da frequência. Para a análise no domínio do tempo, mede-se cada intervalo RR normal (batimentos sinusais) durante um determinado intervalo de tempo, em milissegundos, com base nos métodos estatísticos ou geométricos (média, desvio padrão e índices derivados do histograma ou do mapa de coordenadas cartesianas dos intervalos RR) (ANIS JUNIOR, 2000). São índices no domínio do tempo:

- SDNN: desvio padrão de todos os intervalos RR normais gravados em um intervalo de tempo, expresso em ms;
- SDANN: desvio padrão das médias dos intervalos RR normais, a cada 5 minutos, em um intervalo de tempo, expresso em ms;
- SDNNi: média do desvio padrão dos intervalos RR normais a cada 5 minutos, expresso em ms;
- rMSSD: raiz quadrada da média do quadrado das diferenças entre intervalos RR normais adjacentes, em um intervalo de tempo, expresso em ms;
- pNN50: porcentagem dos intervalos RR adjacentes com diferença de duração maior que 50ms.

Os SDNN, SDANN e SDNNi são obtidos a partir de registros de longo prazo e representam a atividade simpática e parassimpática, mas não permitem distinguir quando as alterações na VFC são devidas ao aumento da atividade simpática ou parassimpática. Os índices rMSSD e pNN50 representam a atividade parassimpática (ANIS JUNIOR, 2000; MCCRATY; SHAFFER, 2015; VANDERLEI et al., 2009).

Outra possibilidade para processar intervalos RR no domínio do tempo é a partir de métodos geométricos, através do índice triangular e o gráfico de Lorenz (ou Poincaré Plot). Estes apresentam intervalos RR em padrões geométricos e diversas abordagens são utilizadas para derivar medidas de VFC a partir deles (VANDERLEI et al., 2009). O índice triangular é calculado com base na construção de um histograma de densidade de intervalos RR normais, que mostra no eixo horizontal (eixo x), o comprimento dos intervalos RR e o eixo vertical (eixo y), a frequência em que cada intervalo ocorre. A junção dos pontos das colunas do histograma forma uma figura em forma de triângulo e a largura da base do triângulo expressa a

variabilidade dos intervalos RR. O índice triangular (correspondente à base do triângulo) pode ser calculado dividindo a área (correspondente ao número total de intervalos RR usados na construção da figura) e a altura (correspondente ao número de intervalos RR com frequência modal) do triângulo (JOHN CAMM et al., 1996; VANDERLEI et al., 2009). O gráfico de Poincaré é um método para análise dinâmica da VFC, que representa uma série temporal dentro de um plano cartesiano. A análise do gráfico de Poincaré pode ser realizada de forma qualitativa (visual), avaliando a forma da figura formada, ou quantitativo, ajustando a elipse do intervalo (JOHN CAMM et al., 1996; VANDERLEI et al., 2009).

No domínio da frequência, a densidade de potência espectral é a mais utilizada quando se trata de indivíduos em condições de repouso. Este domínio decompõe a VFC em componentes oscilatórios fundamentais, sendo os principais:

- HF (*High Frequency*) - componente de alta frequência: corresponde à modulação respiratória e é um indicador da atuação do nervo vago sobre o coração (de 0,15 a 0,4Hz);

- LF (*Low Frequency*) - componente de baixa frequência: decorrente da ação conjunta dos componentes vagal e simpático sobre o coração, com predominância do simpático (de 0,04 e 0,15Hz);

- VLF (*Very Low Frequency*) - componente de muito baixa frequência e ULF (*Ultra Low Frequency*) - ultrabaixa frequência: índices menos utilizados cuja explicação fisiológica não está bem estabelecida e parece estar relacionada ao sistema renina-angiotensina-aldosterona, à termorregulação e ao tônus vasomotor periférico (JOHN CAMM et al., 1996; VANDERLEI et al., 2009).

A razão LF/HF reflete as alterações absolutas e relativas entre os componentes simpático e parassimpático do SNA, caracterizando o balanço autonômico ou também chamado de balanço simpatovagal do coração (MONTANO et al., 2009).

Além disso, a normalização dos dados da análise espectral pode ser usada para minimizar os efeitos das mudanças na banda VLF. Isso é determinado pela divisão do poder de um determinado componente (LF ou HF) pelo espectro total de potência, menos o componente VLF e multiplicado por 100 (LF ou HF/Total Power – VLF) x 100) (JOHN CAMM et al., 1996; VANDERLEI et al., 2009). Para análise dos índices da VFC usando métodos lineares e múltiplos, softwares são utilizados (TARVAINEN et al., 2014).

O método não-linear é determinado por interações complexas de variáveis hemodinâmicas, eletrofisiológicas e humorais, bem como por regulações nervosas autonômicas e centrais. Especulou-se que a análise da VFC com base nos métodos não linear poderia elucidar

informações valiosas para a interpretação fisiológica da VFC e para a avaliação do risco de morte súbita (JOHN CAMM et al., 1996).

2.4 HIPERTENSÃO ARTERIAL (HA)

A hipertensão arterial (HA) é o principal fator de risco para doenças cardiovasculares, sendo considerada um grave problema de saúde pública responsável por cerca de 7,1 milhões de mortes ao ano no mundo e 50% das mortes por doença cardiovascular, atingindo 32,5% dos brasileiros adultos, e mais de 60% dos idosos (MALACHIAS et al., 2016). Mundialmente, estima-se que 54% dos casos de acidente vascular cerebral e 47% dos infartos agudos do miocárdio estejam relacionados a elevados níveis pressóricos (LAWES; HOORN; RODGERS, 2008).

Atualmente, a hipertensão acomete um bilhão de pessoas em todo o mundo e, estima-se que para 2025, a prevalência desta doença seja superior a 1,5 bilhões de pessoas (BENJAMIN et al., 2017). Segundo a *World Health Association*, este aumento se deve aos fatores de risco comportamentais e ao envelhecimento populacional (WHA, 2013).

A HA é caracterizada como uma doença crônica não transmissível, de causas multifatoriais associada a alterações funcionais, estruturais e metabólicas (MALACHIAS et al., 2016). De acordo com a *American Heart Association* (2017) e com a *World Health Association* (WHA) (2013), os principais fatores de risco para a HA são divididos em modificáveis, como hábitos de vida, os quais incluem: o sobrepeso ou obesidade, o sedentarismo, o consumo abusivo de bebidas alcoólicas, o tabagismo, o consumo excessivo de sal e o estresse. E não modificáveis, como idade, raça, sexo e a predisposição genética (BENJAMIN et al., 2017; WHA, 2013).

Segundo a *American Heart Association* e *American College of Cardiology*, a classificação de acordo com a medida casual no consultório, para pessoas acima de 18 anos é dividida da seguinte maneira (WHELTON et al., 2017):

Tabela 1 - Classificação da Pressão Arterial.

Classificação	Pressão sistólica (mmHg)	Pressão diastólica (mmHg)
Normal	<120	<80
Elevada	120 - 129	<80
Hipertensão estágio 1	130-139	80-89
Hipertensão estágio 2	≥140	≥90
Crise Hipertensiva	>180	>120

Fonte: (*American Heart Association e Americann College of Cardiology, 2017*).

Diferentes mecanismos de controle estão envolvidos na manutenção da PA, regulando o calibre e a reatividade vascular, a distribuição de fluido dentro e fora dos vasos e o débito cardíaco. Os mecanismos de controle da PA interagem para garantir a PA em níveis adequados nas mais diversas situações. E quando ocorrem disfunções desses mecanismos de controle há uma alteração na PA (IRIGOYEN; CONSOLIM-COLOMBO; KRIEGER, 2001). Dentre estes mecanismos de controle da PA, destacam-se os neurais. (SANJULIANI, 2002).

Os reflexos cardiovasculares (barorreflexo e quimiorreflexo) promovem ajustes cardiovasculares por meio do SNA, através das porções simpática e parassimpática, cuja atividade é gerada e modulada no SNC. Alterações na PA geram potenciais de ação que são transmitidos aos neurônios sensitivos dos gânglios até o Núcleo Trato Solitário (NTS) na medula. A partir deste local, os sinais são enviados para os núcleos centrais que incluem os neurônios pré-ganglionares simpáticos, pré-ganglionares parassimpáticos e o nervo vago (OLIVA; BAKRIS, 2014). Esses sistemas reflexos aferentes envolvidos no controle da circulação têm como objetivo principal monitorar a PA e informar ao SNC sobre possíveis alterações nesse parâmetro fisiológico a fim de que a mesma seja mantida constante (ACCORSI-MENDONÇA et al., 2005).

Com isto, como dito anteriormente, o SNA, através de desequilíbrios em sua atividade, torna-se um dos principais fatores desencadeantes no desenvolvimento e na manutenção da HA (CHOBANIAN et al., 2003; HERING et al., 2013; SALES et al., 2012). Este sistema tem uma importante participação no controle da PA e pode estar alterado em pacientes com HA, pois seu inadequado funcionamento induz aumento do débito cardíaco (DC) e da resistência vascular periférica (RVP), mantendo a PA elevada (SANJULIANI, 2002). E os altos índices sustentados ao longo do tempo contribuem para desencadear as lesões nos órgão alvos (rins, coração, cérebro), além das doenças renais, metabólicas e cardiovasculares (NOBRE et al., 2010; WHA, 2013).

Para o controle e adequado manejo da PA elevada e de suas consequências é imprescindível a identificação e o acompanhamento dos pacientes hipertensos pelos serviços de saúde, pois tratamentos farmacológicos e não farmacológicos são capazes de melhorar o prognóstico da doença e a qualidade de vida das pessoas (ZATTAR et al., 2013).

2.5 TRATAMENTOS

A medida medicamentosa é o principal tratamento para a hipertensão (WHELTON et al., 2017). Dentre os medicamentos tem-se os diuréticos, inibidores da enzima conversora de angiotensina (ECA), bloqueador do receptor de angiotensina (BRA), bloqueadores do canal de cálcio (CCB), os antagonistas dos receptores beta-adrenérgicos (β -bloqueadores), entre outros (WHELTON et al., 2017). Entretanto, estes medicamentos podem causar efeitos colaterais, tais como hipotensão arterial, insuficiência cardíaca, broncoespasmo (BOSCO; BRAZ, 2001) ou doenças como acidente vascular encefálico (AVE) e diabetes mellitus (KUYPER; KHAN, 2014). Além destes efeitos colaterais, pacientes com hipertensão resistente (hipertensão descontrolada apesar do uso de ≥ 3 medicamentos anti-hipertensivos) (DUDENBOSTEL et al., 2016) ou refratária (nova definição para um subgrupo fenotípico extremo que permanecem descontrolados apesar do uso de ≥ 5 agentes anti-hipertensivos) (MODOLO et al., 2015) não evoluem bem com o manejo farmacológico.

Estudos têm demonstrado à eficácia do manejo não farmacológico da hipertensão, na redução do sistema nervoso simpático e consequentemente no aumento do sistema nervoso parassimpático (BERNARDI et al., 2001; GKALIAGKOUSI; GAVRIILAKI; DOUMA, 2015; HERING et al., 2013). Dentre as principais medidas não medicamentosa encontram-se as mudanças na dieta alimentar (SALES et al., 2012), a prática de exercícios físicos e/ou atividades físicas (GKALIAGKOUSI; GAVRIILAKI; DOUMA, 2015) e exercícios respiratórios (BERNARDI et al., 2001; HERING et al., 2013).

Além das terapias não farmacológicas já citadas, a eletroterapia vem sendo estudada, pois apresenta-se com potencial terapêutico no manejo da hipertensão.

2.6 ELETROTERAPIA

A eletroterapia compreende uma série de recursos terapêuticos para o tratamento de diferentes disfunções e/ou patologias. Para isto, é necessário conhecermos suas diferentes características e parâmetros. Dentre estes, temos:

2.6.1 Classificação das correntes elétricas

- Corrente Contínua: caracterizada por um fluxo contínuo de elétrons, sempre no mesmo sentido ou na mesma direção. Esta corrente é polarizada. Exemplo: corrente galvânica (ROBINSON; SNYDER-MACKER, 2010).

- Corrente Alternada ou Bidirecional: caracterizada por um fluxo bidirecional contínuo de elétrons. O fluxo desta corrente muda constantemente de direção, revertendo à polaridade, tornando-a uma corrente não polarizada. Terapeuticamente, possui frequência na faixa de 1.000 Hz a 10.000 Hz (média frequência). Os impulsos se alternam entre as fases positivas e negativas. Nesta corrente não há polaridade. Exemplo: Corrente Interferencial (CI) (ROBINSON; SNYDER-MACKER, 2010).

- Corrente Pulsada: fluxo não-contínuo de correntes diretas ou alternadas, caracterizada por um fluxo uni ou bidirecional de elétrons que periodicamente param por um período finito. Terapeuticamente, possui frequência na faixa de 1 a 1.000 Hz (baixa frequência). Exemplo de corrente: Estimulação elétrica nervosa transcutânea (TENS) e estimulação elétrica funcional (FES) (NELSON; HAYES; CURRIER, 2003; ROBINSON; SNYDER-MACKER, 2010).

As frequências das correntes são classificadas como: baixa (<1000 Hz), média (1.000 Hz a 10.000 Hz) ou alta (>10.000 Hz). (ROBINSON; SNYDER-MACKER, 2010).

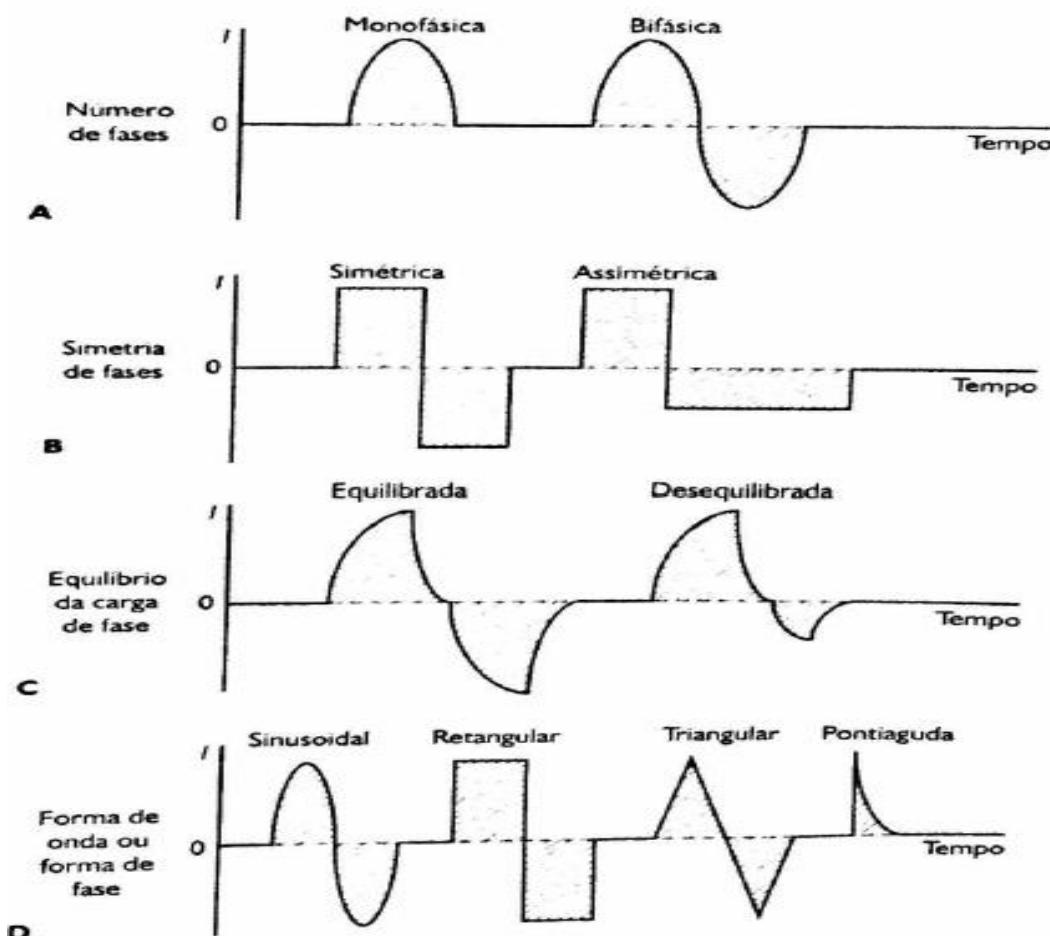
2.6.2 Formas de ondas elétricas

As ondas elétricas se diferenciam pelas suas características, as quais compreendem o número de fases, a simetria e as formas de onda. Essas características estão representadas na Figura 1. As formas de onda podem diferenciar-se quanto ao número de fases. Assim, os pulsos podem ser monofásicos (as partículas carregadas movem-se em uma mesma direção, de acordo com sua carga, indicando que existe apenas uma fase para cada pulso), bifásicos (as partículas carregadas movem-se primeiro em uma direção e depois na direção oposta, indicando que duas fases opostas estão contidas em um único pulso) e até mesmo trifásica ou polifásica (Figura 1A).

Em relação à simetria, estas podem ser simétricas (quando a primeira for à imagem de espelho da segunda fase de um pulso bifásico, sendo o fluxo da corrente iguais nas duas direções) ou assimétricas (a primeira fase de um pulso bifásico não for à imagem espelho da segunda fase, sendo o fluxo das correntes diferente em cada uma das direções) (Figura 1B).

Além disso, são classificadas quanto ao equilíbrio de cargas (equilibrada ou desequilibrada) (Figura 1C). As formas de onda e a forma geométrica de um único pulso ou ciclo da corrente alternada em um gráfico de corrente versus tempo. Estas formas podem ser: retangular, quadrada, triangular, dente-de-serra, exponencial e sinusoidal (Figura 1D) (NELSON; HAYES; CURRIER, 2003; ROBINSON; SNYDER-MACKER, 2010).

Figura 1 - Características descritivas de formas de onda.



Fonte: (ROBINSON; SNYDER-MACKER, 2010).

2.6.3 Frequência

É o número de pulsos elétricos produzidos por segundos. Sua unidade é medida em Hertz (Hz). Por exemplo: 10 Hz = 10 potências de ação (ROBINSON; SNYDER-MACKER, 2010). As frequências de pulso podem ser classificadas em correntes, como a TENS, como: baixa (≤ 50 Hz) ou alta (≥ 50 Hz). Além disso, há relação inversa entre frequência e largura do

pulso ($f=1/T$). Assim, para aumentar a frequência é necessário diminuir a largura de pulso (ROBINSON; SNYDER-MACKER, 2010).

2.6.4 Largura ou duração de pulso

A largura de pulso é definida pela quantidade de tempo que as cargas elétricas irão passar em um pulso. É expresso geralmente em segundos, milissegundos (ms) ou microssegundos (μs). (ROBINSON; SNYDER-MACKER, 2010).

2.6.5 Amplitude ou intensidade da corrente

Definida pelo tamanho do estímulo aplicado. Geralmente é medido em miliampéres (mA). Sendo que, quanto maior a intensidade, maior é o efeito de despolarização nas estruturas subjacentes aos eletrodos e deve ser aumentada ao longo da aplicação para evitar acomodação. Este parâmetro contribui para a fadiga (ROBINSON; SNYDER-MACKER, 2010).

2.6.6 Tempo *on/off*

O período de estimulação (*on*) com relação ao período de repouso (*off*) em uma sessão. O tempo *on* determina por quanto tempo (em segundos) vai ser mantida a contração. Neste tempo, o trem de pulso é fornecido em aplicação terapêutica. O tempo *off* é o tempo entre os trens de pulso, garantindo um período de recuperação para os nervos e músculos estimulados (ROBINSON; SNYDER-MACKER, 2010).

2.6.7 Rampa de subida e rampa de descida

Permite ajustar o número de segundos sobre os quais a amplitude ou o pulso irá aumentar ou diminuir de forma gradual até um valor máximo ajustado pelo controle de amplitude. O início gradual de estimulação produz contrações que imitam de forma mais exata aquelas produzidas em atividades funcionais durante a ativação muscular voluntária (ROBINSON; SNYDER-MACKER, 2010).

2.7 CORRENTE INTERFERENCIAL (CI)

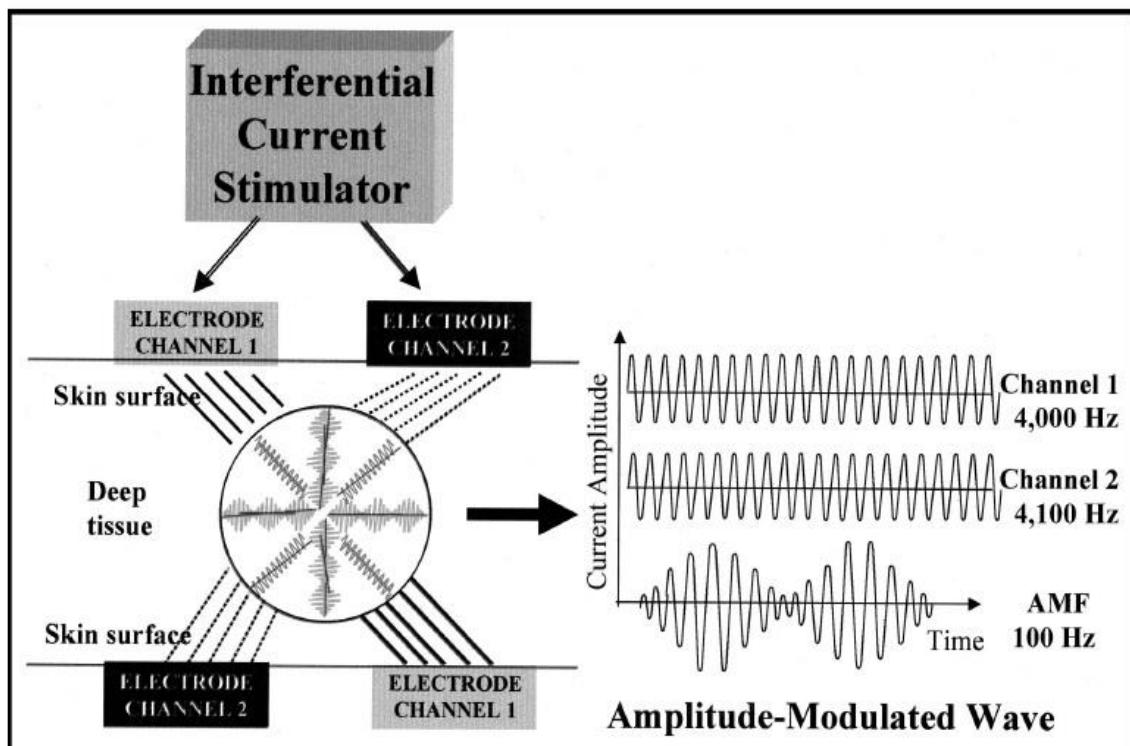
A corrente interferencial (CI) foi descrita pela primeira vez por Neméc na Áustria no final dos anos 50 e foi introduzida comercialmente depois dos anos 70 (GANNE, 1976). Trata-se de uma forma de estimulação elétrica transcutânea, descrita como a aplicação de duas fases

de correntes de média frequência (2 ou 4 KHz) que são transmitidas através da superfície da pele (PIVETTA; BERTOLINI, 2012; YOUN; LEE; LEE, 2016).

A CI é uma das modalidades eletroterapêuticas mais utilizadas na prática clínica. É indicada para aumentar a força e a resistência muscular, reeducação muscular, para produzir analgesia, promover a recuperação do tecido, redução de edemas e diminuir a espasticidade (OZCAN; WARD; ROBERTSON, 2004; PIVETTA; BERTOLINI, 2012; ROBINSON; SNYDER-MACKER, 2010).

O princípio da CI é produzir duas correntes de média frequência com frequências levemente diferentes que interfiram uma com a outra. Assim, uma nova corrente é estabelecida, denominada amplitude de modulação da frequência (AMF). A frequência de corrente resultante será a média das duas. Por exemplo: se a corrente A for 4.000 Hz e a B de 4.100 Hz, a resultante será de 4050 Hz (AMF de 100 Hz). As correntes de média frequência (faixa de 1.000 Hz a 10.000 Hz) (ROBINSON; SNYDER-MACKER, 2010) passarão mais facilmente através da pele do que correntes de baixa frequência devido à impedância mais baixa, gerando efeitos mais profundos nos tecidos (DOHNERT; BAUER; PAVÃO, 2015; SANTOS et al., 2013) (figura 2).

Figura 2 – Amplitude de modulação da frequência (AMF).

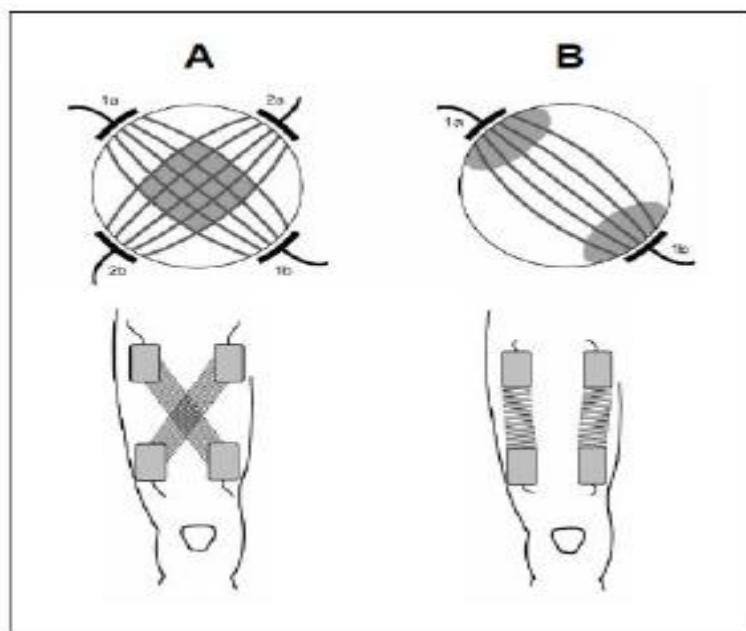


Fonte: (JOHNSON; TABASAM, 2003).

A AMF, tradicionalmente é considerada como sendo o componente efetivo da CI, simulando as correntes de baixa frequência e criando a estimulação diferencial de nervos e certos tipos de tecidos. A partir dessa definição, observa-se que a CI é uma forma semelhante à estimulação elétrica nervosa transcutânea (TENS) (PALMER et al., 1999). A importância da AMF é questionável, uma vez que existe uma falta de efeitos que evidenciam diferenças significativas com diferentes valores de AMF (PALMER et al., 2004).

Além disso, há diferentes formas de aplicação da CI. Está pode ser fornecida na pele de forma bipolar ou de forma tetrapolar. Na tetrapolar há máxima estimulação ocorrerá a 45° aos eletrodos. Nesta forma, a modulação deve-se ao fato de tanto as amplitudes de corrente quanto suas direções precisarem ser somadas, ou seja, uma adição de vetores, aumentando a área efetiva de tratamento. Por outro lado, na aplicação bipolar ocorre a propagação da onda interferencial de forma linear, onde a corrente passa de um eletrodo para outro (Figura 3) (AGNE, 2013; ROBINSON; SNYDER-MACKER, 2010). Entretanto, ainda não foram demonstradas uma maior superioridade em relação à eficácia do método bipolar comparado ao tetrapolar (OZCAN; WARD; ROBERTSON, 2004).

Figura 3 - Exemplo de aplicação da CI nos métodos tetrapolar (A) e bipolar (B) na região anterior da coxa.



Fonte: (OZCAN; WARD; ROBERTSON, 2004).

Existem diferentes características elétricas disponíveis no dispositivo interferencial, algumas delas permite ao usuário ajustar tais características (JOHNSON; TABASAM, 2003).

Uma dessas características na qual é possível ajustar é o ΔF. Este é uma variação no AMF que provoca aumento e diminuição da frequência em padrões pré-definidos no equipamento, que varia de 1 a 100 Hz. Assim, se AMF de 100 Hz, com ΔF de 50 Hz, a variação de modulação ocorrerá entre 100-150 Hz. Esse fato também é usado para evitar o acomodação, pois, além da intensidade, a alteração de frequência é outro fator que combate a acomodação (PIVETTA; BERTOLINI, 2012).

A aplicação da CI em locais onde se concentram maiores quantidades de estruturas como vasos sanguíneos ou gânglios podem produzir modulações diferentes. Um exemplo é a aplicação na região do gânglio estrelado, podendo influenciar a perfusão vascular periférica (JIN; HWANG; CHO, 2017; SANTOS et al., 2013). O gânglio estrelado é composto por um grupo de nervos localizado na região cervical (C8-T4) e é formado pela fusão dos gânglios cervical e inferior primeiro torácico (BARKER et al., 2007). Porém, os efeitos da CI, neste local, sobre o fluxo sanguíneo ainda não está totalmente comprovados devido à falta de evidências (GUGLIELMIN, 2013).

2.8 EFEITOS DA CORRENTE INTERFERENCIAL (CI) NO BALANÇO AUTONÔMICO E PRESSÃO ARTERIAL (PA)

A aplicação da eletroestimulação sensorial com corrente de baixa frequência através da estimulação elétrica nervosa transcutânea (TENS) vem sendo pesquisadas com foco nos seus efeitos sobre o balanço autonômico, fluxo sanguíneo, mecanismos de vasodilatação e consequentemente na PA. Tem-se sugerido que a aplicação dessa corrente nos gânglios estrelados pode induzir a uma vasodilatação local (DA SILVA et al., 2015), ter impacto favorável no aumento da atividade parassimpática e da redução da atividade simpática (SARTORI et al., 2018; STEIN et al., 2011) e gerar efeitos sobre o reflexo pressórico (VIEIRA et al., 2012), apresentando-se com potencial terapêutico no manejo da hipertensão. A neuromodulação, gerada por essas correntes, pode variar dependendo dos parâmetros utilizados (STEIN et al., 2011). Porém, estudos com média frequência, como a Corrente Interferencial, ainda são escassos nestas variáveis. Para entendermos melhor os possíveis efeitos da CI, será necessária uma breve relação desta corrente com a TENS.

Lembrando que essas correntes (TENS e CI) diferenciam-se desde os tipos de corrente (TENS é pulsada, já a CI alternada), frequência (TENS é de baixa frequência e a CI média), o modo de aplicação (TENS bipolar somente e a CI pode ser tanto bipolar quanto tetrapolar) (AGNE, 2013; ROBINSON; SNYDER-MACKER, 2010) e a profundidade no qual cada uma

dessas correntes alcança nos tecidos (CI é mais profunda) (DOHNERT; BAUER; PAVÃO, 2015).

Em um estudo de Wong e Jette (1984) realizado com voluntários saudáveis, submetidos à aplicação da TENS (2 e 85 Hz) nos membros superiores, houve aumento na modulação simpática, embora os resultados não sejam conclusivos quanto ao efeito de cada frequência. Os autores oferecem duas explicações para este aumento simpático. As fibras nervosas vasoconstritoras simpáticas podem ter sido estimuladas pela TENS e que a vasoconstrição de vasos sanguíneos pode ter ocorrido devido a um aumento na demanda de sangue pela contração dos músculos gerada pela TENS (WONG; JETTE, 1984).

A TENS de baixa frequência (10Hz) foi capaz de reduzir a atividade do sistema nervoso simpático e aumentar a do sistema nervoso parassimpático, quando aplicada na região ganglionar paravertebral em voluntários saudáveis. Já a TENS de alta frequência promoveu efeitos opostos (STEIN et al., 2011). Stein et al. (2011) afirma que a região onde a TENS é aplicada pode interferir nesses resultados.

As diferentes frequências da TENS aplicadas ao longo do plexo braquial foi estudada por De Nardi et al. (2017). Observou-se que houve modificação no equilíbrio simpático-vagal, onde a TENS de baixa frequência (10 Hz) aumentou a atividade simpática e diminuiu a atividade parassimpática. Por outro lado, a TENS de alta frequência (100 Hz) apresentou efeitos opostos, o que reforça os efeitos sobre o balanço autonômico em voluntários saudáveis (NARDI et al., 2017). Utilizando os mesmos parâmetros e locais de aplicação, Franco et al. (2014) afirmou que a TENS modificou a resposta venosa e que a baixa frequência (10Hz) aumenta e a alta frequência (100Hz) diminui a sensibilidade dos receptores a1-adrenérgicos, demonstrando que diferentes frequências de estímulos promovem efeitos opostos sobre esses receptores. No sistema cardiovascular, o receptor a1-adrenérgico altera a vasomotricidade, modulando a resistência vascular periférica por venoconstrição e cooperando com ajustes da pressão arterial sistêmica pelo retorno venoso (FRANCO et al., 2014). Além disso, a TENS (80Hz) em pacientes com insuficiência cardíaca crônica, aplicada perifericamente na região do pé para avaliar atividade barorreflexa, mostrou aumentar esta variável (GADEMAN et al., 2011).

Já Kamali et al. (2017) comparou a TENS baixa frequência (4Hz) nos gânglios simpáticos toracolombares, pontos de acupuntura (perna) e no pé. Avaliaram o fluxo sanguíneo periférico. Os resultados demonstraram que a TENS nos gânglios simpáticos nos níveis de T12, L1 e L2 aumentou o fluxo sanguíneo dos membros inferiores comparado pontos de acupuntura (KAMALI et al., 2017).

A TENS (80Hz) também mostrou atenuar a redistribuição do fluxo sanguíneo durante a oclusão circulatória pós-exercício em indivíduos saudáveis, o que suporta a hipótese de que o TENS num momento agudo melhora o fluxo sanguíneo do músculo periférico e diminui a atividade simpática avaliada pela VFC. Sugeriu-se que esses efeitos podem estar ligados à liberação de β -endorfina por um efeito agonista sobre os receptores μ -opioides locais, o que parece ser um mecanismo fundamental para a modulação da PA, aumentando a liberação de oxigênio para o músculo (TOMASI et al., 2015).

Da Silva et al. (2015) demonstram que a TENS (80 Hz) aumentou o efeito vasodilatador local, o que pode contribuir para reduzir a PA (DA SILVA et al., 2015). Entre os mecanismos que podem explicar esta ação anti-isquêmica estão: a inibição da vasoconstrição simpática, a liberação de peptídeos vasodilatadores de neurônios sensoriais e o efeito da bomba de contrações musculares (VILELA-MARTIN et al., 2016).

Sartori et al. (2017) avaliaram efeitos agudos da baixa (4Hz) e alta (100Hz) frequência da TENS localizada na região paravertebral ganglionar na modulação do sistema nervoso em indivíduos com hipertensão. A TENS de baixa frequência melhorou o controle autonômico cardiovascular, reduzindo a modulação simpática e aumentando a modulação parassimpática. Porém na PA esta frequência não gerou mudanças. A TENS de 100Hz aumentou a PAD. Além disso, citam que as respostas distintas das interações do sistema nervoso autônomo, podem ser determinadas de acordo com a metodologia dos estudos (SARTORI et al., 2018). Vieira et al. (2012) mostraram que a estimulação da TENS (80Hz), também na região paravertebral ganglionar, atenua a PA e as respostas vasoconstritoras durante a ativação do exercício e metaborreflexo, associadas à melhora do equilíbrio simpatovagal em indivíduos saudáveis jovens e idosos (VIEIRA et al., 2012). Porém Lazarou et al. (2009) trouxeram que a TENS, aplicada no nervo radial, foi incapaz de produzir um efeito significativo sobre a BP, independentemente da intensidade (LAZAROU et al., 2009). Assim como Silverdal et al. (2012) que comparou a TENS baixa frequência (2Hz) com medicação anti-hipertensiva (felodipina), aplicada em pontos de acupuntura no braço, e não obteve diferenças da PA com a TENS (SILVERDAL et al., 2012).

Guglielmin (2013) comparou os efeitos da TENS alta frequência (80 Hz) e da CI com AMF em alta frequência (100 Hz) aplicados na região ganglionar (de C7 a T4) sobre a variabilidade da frequência cardíaca (VFC) em voluntários jovens saudáveis durante exercício físico. Demonstraram que ambas foram eficazes para aumentar o fluxo sanguíneo muscular periférico através de uma maior atenuação em metaborreflexo muscular e tônus vasoconstritor durante o exercício, porém a CI indicou um maior efeito vasodilatador do que a TENS. Além

disso, a CI diminuiu a modulação VFC em indivíduos saudáveis, com o aumento do componente HF e diminuindo LF e LF/HF após o exercício com ou sem oclusão circulatória do músculo (GUGLIELMIN J.Z, 2013).

Santos et al. (2013) também avaliaram os efeitos da CI com AMF de 100Hz no metaborreflexo muscular antes do exercício na região ganglionar paravertebral em indivíduos saudáveis. A CI atenuou as respostas periféricas causadas pela atividade do metaborreflexo muscular, mantendo o fluxo sanguíneo periférico e a resistência vascular periférica dentro da normalidade. Esses achados contribuem para uma melhor compreensão dessa terapia.

Em outro estudo, investigaram as mudanças no fluxo sanguíneo nos diferentes parâmetros da CI (AMF 100Hz + 10-20 mA, AMF 5 Hz + 45-50 mA e AMF 100 Hz + 80-90 mA). A AMF 100 Hz à nível sensorial (10-20 mA) reduziu do diâmetro do vaso e aumentou levemente o fluxo sanguíneo avaliados imediatamente e 30 minutos após a aplicação, mas na estimulação AMF 5Hz ao nível sensório-motor (45-50 mA) os resultados sobre os aumentos do diâmetro do vaso e do fluxo sanguíneo foram muito mais pronunciados. Os autores sugeriram que a AMF de 5Hz e a alta intensidade apresentam resultados mais promissores no aumento do fluxo sanguíneo local (JIN; HWANG; CHO, 2017).

Noble e Henderson (2000) mostraram que a CI (10-20 Hz), aplicada através de eletrodos de sucção no quadríceps, produziu um aumento no fluxo sanguíneo cutâneo com um aumento concomitante na temperatura da pele. Estes resultados sugerem que o efeito fisiológico subjacente é a vasodilatação, através da inibição do sistema nervoso simpático (NOBLE et al., 2000). Por outro lado, a CI (AMF 90-100 Hz) aplicada no gânglio estrelado em indivíduos assintomáticos por 10 minutos não causou vasodilatação do antebraço em indivíduos assintomáticos. Tal estudo questionou a teoria de que o IC é capaz de bloquear os impulsos vasoconstritores simpáticos nos nervos periféricos (INDERGAND; MORGAN, 1995). Percebe-se que ainda há poucas publicações a respeito de sua utilidade clínica ou mesmo de suas premissas fisiológicas básicas desta corrente. A seguir será apresentada tabela com variáveis dos estudos citados anteriormente.

Tabela 2 – Revisão das variáveis dos estudos.

Estudo	Desfechos	População	Local aplicado	Corrente	Frequência
Vieira et al. (2012)	Metaborreflexo e VFC (no exercício)	Jovens e idosos saudáveis	Central (C7-T4)	TENS	80 Hz
Tomasi et al. (2015)	VO2, VE/VCO2, VO2/FC	Saudáveis	Central (C7-T4)	TENS	80 Hz
Sartori et al. (2018)	VFC	Hipertensos	Central (T1-L2)	TENS	4 Hz x 100 Hz
Stein et al. (2011)	VFC	Saudáveis	Central (T1-L2)	TENS	10 Hz x 100 Hz
Kamali et al. (2017)	Fluxo sang.		Central (T12, L1 e L2), periférico (Perna) e periférico (Pé)	TENS	4 Hz
De Nardi et al. (2017)	VFC	Saudáveis	Periférico (Plexo braquial)	TENS	10 x 100 Hz
Franco et al. (2014)	Reatividade vascular venosa	Saudáveis	Periférico (Plexo braquial)	TENS	10 x 100 Hz
Gademan et al. (2011)	Barorreflexo	Insuficiência Cardíaca	Periférico (Pé)	TENS	80 Hz
Silverdal et al. (2012)	PA (tens x medicação)	Hipertensos	Periférico (braço)	TENS	2 HZ
Da Silva et al. (2015)	Rigidez arterial	Saudáveis	Central (C7-T4)	TENS	80 Hz
Lazarou et al. (2009)	Dor e PA	Saudáveis	Periférico (braço)	TENS	2 Hz (diferentes intensidades) 10-20 Hz x 80-
Noble et al (2000)	Fluxo sanguíneo cutâneo	Saudáveis	Periférico (Quadríceps)	CI	100 Hz x 10-100 Hz
Santos et al. (2013)	Metaborreflexo	Saudáveis	Central (C7-T4)	CI	25 Hz x 100 Hz 100Hz (10-20mA)
Jin et al. (2017)	Fluxo sanguíneo	Saudáveis	Central (T1- T4)	CI	x 5 Hz (45-50mA) x 100hz (80- 90mA)
Indergand e Morgan (1995)	Fluxo Sanguíneo	Saudáveis	Central (C7)	CI	90-100 Hz

CI: Corrente Interferencial; TENS: Estimulação elétrica nervosa transcutânea; VFC: Variabilidade da frequência cardíaca; PA: Pressão arterial; Hz: Hertz.

2.9 JUSTIFICATIVA/OBJETIVO

O presente trabalho se justifica pelos efeitos previamente demonstrados da eletroterapia sobre a pressão arterial (PA) e no balanço autonômico, e principalmente pelos potenciais efeitos da CI sobre estas variáveis em voluntários normotensos e hipertensos. As alterações dessas correntes elétricas sobre estas variáveis cardiovasculares, apresentam potencial terapêutico e consequentemente relevância clínica, em especial em pacientes hipertensos refratários ou em crises hipertensivas, onde o manejo farmacológico não se apresenta efetivo. Neste contexto, este recurso eletroterápico pode ser uma ferramenta não farmacológica coadjuvante no manejo da hipertensão.

Ressalta-se que esta dissertação comprehende parte de um projeto temático intitulado “Efeitos da estimulação elétrica nervosa transcutânea (TENS) e da corrente interferencial sobre a pressão arterial (PA) e balanço autonômico de voluntários normotensos e pacientes hipertensos”. Neste sentido, o objetivo da pesquisa consistiu em estudar os efeitos da aplicação da CI com AMF em 100 Hz e com AMF em 10 Hz, aplicada na região paravertebral ganglionar (C7-T4), no balanço autonômico e na PA de voluntários saudáveis. Desta forma, determinando os melhores parâmetros dessa corrente elétrica para pacientes hipertensos.

A seguir será apresentado o artigo intitulado “Effects of interferential current on autonomic balance and blood pressure in healthy volunteers: randomized clinical trial” a ser submetido a revista *Physiotherapy* (Qualis A1 na área 21 da CAPES).

3 ARTIGO

EFFECTS OF INTERFERENTIAL CURRENT ON AUTONOMIC BALANCE IN HEALTHY VOLUNTEERS: RANDOMIZED CLINICAL TRIAL

Murilo Rezende Oliveira^a, Juliana Nascimento^a, Natiele Righi^a, Antonio Marcos Vargas da Silva^a, Rodrigo Della Mea Plentz^b, Luis Ulisses Signori^a.

^a Programa de Pós-Graduação em Reabilitação Funcional, Universidade Federal de Santa Maria – UFSM, Santa Maria, RS, Brasil.

^b Programa de Pós-Graduação em Ciências da Reabilitação, Universidade Federal de Ciências da Saúde de Porto Alegre - UFCSPA, Porto Alegre, RS, Brasil.

Contact Information:

Luis Ulisses Signori. Programa de Pós-Graduação em Reabilitação Físico-Funcional, Centro de Ciências da Saúde (CCS), Universidade Federal de Santa Maria - UFSM, Av. Roraima, 1000. Bairro Camobi, ZIP: 97105-900 – Santa Maria – RS [Brasil]. Tel: (55) 55 3220-8234. E-mail: l.signori@hotmail.com

ABSTRACT

Objective: To evaluate the effects of different amplitude-modulated frequency (AMF) at 100Hz and 10Hz of the interferential current (IC) on autonomic balance in healthy volunteers.

Design: Randomized placebo-controlled, crossover study with concealed allocation and assessor blinding.

Settings: Clinical research laboratory.

Participants: Thirty healthy volunteers (21 women), with 23.7 ± 2.7 years old and body mass index (BMI) $23.2 \pm 2.7 \text{ kg/m}^2$.

Interventions: Placebo (equipment turned off), IC with AMF 100Hz and 10Hz were randomized and applied in the paravertebral ganglionar region for 30 minutes, within the period of one week.

Outcome measure: Autonomic balance evaluated by the heart rate variability before and immediately after the interventions.

Results: AMF 10Hz intervention reduced the sympathetic activity (LF n.u.) in 6% (95%CI = -2.2 to -9.9) and an increase in the parasympathetic (HF n.u.) in approximately 6% (95% CI = 2.2 to 9.9). On the other hand, the AMF 100 Hz intervention increased 12% (95%CI = 8.5 to 16.3) to sympathetic activity (LF n.u.) and decreased 12% (95%CI = -8.8 to -16.6) to parasympathetic activity (HF n.u.).

Conclusion: IC changes the autonomic balance in healthy volunteers. The AMF of 10Hz reduces the sympathetic activity and increases parasympathetic, although the AMF of 100Hz has opposite results. The IC with AMF of 10Hz improves the autonomic balance and presents potential effects to be tested in the non-pharmacological management of patients with hyperactive sympathetic system, such as hypertensives and patients with heart failure.

Clinical trial registration number: NCT03258489.

Contribution of the Paper

- The interferential current (CI) applied on the paravertebral ganglionar region for 30 minutes modifies the autonomic balance;
- The amplitude-modulated frequency (AMF) at 10Hz decreased sympathetic activity and increased parasympathetic, but AMF of 100Hz had opposite effects.
- The AMF at 10Hz presents potential effects on the management of patients with hyperactive sympathetic system, such as hypertensives and patients with heart failure;

Key words: Autonomic nervous system. Sympathetic nervous system. Parasympathetic nervous system. Heart Rate. Blood Pressure. Electric Stimulation Therapy.

INTRODUCTION

The autonomic nervous system (ANS) is divided into sympathetic and parasympathetic components [1], where activation of the sympathetic nervous system causes increases in heart rate, peripheral vascular resistance and venous return to the heart, favoring an increase in blood pressure (BP) [2]. On the other hand, the activation of the parasympathetic nervous system favors the reduction of BP [1,2]. The autonomic imbalance, characterized by the hyperactive sympathetic system and the hypoactive parasympathetic system, is associated with cardiovascular diseases, such as hypertension and heart failure [3]. Therapeutic correction of this imbalance is associated with reduction in mortality from cardiovascular diseases [4].

Sensorial electrostimulation has been studied as a therapeutic alternative in the correction of this imbalance [5–7]. The application of transcutaneous electrical nerve stimulation (TENS), which is a low-frequency current (<1000Hz) [8], showed increased baroreflex sensitivity through a somatosensory impulse mediated by the fibers A- δ [9], increase the release of endogenous opioids [10], decrease levels of epinephrine and norepinephrine, generating attenuation of vascular response and vasodilatory responses [11], alter the sensitivity of peripheral α 1-adrenergic receptors [12] and capable of increasing peripheral blood flow through circulatory changes caused by the stimulation of sympathetic postganglionic efferent fibers, reducing peripheral vascular resistance [11,12]. However, the neuromodulation generated by this low frequency current may vary depending on the local of application and parameters used, especially on the frequency used [6,7,12].

Interferential current (IC), another form of sensory electrostimulation, is formed from two different medium-frequency currents, which interfere with each other, resulting in a new electric current, called amplitude-modulated frequency (AMF) [13,14]. A recent study has shown that different AMF (100Hz and 5Hz) of IC applied in the paravertebral region modify the vessel diameter and blood flow of healthy volunteers [15], which suggests a therapeutic potential in reducing sympathetic activity and BP, but such effects have not yet been investigated.

Medium-frequency currents (IC) pass more easily through the skin than low-frequency currents (TENS), due to their lower impedance, generating effects in the deeper tissues [16,17]. These differences in skin propagation and in the depth of the penetration of IC in relation to TENS suggest that this electrical current may be more effective in the

management of autonomic imbalance and the fact that there are yet no studies of the effects of IC on this variable, requiring further investigation. In this sense, the objective of this research was to evaluate the effects of the application of different frequencies (AMF 100Hz and 10Hz) of IC on the autonomic balance in healthy volunteers.

METHODS

Design overview and Settings

The present double-blind, crossover, randomized clinical trial was approved by the institutional ethics committee (Protocol: 2.180.257) and was registered in Clinical trial (Protocol: NCT03258489). Methodologic design was based on the determinations of the 2010 CONSORT statement. The ethical precepts contained in CNS Resolution 466/2012 were respected. Volunteers were informed of the study protocol and provided written informed consent before participating. Data were collected between October 2017 and April 2018 at the Clinical Research Laboratory of Federal University of Santa Maria.

Participants

All enrolled volunteers were literate, both sexes, aged between 20 and 30 years-old, body mass index (BMI) lower than 30 kg/m^2 ; non-smokers; and free of skeletal muscle, rheumatic, cardiovascular, metabolic, neurologic, oncologic, immune, hematologic, psychiatric or cognitive disorders. The enrolled volunteers were not taking any type of medication (except contraceptive).

Participants were instructed not to perform exhaustive exercises (48 hours before) and not to drink beverages containing caffeine or alcohol 12 hours before the exams. On the day of the examinations, volunteers who presented values of blood pressure above normal ($\text{SBP} > 120\text{mmHg}$ and $\text{DBP} > 80\text{mmHg}$) [18] or reported stressful events that occurred in the last 48 hours, would be excluded from the study. From these criteria, three volunteers, who presented BP values above normal, were excluded. The flowchart of the study design is shown in Figure 1.

Interventions

All volunteers underwent the three interventions (Placebo, IC: AMF 100Hz and IC: AMF 10Hz), which were performed within the period of one week. Autonomic balance and blood pressure (BP) measurements were evaluated simultaneously before

and immediately after the interventions. Interventions were previously randomized through the website www.random.org. The information was kept in a sealed brown envelope and was randomly chosen on the day of the exams, with the evaluator and the volunteers blinded about the interventions.

The volunteers were placed in the supine position and remained in this position for one hour and a half (rest: 20min, data collection: 20min, interventions: 30min and data collection: 20min). The temperature of the room was maintained between 21 to 24°C. The skin was duly sanitized with 70% alcohol and the self-adhesive electrodes (5x5 area) were positioned in the tetrapolar form, in the paravertebral ganglionar region, between C7 and T4 [17,19–21], according to Figure 2.

The IC (Dualpex 071® model, Quark Medical, São Paulo, Brazil) was applied for thirty minutes, in continuous flow, with biphasic pulses and a slope of 1/5/1. The IC with AMF 100Hz was used in the following parameters: the current was adjusted to 4000Hz, pulse width of 100 μ s and an AMF variation of 0Hz. IC with AMF 10Hz: current was adjusted to 4000Hz, pulse width of 100 μ s and an AMF variation of 0Hz. Intensity in milliamperes (mA) was adjusted every 5 minutes at the sensorimotor threshold level, without muscle contraction or according to the tolerance to the stimulus informed by the volunteers [6]. The placebo intervention consisted in the repetition of the previous procedures, where the intensity was increased until the sensorial threshold and later the equipment was turned off, remaining in such way until the end of the data collections.

Outcomes and follow-up

The primary outcome measure was autonomic balance, which was assessed by the heart rate variability (HRV) in the time-domain and frequency-domain. Secondary outcome measure was blood pressure (BP).

Heart Rate Variability

The autonomic balance was evaluated through the heart rate variability (HRV) technique using a pulse frequency meter (Polar brand, model 810i, Kempele - Finland). The heart rate acquisition (sample rate – 1000Hz) was performed in time series of the RR intervals and acquired at continuous intervals (10 minutes) before and immediately after the interventions. The data were collected with controlled breathing (12 breaths per minute; I/E: 2/3) for 10 minutes [6]. In HRV analysis, time and frequency domain were

analyzed using an area corresponding to 5 minutes (containing at least 256 consecutive heart beats), which was moved over the visually more stable section of the 10-minute period before and immediately after the electrostimulation of IC.

The analysis was performed by spectral power density. This analysis decomposes the HRV into fundamental oscillatory components, the main ones being: high frequency component (HF) of 0.15 to 0.4Hz, corresponding to respiratory modulation and to the indicator of the vagus nerve acting on the heart; low frequency component (LF) of 0.04 and 0.15Hz, which is due to the joint action of the vagal and sympathetic components on the heart, predominantly sympathetic. Normalized units (n.u.) were obtained by dividing the power of a given component by the total power (from which VLF has been subtracted) and multiplying it by 100 (LF ou HF/(Total Power – VLF) x 100) [3]. The LF/HF ratio reflects the absolute and relative changes between the sympathetic and parasympathetic components of the ANS, characterizing the sympatho-vagal balance on the heart [3]. The data were transferred to a computer and the R-R ranges processed to calculate the HRV using the parameters of the Kubios program HRV version 2.1 (Kuopio, Finland, 2012).

The variables in the time-domain were the heart rate (HR), standard deviation of all normal to normal R-R (NN) interval (SDNN), square root of the mean of the squares of successive R-R interval differences (rMSSD), percentage of intervals differing more than 50 ms different from preceding interval (PNN50%) and Triangular Index. At the frequency-domain were total power (TP), low frequency (LF), high frequency (HF) and sympatho-vagal balance ratio (LF/HF).

Blood pressure

Blood pressure (BP) monitoring (Systolic blood pressure - SBP, Diastolic Blood Pressure – DBP and Mean Blood Pressure - MBP) was performed using a multiparametric monitor (Dixtal, model 2021, Manaus, Brazil). The cuff was positioned on the right arm with the patient positioned in the supine position on the stretcher. Data were collected before and immediately after the interventions through three measurements, with a 10 minutes interval between them and the data expressed by means of measures.

Statistical analysis

Data are presented as mean and standard deviation (SD). The Kolmogorov-Smirnov normality test was used. Variables were compared by two-way ANOVA of

repeated measures, followed by Bonferroni *post hoc*. Variations between interventions are reported as mean differences and 95% confidence intervals (95% CI). The α error rate of 5% ($p < 0.05$) was considered.

Sample size

The sample size was calculated based on a previous study data [7]. It was estimated that a sample size of 30 volunteers in each group would have a power of 85% to detect a 11% difference between means (standard deviation 13%) for the sympathetic activity after TENS application, for $\alpha = 0.05$ (5%).

RESULTS

The sample was composed of thirty healthy volunteers (21 women; 13 using contraceptives), with 23.7 ± 2.7 years old, body mass index (BMI) 23.2 ± 2.7 kg/m² and Waist/Hip relation 0.77 ± 0.04 cm.

HRV data in the time domain and frequency in response to different AMF of IC are shown in Table 1. In the time domain, HR was within the limits of normality in all evaluations, but after interventions reduced 4 bpm (95%CI = -1 to -7) in the placebo intervention, 3 bpm (95%CI = 0.2 to -6) at AMF 100Hz and 4 bpm (95%CI = -0.2 to -7) at AMF 10Hz. SDNN remained unchanged in placebo intervention, increased 15.4 ms (95%CI = 2.3 to 28.5) at AMF 100Hz and 13.6 ms (95%CI = 20.1 to 26.7) at AMF 10Hz. rMSSD increased 13.3 ms (95%CI = 1.8 to 24.9) after the placebo intervention and 18.2 ms (95% CI = 6.7 to 29.8) after AMF 10Hz. PNN50% also increased 6.4% (95%CI = -0.4 to 13.3) in the placebo and 9.8% (95%CI = 2.9 to 16.7) at AMF 10Hz. Triangular Index presented differences in time ($p = 0.020$), but was not confirmed Bonferroni posttest ($p > 0.05$) through confidence intervals (Placebo: 95%CI = -2.20 to 2.91; AMF 100Hz: 95%CI = -1.18 to 3.93; AMF 10Hz, 95%CI = -0.41 to 4.69).

In the frequency domain (Table 1), TP presented an increase of 2627 ms² (95%CI = 279 to 4975) at AMF 100Hz and 2768 ms² (95%CI = 419 to 5116) at AMF 10Hz. The power in low frequency range (LF - ms²) increased 784 ms² (95%CI = 340 to 1229) at AMF 100Hz, while the power in high frequency range (HF - ms²) increased 1705 ms² (95%CI = 716 to 2694) at AMF 10Hz.

After data normalization, the placebo intervention did not modify sympathetic (LF) and parasympathetic (HF) activities. The AMF 100 Hz intervention increased 12%

(95%CI = 8.5 to 16.3) to sympathetic activity (LF n.u.) and decreased 12% (95%CI = -8.8 to -16.6) to parasympathetic activity (HF n.u.) in relation to the period prior to application (Figure 3A). On the other hand, after the application of AMF 10Hz, there were opposite effects, observing a reduction of sympathetic activity (LF n.u.) in 6% (95%CI = -2.2 to -9.9) and an increase in the parasympathetic (HF n.u.) in approximately 6 % (95% CI = 2.2 to 9.9) (Figure 3B). The AMF 100Hz and 10Hz presented different results after the application, where the AMF 100Hz increased sympathetic activity in 16% and reduced parasympathetic activity 16% (95%CI = 6.6 to 25.3) in relation to AMF 10Hz. Only the AMF 100Hz increased the LF (n.u.) in 9.7% (95%CI = 0.5 to 19.0) and reduced the HF (n.u.) in 9.7% (95%CI = -0.4 to -19.0) compared to placebo.

LF/HF ratio increased 0.4 (95%CI = 0.3 to 0.6) after application of AMF 100Hz and decreased 0.2 (95%CI = -0.02 to -0.3) after AMF 10Hz (Figure 3C). LF/HF decreased 0.5 (95%CI = -0.2 to -0.8) between frequencies (100Hz vs 10Hz). AMF 100Hz increased this ratio by 0.3 (95%CI = 0 to 0.7) compared to placebo. Data of the Blood Pressure are shown in table 2. SBP, DBP and MBP no differences were found between interventions, time and in the interaction in the study (Table 2).

DISCUSSION

The results demonstrate that the different AMF of IC applied in the paravertebral ganglionar region (C7 to T4) modify the autonomic balance of healthy volunteers. AMF 10Hz reduced sympathetic activity (LF) and increased parasympathetic (HF) of healthy volunteers. On the other hand, the AMF 100Hz presented opposite results. Also, the different AMF of IC did not modify BP.

Research on the IC effects on the cardiovascular system is scarce. AMF is considered to be the effective component of IC, simulating low frequency currents such as TENS [22]. However, these currents differ in relation to the frequency of their currents (TENS is low-frequency and IC medium-frequency) [8] and the depth in which each of them reaches the tissues [16,17]. Although these currents are electrically different and the depth reached in the tissues, studies have shown similar results when compared in analgesia [16,23]. In this sense, in part, we will refer to TENS in the discussion of the results of the present study.

The site of application was chosen according to previous studies with the use of TENS [19–21] and IC [17]. In this place, the anatomical organization of the ANS occurs

with the presence of the ganglia that store the cellular bodies of the postganglionic sympathetic neurons, from which the axons forming the cardiac nerves to the periphery leave [1]. Due to this anatomical location, sensory stimulation in this region favors changes in the autonomic nervous system [5] and repercussions on peripheral blood flow [11].

In the present study, the IC with AMF 10Hz improved the autonomic balance, as it reduced sympathetic activity and increased parasympathetic activity. Previous studies have shown that the stimulation of IC with AMF 5Hz (bipolar application in T1-T4) [15] and AMF 10-20Hz (applied in the quadriceps) [24] increased blood flow, reinforcing the findings of the present study. TENS (10Hz) applied on the paravertebral ganglionar rengion presented similar results to this research [6] and meta-analysis showed that the TENS (<50Hz) reduces SBP in healthy volunteers [25], showing that lower frequencies present better results on the balance autonomic and BP in these sensory stimuli. In addition, TENS (<4Hz) demonstrated to reduce sympathetic activity by increasing the release of endogenous opioids in the ANS [10]. We believe that increasing of endogenous opioids also occur with the AMF 10Hz IC.

The AMF 100Hz increased sympathetic activity and reduced parasympathetic, which was demonstrated in the present study. Previous study has shown that the AMF 100Hz of IC decreased vessel diameter and increased blood flow (bipolar form application in T1-T4), which is due to the increase in sympathetic activity [15]. Our results also agree with a previous study using TENS 100Hz, applied to the paravertebral ganglionar region, that demonstrated the increase of the sympathetic activity and reduction of the parasympathetic evaluated by the HRV technique [6]. Wong e Jette (1984) suggest that increased sympathetic activity may be related to vasoconstricting sympathetic fiber stimulation, generated by increased blood flow demand, producing pain relief [26].

The different AMF (100Hz and 10Hz) of the IC had opposite results, which also have been demonstrated with the different frequencies and sites of TENS application [6,7,12]. Such results reinforce that the cardiovascular effects, induced by sensorial electro stimulation, depend on the parameters used (frequency, place of application of electrodes, duration of the stimulus) and on the population studied [7,12,15,25].

The BP in relation to the different frequencies of AMF of IC remained unchanged. These results have already been demonstrated in studies that applied TENS (<4Hz) and did not identify alterations in BP in healthy subjects [27] and hypertensive

patients [5,28]. However, the TENS (<50Hz) reduced BP in healthy volunteers [25] and TENS (80Hz) reduced SBP in young healthy volunteers [21]. These studies suggest that TENS is more effective than IC in the reduction of BP in healthy volunteers and hypertensive patients, but studies comparing these different sensorial stimuli have not yet been performed in these populations.

The absence of evaluation of plasma catecholamines and the duration of these effects on the autonomic balance and the method of assessing blood pressure through the casual measure are presented as limitations of the study. Among the clinical implications, the effects of IC with AMF 10Hz, in the paravertebral ganglionar region, become a potential non-invasive and non-pharmacological approach to be tested to improve the autonomic balance of patients with sympathetic hyperactivity, such as resistant hypertensive and patients with heart failure.

CONCLUSION

The application of IC applied in the paravertebral ganglionar region modifies the autonomic balance of healthy volunteers. The AMF of 10Hz reduces the sympathetic activity and increases parasympathetic, although the AMF of 100Hz has opposite results. The IC with AMF of 10Hz improves the autonomic balance and presents potential effects to be tested in the non-pharmacological management of patients with hyperactive sympathetic system, such as hypertensives and patients with heart failure.

Ethical Approval: Ethics approval was obtained from the University of Santa Maria (UFSM) Human Research Ethics Committee (Protocol: 2.180.257).

Funding: This study was supported by the National Council of Technological and Scientific Development and Coordination of Improvement of Higher Education Personnel.

Conflict of Interest: There is no conflict of interest.

References

- [1] Shen MJ, Zipes DP. Role of the autonomic nervous system in modulating cardiac arrhythmias. *Circ Res* 2014;114:1004–21. doi:10.1161/CIRCRESAHA.113.302549.
- [2] Shafi T, Mullangi S, Jaar BG, Silber H. Autonomic dysfunction as a mechanism of intradialytic blood pressure instability. *Semin Dial* 2017;30:537–44. doi:10.1111/sdi.12635.
- [3] Mccraty R, Shaffer F. Heart Rate Variability: New Perspectives on Physiological Mechanisms, Assessment of Self-regulatory Capacity, and Health Risk. *Glob Adv Heal Med* 2015;4:46–61. doi:10.7453/gahmj.2014.073.
- [4] Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2013;34:2159–219. doi:10.1093/eurheartj/eht151.
- [5] Sartori S, Stein C, Coronel C, Macagnan F, Plentz R. Effects of transcutaneous electrical nerve stimulation in autonomic nervous system of hypertensive patients: a randomized controlled trial. *Curr Hypertens Rev* 2018;14.
- [6] Stein C, Dal Lago P, Ferreira JB, Casali KR, Plentz RDM. Transcutaneous electrical nerve stimulation at different frequencies on heart rate variability in healthy subjects. *Auton Neurosci Basic Clin* 2011;165:205–8. doi:10.1016/j.autneu.2011.07.003.
- [7] Nardi AT de, Hauck M, Franco OS, Paulitsch FDS, Silva AMV da, Signori LU. Different frequencies of transcutaneous electrical nerve stimulation on sympathetic-vagal balance. *Acta Sci Heal Sci* 2017;39:9. doi:10.4025/actascihealthsci.v39i1.32854.
- [8] Robinson AJ, Snyder-Mackler L. Clinical Electrophysiology: Electrotherapy and Electrophysiologic Testing. 3°. 2008.
- [9] Gademan MGJ, Sun Y, Han L, Valk VJ, Schalij MJ, Van Exel HJ, et al. Rehabilitation: Periodic somatosensory stimulation increases arterial baroreflex sensitivity in chronic heart failure patients. *Int J Cardiol* 2011;152:237–41. doi:10.1016/j.ijcard.2010.07.022.
- [10] Campbell TS, Ditto B. Exaggeration of blood pressure-related hypoalgesia and reduction of blood pressure with low frequency transcutaneous electrical nerve stimulation 2002;473–81.
- [11] Kamali F, Mirkhani H, Nematollahi A, Heidari S, Moosavi E, Mohamadi M. The Effect of Transcutaneous Electrical Nerve Stimulation of Sympathetic Ganglions and Acupuncture Points on Distal Blood Flow. *JAMS J Acupunct Meridian Stud* 2017;10:120–4. doi:10.1016/j.jams.2017.01.003.

- [12] Franco OS, Paulitsch FS, Pereira APC, Teixeira AO, Martins CN, Silva AM V, et al. Effects of different frequencies of transcutaneous electrical nerve stimulation on venous vascular reactivity. *Brazilian J Med Biol Res* 2014;47:411–8. doi:10.1590/1414-431X20143767.
- [13] Youn J-IJ-I., Lee HS. HS, Lee SS. Determination of effective treatment duration of interferential current therapy using electromyography. *J Phys Ther Sci* 2016;28:2400–3. doi:10.1589/jpts.28.2400.
- [14] Mendonça Araújo F, Alves Menezes M, Martins de Araújo A, Abner Dos Santos Sousa T, Vasconcelos Lima L, Ádan Nunes Carvalho E, et al. Validation of a New Placebo Interferential Current Method: A New Placebo Method of Electrostimulation. *Pain Med* 2017;18:86–94. doi:10.1093/pmw/pnw039.
- [15] Jin H-K, Hwang T-Y, Cho S-H. Effect of electrical stimulation on blood flow velocity and vessel size. *Open Med* 2017;12:5–11. doi:10.1515/med-2017-0002.
- [16] Dohnert MB, Bauer JP, Pavão TS. Study of the effectiveness of interferential current as compared to transcutaneous electrical nerve stimulation in reducing chronic low back pain. *Rev Dor* 2015;16:27–31. doi:10.5935/1806-0013.20150006.
- [17] Santos F V., Chiappa GR, Vieira PJC, Umpierre D, Ribeiro JP, Cipriano G. Interferential electrical stimulation improves peripheral vasodilatation in healthy individuals. *Brazilian J Phys Ther* 2013;17:281–8. doi:10.1590/S1413-35552012005000092.
- [18] Whelton PK, Carey RM, Aronow WS, Ovbiagele B, Casey DE, Smith SC, et al. 2017 Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults A Report of the American College of Cardiology / American Heart Association T. 2017. doi:10.1161/HYP.000000000000065/-/DC1.The.
- [19] Vieira PJC, Ribeiro JP, Cipriano G, Umpierre D, Cahalin LP, Moraes RS, et al. Effect of transcutaneous electrical nerve stimulation on muscle metaboreflex in healthy young and older subjects. *Eur J Appl Physiol* 2012;112:1327–34. doi:10.1007/s00421-011-2084-z.
- [20] Tomasi FP, Chiappa G, Maldaner da Silva V, Lucena da Silva M, Lima ASCGB, Arena R, et al. Transcutaneous Electrical Nerve Stimulation Improves Exercise Tolerance in Healthy Subjects. *Int J Sport Med* 2015;2–6.
- [21] da Silva ML, Chiappa GR, da Silva VM, Neves LMT, de Lima ACGB, Tomasi FP, et al. Effect of transcutaneous electrical nerve stimulation on peripheral to central blood pressure ratio in healthy subjects. *Clin Physiol Funct Imaging* 2015;36:293–7. doi:10.1111/cpf.12227.
- [22] Palmer ST, Martin DJ, Steedman WM, Ravey J. Alteration of interferential current and transcutaneous electrical nerve stimulation frequency: Effects on nerve excitation. *Arch Phys Med Rehabil* 1999;80:1065–71. doi:10.1016/S0003-9993(99)90062-X.

- [23] de Almeida CC, Silva VZM da, Júnior GC, Liebano RE, Durigan JLQ. Transcutaneous electrical nerve stimulation and interferential current demonstrate similar effects in relieving acute and chronic pain: a systematic review with meta-analysis. *Brazilian J Phys Ther* 2018. doi:10.1016/j.bjpt.2017.12.005.
- [24] Noble J, Henderson G, Fiona A, Cramp L, Deirdre M, Walsh M, et al. The effect of interferential therapy upon cutaneous blood flow in humans. *Clin Physiol* 2000;20:2–7.
- [25] Campos F V., Neves LM, Da Silva VZ, Cipriano GF, Chiappa GR, Cahalin L, et al. Hemodynamic Effects Induced by Transcutaneous Electrical Nerve Stimulation in Apparently Healthy Individuals: A Systematic Review with Meta-Analysis. *Arch Phys Med Rehabil* 2015;97:826–35. doi:10.1016/j.apmr.2015.08.433.
- [26] Wong RA, Jette DU. Changes in sympathetic tone associated with different forms of transcutaneous electrical nerve stimulation in healthy subjects. *Phys Ther* 1984;64:478–82.
- [27] Lazarou L, Kitsios A, Lazarou I, Sikaras E, Trampas A. Effects of Intensity of Transcutaneous Electrical Nerve Stimulation (TENS) on Pressure Pain Threshold and Blood Pressure in Healthy Humans. *Clin J Pain* 2009;25:773–80. doi:10.1097/AJP.0b013e3181a7ece3.
- [28] Silverdal J, Mourtzinis G, Stener-Victorin E, Mannheimer C, Manhem K. Antihypertensive effect of low-frequency transcutaneous electrical nerve stimulation (TENS) in comparison with drug treatment. *Blood Press* 2012;21:306–10. doi:10.3109/08037051.2012.680737.

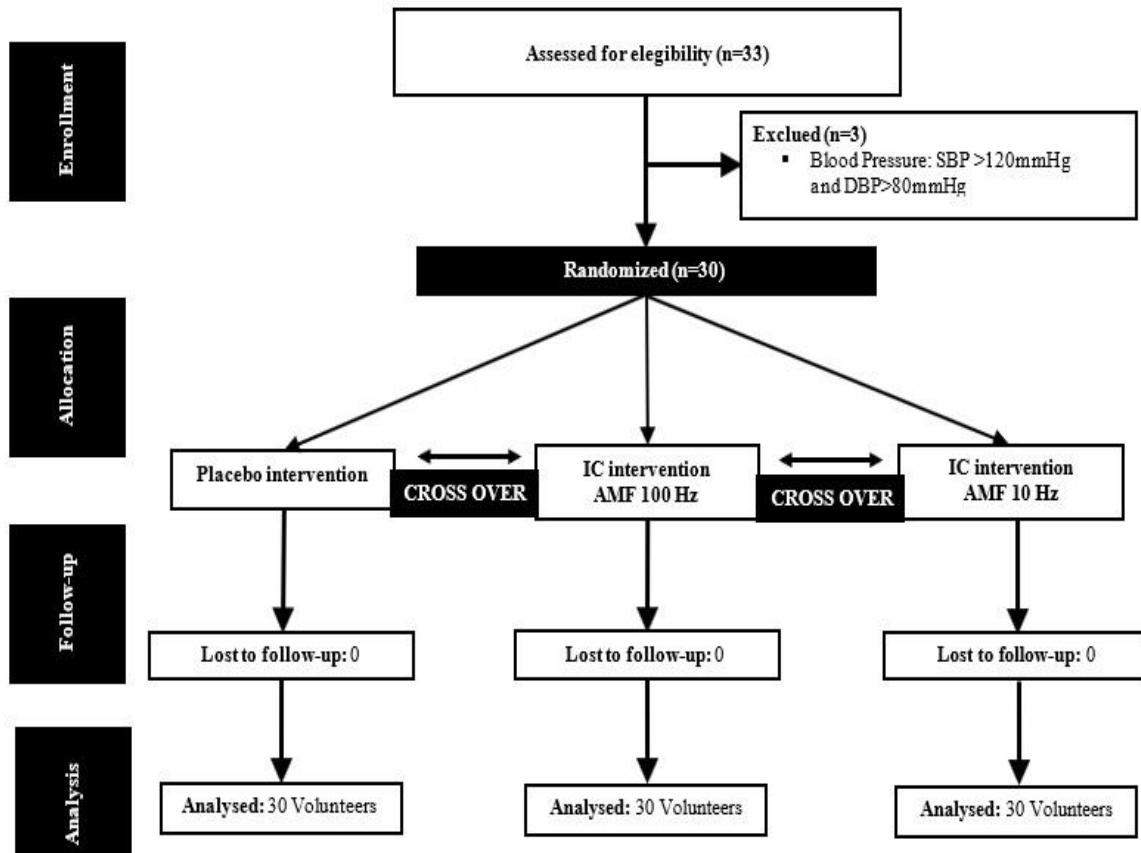


Figure 1.

Flow Diagram of study.

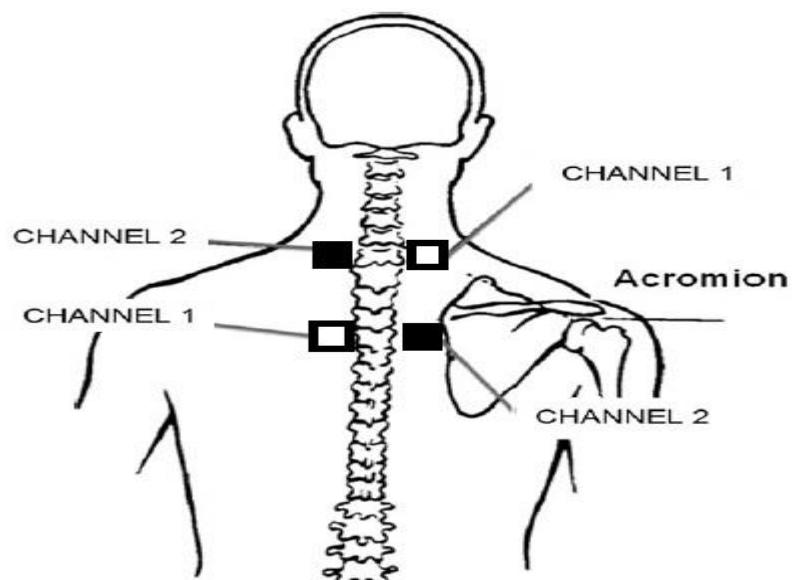


Figure 2

Local of electrodes (paravertebral ganglionar region - C7 and T4).

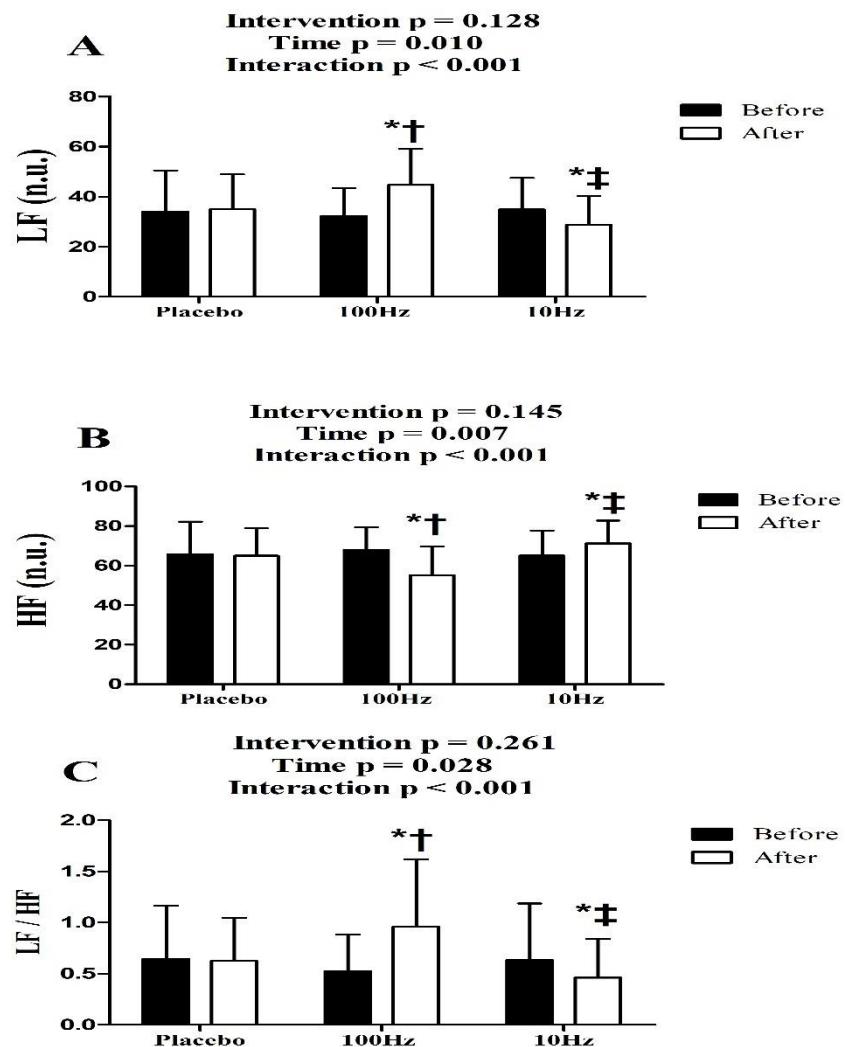


Figure 3

The sympathetic-vagal balance.

Data are presented as mean \pm standard deviation (SD); A: LF (n.u.): panels of spectral parameters of low frequency normalized component; B: HF (n.u.): high frequency normalized component; C: LF/HF: sympathovagal balance ratio LF(ms²) / HF(ms²); * p < 0.05 vs Before; † p < 0.05 vs Placebo; ‡ p < 0.05 vs 100Hz.

Table 1

Results of heart rate variability data.

Variables		Placebo	AMF 100Hz	AMF 10Hz	p		
					Intervention	Time	Interaction
Time-Domain							
HR (bpm)	Before	69.6±11.0	67.8±11.4	70.1±12.4	0.828	<0.001	0.578
	After	65.4±10.0*	64.9±11.6*	65.7±8.9*			
SDNN (ms)	Before	76.7±32.4	73.7±28.0	75.1±27.6	0.997	<0.001	0.651
	After	86.0±31.5	89.1±31.3*	88.7±34.3*			
rMSSD (ms)	Before	64.7±27.6	71.1±39.3	65.6±35.9	0.937	<0.001	0.031
	After	78.0±39.2*	73.5±38.1	83.8±48.0*			
PNN50 (%)	Before	37.2±17.6	39.6±20.1	35.1±19.1	0.995	0.001	0.063
	After	43.7±18.3*	40.9±17.3	44.9±19.7*			
Triangular Index	Before	16.9±5.6	15.2±4.1	14.9±5.3	0.446	0.020	0.411
	After	17.3±4.9	16.5±4.5	17.0±4.3			
Frequency Domain							
TP (ms²)	Before	6583±6329	5713±4969	5995±4469	0.966	0.002	0.437

		After	7762±5673	8340±5705*	8763±7326*			
LF (ms²)	Before		1349±1017	1290±1073	1305±986	0.641	<0.001	0.068
	After		1667±1348	2075±1600*	1520±1217			
HF (ms²)	Before		2592±2164	2950±3012	2467±2104	0.757	0.004	0.004
	After		3270±2949	2673±2733	4171±4274*			

Data are presented as mean ± standard deviation (SD); AMF: amplitude-modulated frequency; HR: Heart Rate (bpm min.-1); SDNN: standard deviation of all normal to normal R-R (NN) interval; rMSSD: Square root of the mean of the squares of successive R-R interval differences; pNN50: percentage of intervals differing more than 50 ms different from preceding interval; Total power (TP ms²): The variance of RR intervals over the temporal segment; LF (ms²): Power in low frequency range (0.04-0.15 Hz); HF (ms²): Power in high frequency range (0.15-0.4 Hz); * p < 0.05 vs Before; † p < 0.05 vs Placebo; ‡ p < 0.05 vs 100Hz.

Table 2

Results of Blood Pressure (BP).

Variables		Placebo	AMF 100Hz	AMF 10Hz	p		
					Intervention	Time	Interaction
SBP (mmHg)	Before	109.3 ± 6.5	111.5 ± 7.1	109.4 ± 6.8	0.367	0.607	0.342
	After	110.6 ± 7.4	111.7 ± 8.9	108.7 ± 7.8			
DBP (mmHg)	Before	63.0 ± 5.4	63.5 ± 5.6	62.6 ± 5.0	0.514	0.126	0.998
	After	63.9 ± 5.6	64.6 ± 6.8	62.3 ± 4.9			
MBP (mmHg)	Before	78.5 ± 5.2	79.5 ± 5.3	78.2 ± 5.2	0.397	0.177	0.175
	After	79.4 ± 6.6	80.3 ± 6.7	77.8 ± 5.3			

Data are presented as mean ± standard deviation; AMF: amplitude-modulated frequency; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MBP: Mean Blood Pressure.

4 CONCLUSÃO

Esta dissertação faz parte de um projeto temático intitulado “Efeitos da estimulação elétrica nervosa transcutânea (TENS) e da corrente interferencial (CI) sobre a pressão arterial e balanço autonômico de voluntários normotensos e pacientes hipertensos”. A presente dissertação apresenta os resultados das diferentes frequências da CI em voluntários saudáveis, visando estabelecer os parâmetros mais adequados dessa estimulação sensorial para futuros estudos em população hipertensa.

Neste sentido, a CI foi aplicada na região paravertebral ganglionar por 30 minutos, no modo contínuo, com pulsos bifásicos, com *slope* de 1/5/1, frequência da corrente de 4000Hz, largura do pulso de 100 μ s e sem variação da AMF. A CI com AMF em 10Hz modificou o balanço autonômico de voluntários saudáveis, diminuindo a atividade simpática e aumentando atividade parassimpática. Entretanto, a CI com AMF em 100Hz apresentou resultados opostos.

Os resultados sugerem que a AMF em 10Hz seja mais adequada para ser testado em pacientes hipertensos, pois este recurso eletroterápico é uma possível ferramenta não farmacológica coadjuvante no manejo da hipertensão, em especial os hipertensos refratários e resistentes a medicação. Salienta-se também que esses resultados devem ser comparados com a TENS nesta população, para verificarmos qual destas correntes apresenta um potencial de efeito maior, sabendo que os efeitos hemodinâmicos, induzidos por estas correntes, podem depender tanto da frequência, do local de aplicação dos eletrodos e da população estudada.

REFERÊNCIAS

- ACCORSI-MENDONÇA, D. et al. Controle neural da circulação e hipertensão arterial. **Revista Brasileira de Hipertensao**, v. 12, n. 4, p. 236–241, 2005.
- ACHARYA, U. R. et al. Heart rate variability: A review. **Medical and Biological Engineering and Computing**, v. 44, n. 12, p. 1031–1051, 2006.
- AGNE, J. E. **Eletrotermofototerapia**. 1º ed. Santa Maria: [s.n.].
- ANGELIS, K. DE; SANTOS, M. B. S. S.; IRIGOYEN, M. C. Sistema nervoso autônomo e doença cardiovascular. **Revista da Sociedade de Cardiologia do Rio Grande do Sul**, v. 13, n. 03, p. 1–7, 2004.
- ANIS JUNIOR, R. Compreendendo melhor as medidas de análise da variabilidade da frequência cardíaca. **J Diag Cardiol**, n. January 2000, 2000.
- BARKER, R. et al. The influence of stellate ganglion transcutaneous electrical nerve stimulation on signal quality of pulse oximetry in prehospital trauma care. **Anesthesia and Analgesia**, v. 104, n. 5, p. 1150–1153, 2007.
- BENJAMIN, E. J. et al. **Heart Disease and Stroke Statistics'2017 Update: A Report from the American Heart Association**. [s.l: s.n.], v. 135
- BERNARDI, L. et al. Slow breathing reduces chemoreflex response to hypoxia and hypercapnia, and increases baroreflex sensitivity. **Journal of Hypertension**, v. 19, n. 12, p. 2221–2229, 2001.
- BOSCO, F. A. P.; BRAZ, J. R. C. Beta-Bloqueadores em Anestesiologia: Aspectos Farmacológicos e Clínicos*. **Revista Brasileira de Anestesiologia**, v. 51, n. 5, p. 431–447, 2001.
- BRUNO, R. M. et al. Interactions between sympathetic nervous system and endogenous endothelin in patients with essential hypertension. **Hypertension**, v. 57, n. 1, p. 79–84, 2011.
- CHOBANIAN, A. V. et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. **Hypertension**, v.

42, n. 6, p. 1206–1252, 2003.

DA SILVA, M. L. et al. Effect of transcutaneous electrical nerve stimulation on peripheral to central blood pressure ratio in healthy subjects. **Clinical Physiology and Functional Imaging**, v. 36, n. 4, p. 293–297, 2015.

DOHNERT, M. B.; BAUER, J. P.; PAVÃO, T. S. Study of the effectiveness of interferential current as compared to transcutaneous electrical nerve stimulation in reducing chronic low back pain. **Revista Dor**, v. 16, n. 1, p. 27–31, 2015.

DUDENBOSTEL, T. et al. Refractory hypertension: A novel phenotype of antihypertensive treatment failure. **Hypertension**, v. 67, n. 6, p. 1085–1092, 2016.

ERDOGAN, D. et al. Effects of normal blood pressure, prehypertension, and hypertension on autonomic nervous system function. **International Journal of Cardiology**, v. 151, n. 1, p. 50–53, 2011.

FRANCO, O. S. et al. Effects of different frequencies of transcutaneous electrical nerve stimulation on venous vascular reactivity. **Brazilian Journal of Medical and Biological Research**, v. 47, n. 5, p. 411–418, 2014.

GADEMAN, M. G. J. et al. Rehabilitation: Periodic somatosensory stimulation increases arterial baroreflex sensitivity in chronic heart failure patients. **International Journal of Cardiology**, v. 152, n. 2, p. 237–241, 2011.

GANNE, J. M. INTERFERENTIAL THERAPY¹ From a paper presented to the Physiotherapy Society of South Australia, April, 1975. **Australian Journal of Physiotherapy**, v. 22, n. 3, p. 101–110, 1976.

GKALIAGKOUSI, E.; GAVRIILAKI, E.; DOUMA, S. Effects of acute and chronic exercise in patients with essential hypertension: Benefits and risks. **American Journal of Hypertension**, v. 28, n. 4, p. 429–439, 2015.

GUGLIELMIN J.Z. **Efeitos da estimulação elétrica nervosa transcutânea e da corrente interferencial sobre o comportamento metaboreflexo muscular.** [s.l.] Universidade Federal do Rio Grande do Sul, 2013.

HERING, D. et al. Effects of acute and long-term slow breathing exercise on muscle

sympathetic nerve activity in untreated male patients with hypertension. **Journal of Hypertension**, v. 31, n. 4, p. 739–746, 2013.

INDERGAND, H. J.; MORGAN, B. J. Effect of interference current on forearm vascular resistance in asymptomatic humans. **Physical Therapy**, v. 75, n. 4, p. 306–312, 1995.

IRIGOYEN, M. C.; CONSOLIM-COLOMBO, F. M.; KRIEGER, E. M. Controle cardiovascular: regulação reflexa e papel do sistema nervoso simpático. **Rev Bras Hipertens**, v. 8, n. 1, p. 55–62, 2001.

JIN, H.-K.; HWANG, T.-Y.; CHO, S.-H. Effect of electrical stimulation on blood flow velocity and vessel size. **Open Medicine**, v. 12, n. 1, p. 5–11, 2017.

JOHN CAMM, A. et al. Guidelines Heart rate variability. **European Heart Journal**, v. 17, p. 354–381, 1996.

JOHNSON, M. I.; TABASAM, G. An investigation into the analgesic effects of different frequencies of the amplitude-modulated wave of interferential current therapy on cold-induced pain in normal subjects. **Archives of Physical Medicine and Rehabilitation**, v. 84, n. 9, p. 1387–1394, 2003.

JOYNER, M. J.; CHARKOUDIAN, N.; WALLIN, B. G. A sympathetic view of the sympathetic nervous system and human blood pressure regulation. **Experimental Physiology**, v. 93, n. 6, p. 715–724, 2008.

KAMALI, F. et al. The Effect of Transcutaneous Electrical Nerve Stimulation of Sympathetic Ganglions and Acupuncture Points on Distal Blood Flow. **JAMS Journal of Acupuncture and Meridian Studies**, v. 10, n. 2, p. 120–124, 2017.

KUYPER, L. M.; KHAN, N. A. Atenolol vs nonatenolol β -blockers for the treatment of hypertension: A meta-analysis. **Canadian Journal of Cardiology**, v. 30, n. 5 S, p. S47–S53, 2014.

LA ROVERE, M. T. et al. Baroreflex sensitivity and heart-rate variability in prediction of total cardiac mortality after myocardial infarction. ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) Investigators. **Lancet (London, England)**, v. 351, n. 9101, p. 478–84, 1998.

LAWES, C. M.; HOORN, S. VANDER; RODGERS, A. Global burden of blood-pressure-related disease, 2001. **The Lancet**, v. 371, n. 9623, p. 1513–1518, 2008.

LAZAROU, L. et al. Effects of Intensity of Transcutaneous Electrical Nerve Stimulation (TENS) on Pressure Pain Threshold and Blood Pressure in Healthy Humans. **The Clinical Journal of Pain**, v. 25, n. 9, p. 773–780, 2009.

LUCINI, D. et al. Correlation between baroreflex gain and 24-h indices of heart rate variability. **Journal of Hypertension**, v. 20, n. 8, p. 1625–1631, 2002.

MALACHIAS, M. V. B. et al. 7^a Diretriz Brasileira De Hipertensão Arterial. v. 107, p. 1–103, 2016.

MANCIA, G. et al. 2013 ESH/ESC guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). **European Heart Journal**, v. 34, n. 28, p. 2159–2219, 2013.

MCCRATY, R.; SHAFFER, F. Heart Rate Variability: New Perspectives on Physiological Mechanisms, Assessment of Self-regulatory Capacity, and Health Risk. **Global Advances in Health and Medicine**, v. 4, n. 1, p. 46–61, 2015.

MODOLO, R. et al. Refractory and resistant hypertension: Characteristics and differences observed in a specialized clinic. **Journal of the American Society of Hypertension**, v. 9, n. 5, p. 397–402, 2015.

MONTANO, N. et al. Heart rate variability explored in the frequency domain: A tool to investigate the link between heart and behavior. **Neuroscience and Biobehavioral Reviews**, v. 33, n. 2, p. 71–80, 2009.

NARDI, A. T. DE et al. Different frequencies of transcutaneous electrical nerve stimulation on sympatho-vagal balance. **Acta Scientiarum. Health Sciences**, v. 39, n. 1, p. 9, 2017.

NELSON, R. M.; HAYES, K. W.; CURRIER, D. P. **Eletroterapia Clínica**. 3º edição ed. [s.l: s.n.].

NOBLE, J. et al. The effect of interferential therapy upon cutaneous blood flow in

humans. **Clinical physiology (Oxford, England)**, v. 20, n. 1, p. 2–7, 2000.

NOBRE, F. et al. VI Diretrizes Brasileiras de Hipertensão. **VI Diretrizes Brasileiras de Hipertensão - Sociedade Brasileira de Cardiologia**, v. 95, p. 1–51, 2010.

OLIVA, R. V.; BAKRIS, G. L. Sympathetic Activation in Resistant Hypertension: Theory and Therapy. **Seminars in Nephrology**, v. 34, n. 5, p. 550–559, 2014.

OZCAN, J.; WARD, A. R.; ROBERTSON, V. J. A comparison of true and premodulated interferential currents. **Archives of Physical Medicine and Rehabilitation**, v. 85, n. 3, p. 409–415, 2004.

PALMER, S. T. et al. Alteration of interferential current and transcutaneous electrical nerve stimulation frequency: Effects on nerve excitation. **Archives of Physical Medicine and Rehabilitation**, v. 80, n. 9, p. 1065–1071, 1999.

PALMER, S. T. et al. Effects of Electric Stimulation on C and A Delta Fiber-Mediated Thermal Perception Thresholds. **Archives of Physical Medicine and Rehabilitation**, v. 85, n. 1, p. 119–128, 2004.

PIVETTA, K. M.; BERTOLINI, G. R. F. ΔF efects on the interferential current accommodation in healthy subjects. **Revista Brasileira de Medicina do Esporte**, v. 18, n. 5, p. 330–332, 2012.

PUMPRLA, J. et al. Functional assessment of heart rate variability: Physiological basis and practical applications. **International Journal of Cardiology**, v. 84, n. 1, p. 1–14, 2002.

ROBINSON, A. J.; SNYDER-MACKER, L. **Eletrofisiologia Clínica: Eletroterapia e teste eletrofisiológico**. 3º ed. Porto Alegre: [s.n.].

ROBINSON, A. J.; SNYDER-MACKER, L. **Clinical Electrophysiology: Electrotherapy and Electrophysiologic Testing**. 3º ed. [s.l: s.n.].

SALES, A. R. K. et al. Diet and exercise training reduce blood pressure and improve autonomic modulation in women with prehypertension. **European Journal of Applied Physiology**, v. 112, n. 9, p. 3369–3378, 2012.

SANJULIANI, A. F. Fisiopatologia da hipertensão arterial: conceitos teóricos úteis para a prática clínica. **Revista da SOCERJ**, v. 15, n. 4, p. 210–218, 2002.

SANTOS, F. V. et al. Interferential electrical stimulation improves peripheral vasodilatation in healthy individuals. **Brazilian Journal of Physical Therapy**, v. 17, n. 3, p. 281–288, 2013.

SARTORI, S. et al. Effects of transcutaneous electrical nerve stimulation in autonomic nervous system of hypertensive patients: a randomized controlled trial. **Current Hypertension Reviews**, v. 14, 2018.

SHAFI, T. et al. Autonomic dysfunction as a mechanism of intradialytic blood pressure instability. **Seminars in Dialysis**, v. 30, n. 6, p. 537–544, 2017.

SHEN, M. J.; ZIPES, D. P. Role of the autonomic nervous system in modulating cardiac arrhythmias. **Circulation Research**, v. 114, n. 6, p. 1004–1021, 2014.

SHIELDS, J. W. Heart rate variability with deep breathing as a clinical test of cardiovagal function. **Cleveland Clinic Journal of Medicine**, v. 76, n. SUPPL.2, p. 37–40, 2009.

SILVERDAL, J. et al. Antihypertensive effect of low-frequency transcutaneous electrical nerve stimulation (TENS) in comparison with drug treatment. **Blood Pressure**, v. 21, n. 5, p. 306–310, 2012.

STEIN, C. et al. Transcutaneous electrical nerve stimulation at different frequencies on heart rate variability in healthy subjects. **Autonomic Neuroscience: Basic and Clinical**, v. 165, n. 2, p. 205–208, 2011.

TARVAINEN, M. P. et al. Kubios HRV - Heart rate variability analysis software. **Computer Methods and Programs in Biomedicine**, v. 113, n. 1, p. 210–220, 2014.

THAYER, J. F.; YAMAMOTO, S. S.; BROSSCHOT, J. F. The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. **International Journal of Cardiology**, v. 141, n. 2, p. 122–131, 2010.

TOMASI, F. P. et al. Transcutaneous Electrical Nerve Stimulation Improves Exercise Tolerance in Healthy Subjects. **Int J Sports Med**, p. 2–6, 2015.

VANDERLEI, L. C. M. et al. Basic notions of heart rate variability and its clinical applicability. **Revista brasileira de cirurgia cardiovascular : orgao oficial da Sociedade Brasileira de Cirurgia Cardiovascular**, v. 24, n. 2, p. 205–217, 2009.

VIEIRA, P. J. C. et al. Effect of transcutaneous electrical nerve stimulation on muscle metaboreflex in healthy young and older subjects. **European Journal of Applied Physiology**, v. 112, n. 4, p. 1327–1334, 2012.

VILELA-MARTIN, J. F. et al. Effects of transcutaneous electrical nerve stimulation (TENS) on arterial stiffness and blood pressure in resistant hypertensive individuals: Study protocol for a randomized controlled trial. **Trials**, v. 17, n. 1, p. 1–13, 2016.

WHA. World Health Association. **A global brief on hypertension**, p. 9, 2013.

WHELTON, P. K. et al. **2017 Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults A Report of the American College of Cardiology / American Heart Association T.** [s.l: s.n.].

WONG, R. A.; JETTE, D. U. Changes in sympathetic tone associated with different forms of transcutaneous electrical nerve stimulation in healthy subjects. **Physical Therapy**, v. 64, n. 4, p. 478–482, 1984.

YOUN, J.-I. J.-I. ; LEE, H. S. . H. S.; LEE, S. S.. Determination of effective treatment duration of interferential current therapy using electromyography. **Journal of Physical Therapy Science**, v. 28, n. 8, p. 2400–2403, 2016.

ZATTAR, L. C. et al. Prevalência e fatores associados á pressão arterial elevada, seu conhecimento e tratamento em idosos do sul do Brasil. **Cad. Saúde Pública**, v. 29, n. 3, p. 507–521, 2013.

ANEXOS

ANEXO 1: Normas da revista *Physiotherapy*

GUIDE FOR AUTHORS

The journal editor Michele Harms, welcomes articles for publication in the journal.

Physiotherapy invites papers in the following categories: Original research, systematic and scoping reviews or meta-analysis, theoretical or debate articles (aim for 3000 words excluding abstract and references, with a limit of 40 references); brief reports (750 words and 1 table/figure, with a limit of 10 references); technical reports (1000-2000 words, with a limit of 20 references); and Letters to

the Editor (400 words). While most of our editorials are commissioned, we also welcome editorials that deal with current or controversial topics (1000 words). Please ensure that submissions conform to the **Uniform Requirements for Manuscripts**

Submitted to Biomedical Journals, issued by the International Committee for Medical Journal Editors (J Am Med Assoc 1997;277:927-934; <http://www.icmje.org/index.html>)

Physiotherapy supports the principles of the Committee of Publication Ethics (COPE), which oblige the highest standards of practice on all participants in scientific research and publishing (www.publicationethics.org.uk). It is recognized that it may not be possible to identify or be aware of all transgressions to the code of practice. Complaints to this journal are dealt with by the Editorial Board in line with COPE's code of practice.

BEFORE YOU BEGIN

Ethics in publishing

Please see our information pages on *Ethics in publishing* and *Ethical guidelines for journal publication*.

Human and animal rights

If the work involves the use of animal or human subjects, the author should ensure that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans <http://www.wma.net/en/30publications/10policies/b3/index.html>; EU Directive 2010/63/EU for animal experiments http://ec.europa.eu/environment/chemicals/lab_animals/legislation_en.htm;

Uniform Requirements for manuscripts submitted to Biomedical journals <http://www.icmje.org>. The privacy rights of human subjects must always be observed. Patients' and volunteers' names, initials, and hospital numbers should not be used. It is the author's responsibility to ensure all appropriate consents have been obtained.

Patient anonymity

Studies on patients or volunteers require ethics committee approval and informed consent which should be documented in your paper. Patients have a right to privacy. Therefore identifying information, including patients' images, names, initials, or hospital numbers, should not be included in videos, recordings, written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and you have obtained written informed consent for publication in print and electronic form from the patient (or parent, guardian or next of kin where applicable). If such consent is made subject to any conditions, Elsevier must be made aware of all such conditions. Written consents must be provided to Elsevier on request. Even where consent has been given, identifying details should be omitted if they are not essential. If identifying characteristics are altered to protect anonymity, such as in genetic pedigrees, authors should provide assurance that alterations do not distort scientific meaning

and editors should so note. If such consent has not been obtained, personal details of patients included in any part of the paper and in any supplementary materials (including all illustrations and videos) must be removed before submission.

Declaration of interest

All authors must disclose any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work. Examples of potential competing interests include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding. Authors must disclose any interests in two places: 1. A summary declaration of interest statement in the title page file (if double-blind) or the manuscript file (if single-blind). If there are no interests to declare then please state this: 'Declarations of interest: none'. This summary statement will be ultimately published if the article is accepted.

AUTHOR INFORMATION PACK 12 Jun 2018 www.elsevier.com/locate/physt 5

2. Detailed disclosures as part of a separate Declaration of Interest form, which forms part of the journal's official records. It is important for potential interests to be declared in both places and that the information matches. [More information](#).

Submission declaration and verification

Submission of an article implies that the work described has not been published previously (except in the form of an abstract, a published lecture or academic thesis, see '[Multiple, redundant or concurrent publication](#)' for more information), that it is not under consideration for publication elsewhere, that

its publication is approved by all authors and tacitly or explicitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyrightholder.

To verify originality, your article may be checked by the originality detection service [Crossref Similarity Check](#).

Authorship

All authors should have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

Changes to authorship

Authors are expected to consider carefully the list and order of authors **before** submitting their manuscript and provide the definitive list of authors at the time of the original submission. Any addition, deletion or rearrangement of author names in the authorship list should be made only **before** the manuscript has been accepted and only if approved by the journal Editor. To request such a change, the Editor must receive the following from the **corresponding author**: (a) the reason

for the change in author list and (b) written confirmation (e-mail, letter) from all authors that they agree with the addition, removal or rearrangement. In the case of addition or removal of authors, this includes confirmation from the author being added or removed. Only in exceptional circumstances will the Editor consider the addition, deletion or rearrangement of authors **after** the manuscript has been accepted. While the Editor considers the request, publication of the manuscript will be suspended. If the manuscript has already been published in an online issue, any requests approved by the Editor will result in a corrigendum.

Acknowledgements

All contributors who do not meet the criteria for authorship as defined above should be listed in an acknowledgements section. Examples of those who might be acknowledged include a person who provided purely technical help, writing assistance, or a department chair

who provided only general support. Authors should disclose whether they had any writing assistance and identify the entity that paid for this assistance.

Randomised controlled trials

Randomised controlled trials should be presented according to the CONSORT guidelines. At manuscript submission, authors must include a complete Consolidated Standards of Reporting Trials (CONSORT) flow chart. *Physiotherapy* has adopted the proposal from the International Committee of Medical Journal Editors (ICMJE) which require, as a condition of consideration for publication of clinical trials, registration in a public trials registry. Trials must register at or before the onset of patient enrolment. The clinical trial registration number should be included at the end of the abstract of the article. For this purpose, a clinical trial is defined as any research project that prospectively assigns human subjects to intervention or comparison groups to study the cause and effect relationship between a medical intervention and a health outcome. Studies designed for other purposes, such as to study pharmacokinetics or major toxicity (e.g. phase I trials) would be exempt. Further information can be found at <http://www.icmje.org>. The CONSORT checklist and template flow diagram can be found on <http://www.consort-statement.org>.

REPORTING GUIDELINES

To facilitate the accurate, complete, and transparent improve the quality of reporting of research, *Physiotherapy* supports the initiatives available through the **EQUATOR Network** (Enhancing the QUality and Transparency Of health Research) which houses a database of all reporting guidelines for health research (<http://www.equator-network.org/>). AUTHOR INFORMATION PACK 12 Jun 2018 www.elsevier.com/locate/physt 6 To assist authors and reviewers, the following guidelines are required for all submissions, where possible and relevant. Please include a flow diagram of the study design and a completed checklist at the point of submission. A TiDier checklist should be included where an intervention is described. The following list is relevant to the main study types but is not an exhaustive list. Please refer to the EQUATOR website for further details.

Study type = RANDOMISED CONTROLLED TRIAL

Description = Consolidated Standards of Reporting Trials

Acronym = CONSORT

Study type = OBSERVATIONAL STUDIES

Description = Strengthening the Reporting of Observational studies in Epidemiology

Acronym = STROBE

Study type = SYSTEMATIC REVIEWS

Description = Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Acronym = PRISMA

Study type = QUALITATIVE RESEARCH

Description = Standards for reporting qualitative research

Acronym = SRQR

or

Study type = QUALITATIVE RESEARCH

Description = Consolidated criteria for reporting qualitative research

Acronym = COREQ

Study type = STUDY PROTOCOLS

Description = Standard Protocol Items Recommendations for Interventional Trials

Acronym = SPIRIT

Study type = STUDY INTERVENTIONS (can be used with CONSORT etc)

Description = Template for Intervention Description and Replication

Acronym = TiDier

Study type = DIAGNOSTIC/PROGNOSTIC STUDIES

Description = Standards for the Reporting of Diagnostic Accuracy

Acronym = STARD or TRIPOD

CLINICAL TRIAL REGISTRATION and PROSPERO

As a condition of consideration for publication, clinical trials must be registered at or before the onset of patient enrolment in a public trials registry. The clinical trial registration number should be included at the end of the abstract of the article. For this purpose, a clinical trial is defined as any research project that prospectively assigns human subjects to intervention or comparison groups to study the cause and effect relationship between a medical intervention and a health outcome. Further information can be found at <http://www.icmje.org>. Systematic reviews should also be registered on PROSPERO, an international database of prospectively registered systematic reviews in health and social care (<http://www.crd.york.ac.uk/prospero/>)

Questionnaires

The format of reports for questionnaires and surveys should follow that of research reports where appropriate. In consideration of respondent bias, the editorial board has made a response rate of more than 65% a requirement of publication. On occasion, a lower response rate may be acceptable although this will be judged on a paper-by-paper basis. Sampling frame, subject selection methods and strategies for follow-up of non-responders should be reported. Report responses in the format

(83/300, 28%) - 300 being the number of possible respondents for this item. Percentages should be reported to the nearest integer.

Outcome measures

Where appropriate, please provide details of the validity, reliability and measurement error in the units of measurement of any outcome measure. The Limits of Agreement method is preferred for method comparison studies and reliability studies (see: Altman DG, Bland JM. Measurement in medicine: the analysis of method comparison studies. Statistician 1983; **32**: 307-17. Bland JM, altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; **i**: 307-10

AUTHOR INFORMATION PACK 12 Jun 2018 www.elsevier.com/locate/physt 7

Copyright

Upon acceptance of an article, authors will be asked to complete a 'Journal Publishing Agreement' (see [more information](#) on this). An e-mail will be sent to the corresponding author confirming receipt of the manuscript together with a 'Journal Publishing Agreement' form or a link to the online version of this agreement.

Subscribers may reproduce tables of contents or prepare lists of articles including abstracts for internal circulation within their institutions. [Permission](#) of the Publisher is required for resale or distribution outside the institution and for all other derivative works, including compilations and translations. If excerpts from other copyrighted works are included, the author(s) must obtain written permission from the copyright owners and credit the source(s) in the article. Elsevier has [preprinted forms](#) for use by authors in these cases. For gold open access articles: Upon acceptance of an article, authors will be asked to complete an 'Exclusive License Agreement' ([more information](#)). Permitted third party reuse of gold open access articles is determined by the author's choice of [user license](#).

Author rights

As an author you (or your employer or institution) have certain rights to reuse your work. [More information](#). Elsevier supports responsible sharing Find out how you can [share your research](#) published in Elsevier journals.

Role of the funding source

You are requested to identify who provided financial support for the conduct of the research and/or preparation of the article and to briefly describe the role of the sponsor(s), if any, in study design; in the collection, analysis and interpretation of data; in the writing of the

report; and in the decision to submit the article for publication. If the funding source(s) had no such involvement then this should

be stated. All sources of funding should be declared at the end of the text.

Funding body agreements and policies

Elsevier has established a number of agreements with funding bodies which allow authors to comply with their funder's open access policies. Some funding bodies will reimburse the author for the gold open access publication fee. Details of [existing agreements](#) are available online.

Open access

This journal offers authors a choice in publishing their research:

Subscription

- Articles are made available to subscribers as well as developing countries and patient groups through our [universal access programs](#).

- No open access publication fee payable by authors.

• The Author is entitled to post the [accepted manuscript](#) in their institution's repository and make this public after an embargo period (known as green Open Access). The [published journal article](#) cannot be shared publicly, for example on ResearchGate or Academia.edu, to ensure the sustainability of peerreviewed

research in journal publications. The embargo period for this journal can be found below.

Gold open access

- Articles are freely available to both subscribers and the wider public with permitted reuse.

- A gold open access publication fee is payable by authors or on their behalf, e.g. by their research funder or institution. Regardless of how you choose to publish your article, the journal will apply the same peer review criteria and acceptance standards. For gold open access articles, permitted third party (re)use is defined by the following [Creative Commons user licenses](#):

AUTHOR INFORMATION PACK 12 Jun 2018 www.elsevier.com/locate/physt 8
Creative Commons Attribution (CC BY) Lets others distribute and copy the article, create extracts, abstracts, and other revised versions, adaptations or derivative works of or from an article (such as a translation), include in a collective

work (such as an anthology), text or data mine the article, even for commercial purposes, as long as they credit the author(s), do not represent the author as endorsing their adaptation of the article, and do not modify the article in such a way as to damage the author's honor or reputation.

Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND)

For non-commercial purposes, lets others distribute and copy the article, and to include in a collective work (such as an anthology), as long as they credit the author(s) and provided they do not alter or modify the article.

The gold open access publication fee for this journal is **USD 2500**, excluding taxes. Learn more about Elsevier's pricing policy: <https://www.elsevier.com/openaccesspricing>.
Green open access Authors can share their research in a variety of different ways and Elsevier has a number of green open access options available. We recommend authors see our [green open access page](#) for further information. Authors can also self-archive their manuscripts immediately and enable public access from their institution's repository after an embargo period. This is the version that has been accepted for publication and which typically includes author-incorporated changes suggested during submission, peer review and in editor-author communications. Embargo period: For subscription

articles, an appropriate amount of time is needed for journals to deliver value to subscribing customers before an article becomes freely available to the public. This is the embargo period and it begins from the date the article is formally published online in its final and fully citable form. [Find out more](#). This journal has an embargo period of 12 months.

Language (usage and editing services) Please write your text in good English (American or British usage is accepted, but not a mixture of these). Authors who feel their English language manuscript may require editing to eliminate possible

grammatical or spelling errors and to conform to correct scientific English may wish to use the [English Language Editing service](#) available from Elsevier's WebShop.

Submission

Our online submission system guides you stepwise through the process of entering your article details and uploading your files. The system converts your article files to a single PDF file used in the peer-review process. Editable files (e.g., Word, LaTeX) are required to typeset your article for final publication. All correspondence, including notification of the Editor's decision and requests for revision, is sent by e-mail. Queries may be directed to the Editorial Office: E-mail: physiotherapy@elsevier.com *Submit your article* Please submit your article via <http://ees.elsevier.com/physt/>.

PREPARATION

Double-blind review

This journal uses double-blind review, which means that both the reviewer and author name(s) are not allowed to be revealed to one another for a manuscript under review. The identities of the authors are concealed from the reviewers, and vice versa. For more information please refer to <http://www.elsevier.com/reviewers/peer-review>. The main body of the paper (including the references, figures, tables and any Acknowledgements) should not include any identifying information, such as the authors' names or affiliations. Authors should ensure that the place of origin of the work or study, and/or the organisation(s) that have been involved in the study/development are not revealed in the manuscript – “X” can be used in the manuscript and details can be completed if the manuscript is processed further through the publication process. AUTHOR INFORMATION PACK 12 Jun 2018 www.elsevier.com/locate/physt 9

Peer review

This journal operates a double blind review process. All contributions will be initially assessed by the editor for suitability for the journal. Papers deemed suitable are then typically sent to a minimum of two independent expert reviewers to assess the scientific quality of the paper. The Editor is responsible for the final decision regarding acceptance or rejection of articles. The Editor's decision is final. [More information on types of peer review](#).

Double-blind review

This journal uses double-blind review, which means the identities of the authors are concealed from the reviewers, and vice versa. [More information](#) is available on our website. To facilitate this, please include the following separately:

Title page (with author details): This should include the title, authors' names, affiliations, acknowledgements and any Declaration of Interest statement, and a complete address for the corresponding author including an e-mail address. *Blinded manuscript (no author details):* The main body of the paper (including the references, figures, tables and any acknowledgements) should not include any identifying information, such as the authors' names or affiliations.

Use of wordprocessing software

It is important that the file be saved in the native format of the wordprocessor used. The text should be in single-column format. Keep the layout of the text as simple as possible. Most formatting codes will be removed and replaced on processing the article. In particular, do

not use the wordprocessor's options to justify text. When preparing tables, if you are using a table grid, use only one grid for each individual table and not a grid for each row. If no grid is used, use tabs, not spaces, to align columns. The electronic text should be prepared in a way very similar to that of conventional manuscripts (see also the Guide to Publishing with Elsevier: <http://www.elsevier.com/guidepublication>). Note that source files of figures, tables and text graphics will be required. See also the section on Electronic artwork.

Presentation of manuscript

Please write your text in good English (American or British usage is accepted, not a mixture of these). Use decimal points (not commas), use a space for thousands (10 000 and above). Please try to avoid abbreviations wherever possible. Authors should use person first language: e.g., "patients with arthritis" rather than "arthritis patients". Present the entire manuscript using double spacing, line number and page numbers. Ensure that each new paragraph is clearly indicated. Present tables and figure legends on separate pages at the end of the manuscript. Consult a recent issue of the journal to become familiar with layout and conventions.

Number all pages consecutively. Provide the following data on the title page (in the order given). *Title*. Concise and informative. Titles are often used in information retrieval systems. Avoid abbreviations and formulae where possible.

Author names and affiliations. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name, and, if available, the e-mail address of each author. *Twitter handles.* Twitter handles for one, or all, authors may be included on the title page if authors wish for these to be published. *Corresponding author.* Clearly indicate who is willing to handle correspondence at all stages of refereeing and publication, also post publication. Ensure that telephone and fax numbers (with country and area code) are provided in addition to the e-mail address and the complete postal address. *Present/permanent address.* If an author has moved since the work described in the article was done, or was visiting at the time, a 'Present address' (or 'Permanent address') may be indicated as a footnote to that author's name. The address at which the author actually did the work must be retained as the main, affiliation address. Superscript Arabic numerals are used for such footnotes.

AUTHOR INFORMATION PACK 12 Jun 2018 www.elsevier.com/locate/physt 10

Word count. Provide a word count for the main body of the paper, excluding abstract, acknowledgments, figure legends, tables and references.

Abstracts. A concise and factual abstract is required (maximum length 200 words for an unstructured abstract or 250 words for a structured abstract). An abstract is often presented separate from the article, so it must be able to stand alone. The abstract should be written using the following headings as appropriate:

Objectives: a clear statement of the purpose of the study

Design: describe aspects of the study: randomisation, prospective, blinding, placebo controlled, observational, survey

Setting: include the level of care eg primary, secondary; number of participating centres

Participants: numbers, selection criteria, numbers entering and completing study

Interventions: what were the interventions, how and for how long

Main outcome measures: identify primary outcome measure and any supporting secondary outcome measures

Results: including main finding, point estimate and degree of uncertainty eg: confidence interval for the difference between groups, where appropriate

Conclusions: main conclusion based on results and objective of study, implications

Clinical Trial Registration number

For meta-analyses and systematic reviews, provide a structured summary in line with the PRISMA Statement, including as applicable:

Background or context

Objectives: the clinical question or purpose

Data sources: databases searched and other information sources

Study selection or eligibility criteria, (participants, and interventions)

Study appraisal and synthesis methods (or Data Extraction and Data Synthesis);

Results

Limitations

Conclusion and implications of key findings

Funding: for the systematic review

Systematic review registration number. OPEN ACCESS: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6):

e1000097. doi:10.1371/journal.pmed.1000097

Keywords

Immediately after the abstract, provide a maximum of 6 keywords. Words selected should reflect the essential topics of the article and will be used for indexing purposes. Terms from the Medical Subject Headings (MeSH) list should be used (<http://www.nlm.nih.gov/mesh/>). If suitable MeSH terms are not available, subject specific terms can be used. At the end of the paper, but before the references, please provide three statements:

- Ethical Approval: The organisation providing ethical approval and ethics protocol reference number where appropriate.
- Funding: any sources of funding should be stated.
- Conflict of Interest: Disclosed conflicts will be published if they are believed to be important to readers in judging the manuscript. If there are no conflicts of interest, authors should state that there are none.

Contribution of the Paper

All submissions (with the exception of Brief Reports, Technical Reports, Letters and Editorials) should include a "Contribution of the Paper" statement. This should inform the reader of the key messages of the article/what the paper adds to the current literature, and what new knowledge is added by this study. Please provide clear statements in the form of two or three short bullet points for each. The bullet points should appear under a separate heading Contribution of paper and should be placed after the abstract but before the Keywords in your main manuscript file.

AUTHOR INFORMATION PACK 12 Jun 2018 www.elsevier.com/locate/physt 11

Data Analysis

Presentation of data and subsequent analyses should be clear and transparent. When presenting parametric statistics (eg Mean, Standard deviation) and parametric data analysis, the authors should provide evidence that their data are normally distributed where appropriate. Non-parametric statistics (eg Median, Inter-quartile range) and non-parametric analysis should be used where the data does not fulfil the assumptions for parametric analysis. Report p-values < .05 to 3 digits and values >.05 to 2 digits. Therefore 0.066 should be 0.07 and 0.0003 should be <0.001.

Formatting of funding sources

List funding sources in this standard way to facilitate compliance to funder's requirements:

Funding: This work was supported by the National Institutes of Health [grant numbers xxxx, yyyy]; the Bill & Melinda Gates Foundation, Seattle, WA [grant number zzzz]; and the United States Institutes

of Peace [grant number aaaa]. It is not necessary to include detailed descriptions on the program or type of grants and awards. When funding is from a block grant or other resources available to a university, college, or other research institution, submit the name of the institute or organization that provided the funding.

If no funding has been provided for the research, please include the following sentence: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Artwork

Electronic artwork

General points

- Make sure you use uniform lettering and sizing of your original artwork.
 - Embed the used fonts if the application provides that option.
 - Aim to use the following fonts in your illustrations: Arial, Courier, Times New Roman, Symbol, or use fonts that look similar.
 - Number the illustrations according to their sequence in the text.
 - Use a logical naming convention for your artwork files.
 - Provide captions to illustrations separately.
 - Size the illustrations close to the desired dimensions of the published version.
 - Submit each illustration as a separate file.
- A detailed [guide on electronic artwork](#) is available.

You are urged to visit this site; some excerpts from the detailed information are given here.

Formats

If your electronic artwork is created in a Microsoft Office application (Word, PowerPoint, Excel) then please supply 'as is' in the native document format.

Regardless of the application used other than Microsoft Office, when your electronic artwork is finalized, please 'Save as' or convert the images to one of the following formats (note the resolution requirements for line drawings, halftones, and line/halftone combinations given below):

EPS (or PDF): Vector drawings, embed all used fonts.

TIFF (or JPEG): Color or grayscale photographs (halftones), keep to a minimum of 300 dpi.

TIFF (or JPEG): Bitmapped (pure black & white pixels) line drawings, keep to a minimum of 1000 dpi.

TIFF (or JPEG): Combinations bitmapped line/half-tone (color or grayscale), keep to a minimum of 500 dpi.

Please do not:

- Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); these typically have a low number of pixels and limited set of colors;
- Supply files that are too low in resolution;
- Submit graphics that are disproportionately large for the content.

Color artwork

Please make sure that artwork files are in an acceptable format (TIFF (or JPEG), EPS (or PDF), or MS Office files) and with the correct resolution. If, together with your accepted article, you submit usable color figures then Elsevier will ensure, at no additional charge, that these figures will appear in color online (e.g., ScienceDirect and other sites) regardless of whether or not these illustrations

are reproduced in color in the printed version. **For color reproduction in print, you will receive**

AUTHOR INFORMATION PACK 12 Jun 2018 www.elsevier.com/locate/physt 12
information regarding the costs from Elsevier after receipt of your accepted article. Please indicate your preference for color: in print or online only. [Further information on the preparation of electronic artwork.](#)

Illustration services Elsevier's WebShop offers Illustration Services to authors preparing to submit a manuscript but concerned about the quality of the images accompanying their article. Elsevier's expert illustrators can produce scientific, technical and medical-style images, as well as a full range of charts, tables and graphs. Image 'polishing' is also available, where our illustrators take your image(s) and improve them to a professional standard. Please visit the website to find out more.

Figure captions

Ensure that each illustration has a caption. Supply captions separately, not attached to the figure. A caption should comprise a brief title (**not** on the figure itself) and a description of the illustration. Keep text in the illustrations themselves to a minimum but explain all symbols and abbreviations used.

Permission of borrowed illustrations or table or identifiable clinical photographs

Permission to produce materials (illustrations and tables) must be obtained from the original publishers and authors, and submitted with the typescript. Borrowed material should be acknowledged in the captions in this style - 'Reproduced by kind permission of (publishers) from (reference)'. Written permission to use photographs of identifiable subjects must be provided.

Tables

Please submit tables as editable text and not as images. Tables can be placed either next to the relevant text in the article, or on separate page(s) at the end. Number tables consecutively in accordance with their appearance in the text and place any table notes below the table body. Be sparing in the use of tables and ensure that the data presented in them do not duplicate results described elsewhere in the article. Please avoid using vertical rules and shading in table cells.

References

Generally the search strategy should be reported, including details of the databases searched, the dates searched and the search terms. References will be judged not only on applicability, but also on time since publication. Although it is accepted that occasionally an historical reference is required, the majority of references should be recent. By providing the literature search strategy, this will illustrate

that appropriate dates have been included should there be little recent literature in that area. Responsibility for the accuracy of bibliographic citations lies entirely with the authors. The Vancouver Numbered style of referencing should be used. Authors should aim for 75% of their references to be within the preceding 5 years, with a limit of 40 references (10 references for short communications, 20 references for technical reports). Citations in the text: Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not permitted. Citation of a reference as 'in press' implies that the item has been accepted for publication. *Reference links* Increased discoverability of research and high quality peer review are ensured by online links to the sources cited. In order to allow us to create links to abstracting and indexing services, such as Scopus, CrossRef and PubMed, please ensure that data provided in the references are correct. Please note that incorrect surnames, journal/book titles, publication year and pagination may prevent link creation. When copying references, please be careful as they may already contain errors. Use of the

DOI is encouraged. A DOI can be used to cite and link to electronic articles where an article is in-press and full citation details are not yet known, but the article is available online. A DOI is guaranteed never to change, so you can use it as a permanent link to any electronic article. An example of a citation using DOI for an article not yet in an issue is: VanDecar J.C., Russo R.M., James D.E., Ambeh W.B., Franke M. (2003). Aseismic continuation of the Lesser Antilles slab beneath northeastern Venezuela. *Journal of Geophysical Research*, <https://doi.org/10.1029/2001JB000884>. Please note the format of such citations should be in the same style as all other references in the paper. AUTHOR INFORMATION PACK 12 Jun 2018 www.elsevier.com/locate/physt 13

Web references As a minimum, the full URL should be given and the date when the reference was last accessed. Any further information, if known (DOI, author names, dates, reference to a source publication, etc.), should also be given. Web references can be listed separately (e.g., after the reference list) under a different heading if desired, or can be included in the reference list.

Data references

This journal encourages you to cite underlying or relevant datasets in your manuscript by citing them in your text and including a data reference in your Reference List. Data references should include the following elements: author name(s), dataset title, data repository, version (where available), year, and global persistent identifier. Add [dataset] immediately before the reference so we can properly identify it as a data reference. The [dataset] identifier will not appear in your published article.

Reference management software

Most Elsevier journals have their reference template available in many of the most popular reference management software products. These include all products that support **Citation Style Language styles**, such as **Mendeley** and **Zotero**, as well as **EndNote**. Using the word processor plug-ins from these products, authors only need to select the appropriate journal template when preparing their article, after which citations and bibliographies will be automatically formatted in the journal's style.

If no template is yet available for this journal, please follow the format of the sample references and citations as shown in this Guide. If you use reference management software, please ensure that you remove all field codes before submitting the electronic manuscript. [More information on how to remove field codes](#). Users of Mendeley Desktop can easily install the reference style for this journal by clicking the following link: <http://open.mendeley.com/use-citation-style/physiotherapy> When preparing your manuscript, you will then be able to select this style using the Mendeley plugins for Microsoft Word or LibreOffice.

Reference style Text: Indicate references by number(s) in square brackets in line with the text. The actual authors can be referred to, but the reference number(s) must always be given. *List:* Number the references (numbers in square brackets) in the list in the order in which they appear in the text. *Examples:* Reference to a journal publication: [1] Van der Geer J, Hanraads JA, Lupton RA. The art of writing a scientific article. *J Sci Commun* 2010;163:51–9. Reference to a book: [2] Strunk Jr W, White EB. The elements of style. 4th ed. New York: Longman; 2000. Reference to a chapter in an edited book: [3] Mettam GR, Adams LB. How to prepare an electronic version of your article. In: Jones BS, Smith RZ, editors. Introduction to the electronic age, New York: E-Publishing Inc; 2009, p. 281–304. Data citation: [dataset] [4] Oguro M, Imahiro S, Saito S, Nakashizuka T. Mortality data for Japanese oak wilt disease and surrounding forest compositions, Mendeley Data, v1; 2015. <http://dx.doi.org/10.17632/xwj98nb39r.1> Note shortened form for last page number. e.g., 51–9, and that for more than 6 authors the first 6 should be listed followed by 'et al.'

Video

Elsevier accepts video material and animation sequences to support and enhance your scientific research. Authors who have video or animation files that they wish to submit with their article are strongly encouraged to include links to these within the body of the article. This can be done in the same way as a figure or table by referring to the video or animation content and noting in the body text where it should be placed. All submitted files should be properly labeled so that they directly relate to the video file's content. In order to ensure that your video or animation material is directly usable, please provide the file in one of our recommended file formats with a preferred maximum size of 150 MB per file, 1 GB in total. Video and animation files supplied will be published online in the electronic version of your article in Elsevier Web products, including [ScienceDirect](#). Please supply 'stills' with your files: you can choose any frame from the video or animation or make a separate image. These will be used instead of standard icons and will personalize the link to your video data. For AUTHOR INFORMATION PACK 12 Jun 2018 www.elsevier.com/locate/physt 14 more detailed instructions please visit our [video instruction pages](#). Note: since video and animation cannot be embedded in the print version of the journal, please provide text for both the electronic and the print version for the portions of the article that refer to this content.

AudioSlides

The journal encourages authors to create an AudioSlides presentation with their published article. AudioSlides are brief, webinar-style presentations that are shown next to the online article on ScienceDirect. This gives authors the opportunity to summarize their research in their own words and to help readers understand what the paper is about. [More information and examples are available](#). Authors of this journal will automatically receive an invitation e-mail to create an AudioSlides

presentation after acceptance of their paper.

Supplementary material

Supplementary material such as applications, images and sound clips, can be published with your article to enhance it. Submitted supplementary items are published exactly as they are received (Excel or PowerPoint files will appear as such online). Please submit your material together with the article and supply a concise, descriptive caption for each supplementary file. If you wish to make changes to supplementary material during any stage of the process, please make sure to provide an updated file. Do not annotate any corrections on a previous version. Please switch off the 'Track Changes' option in Microsoft Office files as these will appear in the published version.

Research data

This journal encourages and enables you to share data that supports your research publication where appropriate, and enables you to interlink the data with your published articles. Research data refers to the results of observations or experimentation that validate research findings. To facilitate reproducibility and data reuse, this journal also encourages you to share your software, code, models, algorithms, protocols, methods and other useful materials related to the project. Below are a number of ways in which you can associate data with your article or make a statement about the availability of your data when submitting your manuscript. If you are sharing data in one of these ways, you are encouraged to cite the data in your manuscript and reference list. Please refer to the "References" section for more information about data citation. For more information on depositing, sharing and using research data and other relevant research materials, visit the [research data](#) page.

Data linking

If you have made your research data available in a data repository, you can link your article directly to the dataset. Elsevier collaborates with a number of repositories to link articles on ScienceDirect with relevant repositories, giving readers access to underlying data that gives them a better understanding of the research described. There are different ways to link your

datasets to your article. When available, you can directly link your dataset to your article by providing the relevant information in the submission system. For more information, visit the [database linking page](#). For [supported data repositories](#) a repository banner will automatically appear next to your published article on ScienceDirect. In addition, you can link to relevant data or entities through identifiers within the text of your manuscript, using the following format: Database: xxxx (e.g., TAIR: AT1G01020; CCDC: 734053; PDB: 1XFN).

Mendeley Data

This journal supports Mendeley Data, enabling you to deposit any research data (including raw and processed data, video, code, software, algorithms, protocols, and methods) associated with your manuscript in a free-to-use, open access repository. Before submitting your article, you can deposit the relevant datasets to *Mendeley Data*. Please include the DOI of the deposited dataset(s) in your main manuscript file. The datasets will be listed and directly accessible to readers next to your published article online. For more information, visit the [Mendeley Data for journals page](#). AUTHOR INFORMATION PACK 12 Jun 2018 www.elsevier.com/locate/physt 15

Data statement

To foster transparency, we encourage you to state the availability of your data in your submission. This may be a requirement of your funding body or institution. If your data is unavailable to access or unsuitable to post, you will have the opportunity to indicate why during the submission process, for example by stating that the research data is confidential. The statement will appear with your published article on ScienceDirect. For more information, visit the [Data Statement page](#).

Submission checklist

The following list will be useful during the final checking of an article prior to sending it to the journal for review. Please consult this Guide for Authors for further details of any item.

Ensure that the following items are present:

One author has been designated as the corresponding author with contact details:

- E-mail address
- Full postal address

All necessary files have been uploaded, and contain:

- Keywords
- "Contribution of Paper statement" (in form of two to three bullet points)
- All figure captions
- All tables (including title, description, footnotes)

Further considerations

- Manuscript has been 'spell-checked' and 'grammar-checked'
- References are in the correct format for this journal
- An appropriate flow diagram and checklist has been submitted <http://www.equator-network.org/>

(including the Internet)

- All references mentioned in the Reference list are cited in the text, and vice versa
- Permission has been obtained for use of copyrighted material from other sources (including the Internet)
- Printed version of figures (if applicable) in color or black-and-white
- Indicate clearly whether or not color or black-and-white in print is required. For any further information please visit our customer support site at <http://support.elsevier.com>.

AFTER ACCEPTANCE

Proofs

One set of page proofs (as PDF files) will be sent by e-mail to the corresponding author or a link will be provided in the e-mail so that authors can download the files themselves. Elsevier now provides authors with PDF proofs which can be annotated; for this you will need

to download Adobe Reader version 7 (or higher) available free from <http://get.adobe.com/reader>. Instructions on how to annotate PDF files will accompany the proofs (also given online). The exact system requirements are given at the Adobe site: <http://www.adobe.com/products/reader/tech-specs.html>. If you do not wish to use the PDF annotations function, you may list the corrections (including replies to the Query Form) and return them to Elsevier in an e-mail. Please list your corrections quoting line number. If, for any reason, this is not possible, then mark the corrections and any other comments (including replies to the Query Form) on a printout of your proof and return by fax, or scan the pages and e-mail, or by post. Please use this proof only for checking the typesetting, editing, completeness and correctness of the text, tables and figures. Significant changes to the article as accepted for publication will only be considered at this stage with permission from the Editor. We will do everything possible to get your article published quickly and accurately – please let us have all your corrections within 48 hours. It is important to ensure that all corrections are sent back to us in one communication: please check carefully before replying, as inclusion of any subsequent corrections cannot be guaranteed. Proofreading is solely your responsibility. Note that Elsevier may proceed with the publication of your article if no response is received.

Offprints

The corresponding author will, at no cost, receive a customized [Share Link](#) providing 50 days free access to the final published version of the article on [ScienceDirect](#). The Share Link can be used for sharing the article via any communication channel, including email and social media. For an extra charge, paper offprints can be ordered via the offprint order form which is sent once the article is accepted for publication. Both corresponding and co-authors may order offprints at any time via Elsevier's [Webshop](#). Corresponding authors who have published their article gold open access do not receive a Share Link as their final published version of the article is available open access on ScienceDirect and can be shared through the article DOI link.

AUTHOR INFORMATION PACK 12 Jun 2018 www.elsevier.com/locate/physt 16

AUTHOR INQUIRIES

Visit the [Elsevier Support Center](#) to find the answers you need. Here you will find everything from Frequently Asked Questions to ways to get in touch. You can also [check the status of your submitted article](#) or find out [when your accepted article will be published](#).

© Copyright 2018 Elsevier | <https://www.elsevier.com>