Universidade do Estado do Rio de Janeiro
Centro Biomédico
Faculdade de Ciências Médicas

Hebert Olímpio Júnior

Efeito da estimulação diafragmática elétrica transcutânea na força muscular respiratória, na espessura do diafragma e no tempo de ventilação mecânica de pacientes críticos idosos

Rio de Janeiro
2023

Hebert Olímpio Júnior

Efeito da estimulação diafragmática elétrica transcutânea na força muscular respiratória, na espessura do diafragma e no tempo de ventilação mecânica de pacientes críticos idosos

Tese apresentada, como requisito parcial para obtenção do título de Doutor, ao Programa de Pós-graduação em Ciências Médicas, da Universidade do Estado do Rio de Janeiro.

Orientador Prof. Dr. Agnaldo José Lopes

Coorientador: Prof. Dr. Gustavo Bittencourt Camilo

Rio de Janeiro

2023

CATALOGAÇÃO NA FONTE
UERJ/REDE SIRIUS/BIBLIOTECA CB-A

O46 Olímpio Júnior, Hebert.
Efeito da estimulação diafragmática elétrica transcutânea na força muscular respiratória, na espessura do diafragma e no tempo de ventilação mecânica de pacientes críticos idosos / Hebert Olímpio Júnior. – 2023.
72 f.

Orientadora: Prof. Dr. Agnaldo José Lopes
Coorientador: Prof. Dr. Gustavo Bittencourt Camilo

Tese (Doutorado) – Universidade do Estado do Rio de Janeiro, Faculdade de Ciências Médicas. Pós-graduação em Ciências Médicas.

1. Respiração artificial – Efeitos adversos – Teses. 2. Diafragma – Lesões – Teses. 3. Serviços de saúde para idosos – Teses. 4. Debilidade muscular – Reabilitação. I. Lopes, Agnaldo José. II. Camilo, Gustavo Bittencourt. III. Universidade do Estado do Rio de Janeiro. Faculdade de Ciências Médicas. IV. Título.

CDU 616.8-053.9

Bibliotecário: Felipe Caldonazzo
CRB7/7341

_______________________________ _______________
Assinatura Data

Hebert Olímpio Júnior

Efeito da estimulação diafragmática elétrica transcutânea na força muscular respiratória, na espessura do diafragma e no tempo de ventilação mecânica de pacientes críticos idosos

Tese apresentada, como requisito parcial para obtenção do título de Doutor, ao Programa de Pós-graduação em Ciências Médicas, da Universidade do Estado do Rio de Janeiro.

Aprovada em 25 de abril de 2023.

Orientador: Prof. Dr. Agnaldo José Lopes
Faculdade de Ciências Médicas - UERJ

Banca Examinadora: ____

Prof. Dr. Gustavo Bittencourt Camilo (Coorientador)
Universidade Federal de Juiz de Fora

____

Prof.ª Dra. Cláudia Henrique da Costa
Faculdade de Ciências Médicas - UERJ

____

Prof. Dr. Thiago Thomaz Mafort
Faculdade de Ciências Médicas - UERJ

____

Prof.ª Dra. Cristina Márcia Dias
Centro Universitário Augusto Motta

____

Prof. Dr. Fernando Silva Guimarães
Universidade Federal do Rio de Janeiro

Rio de Janeiro

2023

DEDICATÓRIA

Dedico este título aos meus pais Heberte Olímpio e Mary Aparecida de Carvalho, por terem me proporcionado amor, carinho, educação e grande parte das ferramentas necessárias para que eu pudesse alcançar a tão sonhada vitória. À Thais da Silva Almeida, minha esposa, por ter caminhado ao meu lado desde o início do Programa, reacendendo minhas esperanças quando eu não acreditava mais ser possível chegar até o fim. Sem você eu não teria cumprido minha carga horária e, menos ainda, concluído minha coleta de dados. Ao Leonardo Carvalho Almeida Olímpio e Anna Clara Medina Trogo Olímpio, meus filhos, por terem me ensinado o significado do amor incondicional e por terem me mostrado o sentido real da vida, que está nas coisas simples, nos pequenos atos. O amor que sinto por vocês é imensurável!

AGRADECIMENTOS

Agradeço a Deus, por me abençoar grandiosamente, permitindo que eu enfrentasse todos os desafios e concluísse o meu Doutorado. O Senhor nunca me desamparou, ainda que a minha fé estivesse abalada pelas adversidades.

Agradeço à Thais da Silva Almeida, minha esposa, pela credibilidade depositada no meu potencial, me mostrando que eu sou capaz de realizar meus sonhos e ser feliz. Obrigado amor, por sempre abrir mão dos compromissos para me acompanhar em minha jornada, por me apoiar nos momentos difíceis e, principalmente, por ter me presenteado com o Leonardo, nosso príncipe, que tanto nos ensina a cada dia. Reafirmo que sem sua existência e sem seu suporte, eu não teria propósito para continuar caminhando.

Agradeço ao meu pai, Heberte Olímpio, por ter sido solícito em todo este processo, por se orgulhar das minhas escolhas e por lutar comigo em prol da realização dos meus desejos.

Agradeço a minha mãe, Mary Aparecida de Carvalho, por ter sido porto seguro e motivação, e por ter me mostrado que independente das turbulências vivenciadas eu sou capaz de vencer. Você foi e é essencial.

Agradeço aos meus sogros Joviano Venancio de Almeida Neto e Maria José da Silva Almeida, por todo apoio durante esse processo; vocês foram indispensáveis. Adicionalmente aos meus cunhados queridos, que me preencheram com sua parceria e amizade.

Agradeço ao meu coorientador Gustavo Bittencourt Camilo, por ter me auxiliado com a proposta do trabalho e com a coleta de dados. Considero você um exímio profissional e seu suporte foi fundamental para conclusão da tese.

Agradeço ao professor Dr. Agnaldo José Lopes pelas orientações, pelo incentivo e pelo zelo diante dos meus momentos de aflição. Mesmo diante de inúmeros orientandos e outras tarefas, você é capaz de iluminar o caminho do próximo, e isso sem a menor dúvida é louvável. Você é merecedor de um reconhecimento maior do que já possui não só por ser um grande pesquisador, mas também por ser um grande ser humano.

Agradeço a toda equipe da UERJ, incluindo funcionários, professores, os membros da banca (internos e externos) e alunos por todo o conhecimento compartilhado, paciência e demais contribuições. Este trabalho é de vocês.

RESUMO

OLÍMPIO JÚNIOR, Hebert. *Efeito da estimulação diafragmática elétrica transcutânea na força muscular respiratória, na espessura do diafragma e no tempo de ventilação mecânica de pacientes críticos idosos.* 2023. 72 f. Tese (Doutorado em Ciências Médicas) – Faculdade de Ciências Médicas, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, 2023.

Pacientes críticos internados em UTI podem desenvolver disfunção diafragmática (DD). Entre os músculos afetados pela permanência em VMI na população geral e principalmente nos idosos, pode ser destacado o diafragma, que evolui com uma redução de sua capacidade de gerar tensão pela atrofia de suas fibras musculares. O primeiro artigo teve como objetivo avaliar a influência do EDET sobre os parâmetros hemodinâmicos e vitais de idosos criticamente enfermos sob VMI. O objetivo do segundo artigo foi avaliar a influência da EDET na força muscular respiratória, espessura do diafragma e tempo de ventilação mecânica de pacientes críticos idosos sob cuidados intensivos. Os participantes da pesquisa foram divididos em GC e GE. No primeiro artigo, todos os participantes foram submetidos à avaliação hemodinâmica antes e após a aplicação do EDET. Eles foram submetidos às mesmas etapas de avaliação, e as variáveis pressão arterial sistólica (PAS), pressão arterial diastólica (PAD), pressão arterial média (PAM) e frequência cardíaca foram medidas imediatamente antes e após a intervenção. No segundo artigo, a avaliação foi feita durante o TRE após o desmame da ventilação mecânica, sendo apenas o GE submetido a EDET. As avaliações consistiram na análise da PImáx, na análise da FED através da USG_D e em um *checklist* de prevenção de falha da extubação institucional. A intervenção com EDET teve início 24h após a intubação orotraqueal, e foi realizada duas vezes ao dia, com duração de 30 minutos, até o término do processo de desmame ventilatório. No primeiro artigo foram encontrados os seguintes resultados: a amostra foi composta por 33 homens e 14 mulheres, com média de idade de 69,9 ± 7,64 anos. A média da pressão arterial sistólica pré-EDET e pós-EDET foi de 126,6 ± 23,7 e 122,9 ± 25,9, respectivamente (p = 0,467). A média da pressão arterial diastólica pré- EDET e pós- EDET foi de 71,1 ± 12,2 e 67,7 ± 14,2, respectivamente (p = 0,223). Não houve diferenças significativas na pressão arterial média ou frequência cardíaca entre os momentos pré- EDET e pós- EDET (p = 0,335 e p = 0,846, respectivamente). No segundo artigo foram encontrados os seguintes resultados: a amostra foi composta por 44 pacientes, sendo 28 do sexo feminino, com mediana de idade de 66 (60 – 79). O valor da média referente ao FED nos pacientes do GC foi de 66,88 ± 31,77, ao passo que naqueles pertencentes ao GE, o resultado foi de 99,13 ± 26,75, (p = 0,001). Foi possível observar na variável PImáx o valor de mediana de 65,75 (42,06–95,92) (p=0,005). Os índices preditivos de desmame IRRS e IWI não apresentaram diferença significativa na análise entre os grupos (p = 0,584 e p = 0,102) e, em relação ao tempo de ventilação mecânica, o valor da média no GC foi de 9,21 ± 2,76, enquanto no GE, o resultado foi 6,28 ± 2,68 (p=0,001). A EDET mostrou-se segura hemodinamicamente e também proporcionou redução no tempo de ventilação mecânica, otimizou a PImáx e aumento na FED em pacientes críticos idosos.

Palavras-chave: Estimulação diafragmática elétrica transcutânea. Idosos. Desmame ventilatório.

ABSTRACT

OLÍMPIO JÚNIOR, Hebert. *Effect of transcutaneous electrical diaphragmatic stimulation on the respiratory muscle strength, diaphragm thickness and mechanical ventilation time in critical elderly patients.* 2023. 72 f. Tese (Doutorado em Ciências Médicas) – Faculdade de Ciências Médicas, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, 2023

Critical patients admitted to the ICU may develop diaphragmatic dysfunction (DD). Among the muscles affected by staying on IMV in the general population and especially in the elderly, the diaphragm can be highlighted, which evolves with a reduction in its capacity to generate tension due to the atrophy of its muscle fibers. The first article aimed to evaluate the influence of TEDS on the hemodynamic and vital parameters of critically ill elderly people under IMV. The objective of the second article was to evaluate the influence of TEDS on respiratory muscle strength, diaphragm thickness and duration of mechanical ventilation in elderly critically ill patients under intensive care. Research participants were divided into GC and GE. In the first article, all participants were submitted to hemodynamic evaluation before and after TEDS application. They underwent the same evaluation steps, and the variables systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and heart rate were measured immediately before and after the intervention. In the second article, the evaluation was performed during SBT after weaning from mechanical ventilation, with only the EG undergoing TEDS. The evaluations consisted of MIP analysis, DTF analysis through USGD and an institutional extubation failure prevention checklist. The intervention with TEDS started 24 hours after orotracheal intubation, and was performed twice a day, lasting 30 minutes, until the end of the ventilatory weaning process. In the first article, the following results were found: the sample consisted of 33 men and 14 women, with a mean age of 69.9 ± 7.64 years. Mean pre-EDET and post-EDET systolic blood pressure were 126.6 ± 23.7 and 122.9 ± 25.9, respectively (p = 0.467). Mean pre-EDET and post-EDET diastolic blood pressure was 71.1 ± 12.2 and 67.7 ± 14.2, respectively (p = 0.223). There were no significant differences in mean arterial pressure or heart rate between pre-EDET and post-EDET time points (p = 0.335 and p = 0.846, respectively). In the second article, the following results were found: the sample consisted of 44 patients, 28 female, with a median age of 66 (60 – 79). The mean value referring to the DTF in the CG patients was 66.88 ± 31.77, while in those belonging to the EG, the result was 99.13 ± 26.75, (p = 0.001) . It was possible to observe in the MIP variable the median value of 65.75 (42.06–95.92) (p=0.005). The predictive indices of IRRS and IWI weaning did not present a significant difference in the analysis between the groups (p = 0.584 and p = 0.102) and, in relation to the duration of mechanical ventilation, the mean value in the CG was 9.21 ± 2.76 , while in the EG, the result was 6.28 ± 2.68 (p=0.001). TEDS proved to be hemodynamically safe and also provided a reduction in mechanical ventilation time, optimized MIP and increased EDF in elderly critically ill patients.

Keywords: Transcutaneous electrical diaphragmatic stimulation. Elderly. Weaning.

LISTA DE FIGURAS

LISTA DE ABREVIATURAS E SIGLAS

CPT	Capacidade pulmonar total
Cst	Complacência estática do sistema respiratório
DD	Disfunção diafragmática
DPOC	Doença pulmonar obstrutiva crônica
ED_{CPT}	Espessura diafragmática na capacidade pulmonar total
ED_{CRF}	Espessura diafragmática na capacidade residual funcional
EDET	Estimulação diafragmática elétrica transcutânea
FR	Frequência respiratória
GC	Grupo controle
GE	Grupo experimental
IED	Índice de espessura do diafragma
IWI	Índice integrativo de desmame
PEmáx	Pressão expiratória máxima
PImáx	Pressão inspiratória máxima
SaO_2	Saturação periférica de oxigênio
USG_D	Ultrassonografia diafragmática
UTI	Unidade de terapia intensiva
VMI	Ventilação mecânica invasiva
VR	Volume residual
Vt	Volume corrente

SUMÁRIO

INTRODUÇÃO

A ventilação mecânica invasiva em pacientes idosos críticos

Pacientes submetidos à ventilação mecânica invasiva (VMI) possuem risco aumentado para desenvolvimento de fraqueza muscular logo nas primeiras horas após o processo de intubação orotraqueal. Esses pacientes são expostos, após a intubação aos medicamentos sedativos, ao imobilismo e à ventilação controlada propriamente dita, dentre outros fatores (DEMOULE et al., 2016). Observa-se que aproximadamente 25% a 50% dos pacientes submetidos ao suporte ventilatório invasivo apresentam fraqueza muscular e, dessa proporção, 85% a 95% persistem com comprometimento neuromuscular pelo período de dois a cinco anos (DESAI et al., 2011).

De acordo com Cederwall et al. (2021), a ventilação mecânica na unidade de terapia intensiva (UTI) é um recurso comum e necessário que permite que os pacientes se recuperem das causas subjacentes de insuficiência respiratória ou sistêmica aguda. Alguns pacientes têm uma necessidade prolongada de ventilação mecânica devido a doenças ou distúrbio de base ou devido a falha no desmame ventilatório.

A prevalência e as características dos pacientes que requerem ventilação mecânica prolongada foram relatadas nos Estados Unidos, Canadá, China, Reino Unido e Brasil, com diferentes sistemas de saúde e com variados números de leitos de UTI. Estudos internacionais do Canadá e do Reino Unido relataram que a porcentagem de pacientes que necessitam de ventilação mecânica prolongada (> 21 dias) constitui até 4% de todas as internações em UTI e ocupam de 11 a 29% dos dias de leitos disponíveis, resultando em impacto substancial nos recursos da UTI. Além disso, pacientes com necessidade de ventilação mecânica prolongada apresentam maior mortalidade em comparação com outros pacientes internados na UTI (BOUZA et al., 2021; CEDERWALL et al., 2021).

Os idosos, neste contexto, merecem atenção pelo fato de o processo de transição demográfica ter como uma de suas características a inversão da pirâmide etária (WONG et al., 2006). Com o aumento da expectativa de vida, houve um aumento significativo da população idosa do Brasil. De 2005 para 2015, a proporção de idosos de 60 anos ou mais na população brasileira passou de 9,8% para 14,3%, segundo dados do IBGE (PACÍFICO et al., 2022). Isso acarreta uma maior incidência de admissões destes pacientes em UTI's em relação aos jovens e adultos, tendo em vista que eles representam a maior parcela da população (WONG et al., 2006). Além disso, considerando a tendência de o paciente com idade avançada ser acometido por um maior número de comorbidades, a insuficiência respiratória torna-se mais frequente e, como consequência, contribui também para as internações hospitalares por aumentar a necessidade de suporte ventilatório (DELERME et al., 2008).

Li et al. (2022) analisaram os principais eventos adversos na intubação a partir do início do procedimento, e notaram complicações adicionais de órgãos, como o desenvolvimento de lesão renal aguda e disfunção diafragmática (DD). A lesão renal aguda é uma doença complexa e grave caracterizada por declínio súbito da função renal com consequente aumento de produtos nitrogenados e distúrbios hidroeletrolíticos e ácido-básicos. Rins "envelhecidos" submetidos a alterações estruturais e funcionais que afetam adversamente a capacidade autorregulatória, a vascularização sistêmica e o sistema imunológico aumentam a suscetibilidade à lesão renal aguda na população idosa.

A disfunção diafragmática em pacientes idosos críticos

Dentre os músculos afetados pela permanência em VMI na população geral e, principalmente, nos idosos, destaca-se o diafragma. Esse músculo mostra, em pacientes sob VMI, uma diminuição progressiva de sua capacidade de gerar tensão pela atrofia de suas fibras musculares. Consequentemente, desenvolve-se uma alteração denominada DD (RADELL et al., 2002). Os mecanismos envolvidos com a DD incluem: 1) a redução no número de miofibrilas (que envolvem filamentos de actina e miosina responsáveis pela produção da contração muscular); 2) o estresse oxidativo (indutor da ativação da proteína *forkhead box O1,* envolvida com os processos de gliconeogênese e glicogenólise); e 3) a ativação anormal de uma via responsável pela proteólise de adenosina-trifosfato, a ubiquitina-proteassoma; 4) a DD induzida pela ventilação mecânica (subassistência ou sobreassistência ventilatória). (HUSSAIN et al., 2010; LEVINE et al., 2008; VAN DEN BERG et al., 2017).

A espessura do diafragma diminui rapidamente durante os primeiros dias de VMI em mais de 40% dos pacientes, independente do modo ventilatório. Esse fator é consequência dos níveis mais baixos de esforço inspiratório e dos níveis mais altos de volume de ar para suporte ventilatório. A espessura aumenta em aproximadamente 10% dos pacientes, quando há maior esforço inspiratório e níveis mais baixos de volume de ar para suporte ventilatório (GOLIGHER et al., 2015). Baixos níveis de assistência fornecidos pelo ventilador podem levar à fadiga e desconforto, enquanto o excesso de assistência pode gerar assincronia paciente-ventilador e DD induzida pelo ventilador mecânico (UMBRELLO et al., 2015).

Considerando a característica progressiva da DD e o processo de miotrauma, algumas consequências como o aumento do tempo de VMI, a elevação do risco de complicações respiratórias e o prolongamento do tempo de internação hospitalar poderão ser observadas, caso não seja realizada nenhuma intervenção específica (MATAMIS et al., 2013; SASSOON et al., 1985). Portanto, faz-se necessária a adoção de medidas que permitam a detecção precoce da fraqueza diafragmática, bem como o emprego de condutas que previnam ou tratem esta condição clínica.

Um dos índices mais recentes para prever o resultado dos pacientes após o desmame ventilatório é o índice integrativo de desmame (IWI). De acordo com os estudos realizados até o presente momento, ele apresenta sensibilidade de 99% e especificidade de 86% em predizer o desfecho do desmame do paciente em ventilação mecânica. Esse índice é resultado de três parâmetros básicos, que são, capacidade pulmonar, saturação arterial de oxigênio (SaO_2), frequência respiratória e volume corrente (Vt), e podem ser calculados facilmente sem necessidade da cooperação do paciente com base na seguinte equação: (Cst, Complacência estática do sistema respiratório (Cst) × SaO_2 / frequência respiratória (FR) / Vt. Esse indicador pode ser um índice mais objetivo em relação aos métodos convencionais, porque avalia simultaneamente a função do sistema cardiovascular, do sistema respiratório e da complacência estática respiratória (EBRAHIMABADI, 2017; NEMER et al., 2011).

Avaliação do diagnóstico de disfunção diafragmática

Quanto à avaliação para o diagnóstico da DD, esta pode ser realizada através de instrumentos que mensuram a força muscular inspiratória, a exemplo do manovacuômetro, além de exames de imagem que evidenciam a espessura do diafragma, como a ultrassonografia diafragmática (USG_D) (ATS, 2002; UMBRELLO et al., 2015).

A ultrassonografia é uma técnica eficaz capaz de criar imagens do corpo para fins de diagnóstico e para orientar os procedimentos invasivos, sendo um exame pulmonar emergente e útil na avaliação de algumas doenças do parênquima pulmonar (VOLPICELLI, 2012). É um procedimento simples, seguro e relativamente de baixo custo que, quando utiliza equipamentos adequados e técnicas padronizadas aplicadas por profissionais capacitados, fornece informações relevantes do sistema respiratório que vêm sendo demonstradas ao longo dos últimos anos (DEMI et al., 2014).

Para condução do exame, foi utilizado transdutor de 10 MHz, entre a linha axilar anterior e média, entre a 8ª e 9ª, modo B, modo M para medir a espessura e deslocamento. O uso da ultrassonografia engloba principalmente à análise visual de um produto gerado por uma técnica de imagem padrão, fazendo com que os diagnósticos dependam de interpretações qualitativas e quantitativas. (DEMI et al., 2014).

A ultrassonografia à beira do leito, que já é essencial em vários aspectos da doença crítica, é um método simples e não invasivo de quantificação da atividade contrátil diafragmática. A ultrassonografia pode ser usada para determinar a mobilidade e também pode permitir a visualização direta da espessura do diafragma, o que pode ajudar a identificar pacientes com disfunção do diafragma. (UMBRELLO et al., 2015). A variável referente à força muscular inspiratória na manovacuometria é a pressão inspiratória máxima (PImáx), enquanto a fração de espessura do diafragma, constatada através da USG_D, é representada pela fração de espessamento diafragmático (FED), obtido por meio da diferença entre a espessura do diafragma na capacidade pulmonar total (ED_{CPT}) e na capacidade residual funcional (ED_{CRF}), sendo dividida pela ED_{CRF}. O FED contribui para o diagnóstico inicial da DD e também é relevante para o acompanhamento da evolução da função do músculo durante o período de internação e desmame ventilatório (FERRARI et al., 2014; KIM et al., 2017). Segundo Goligher et al. (2015), a diminuição do FED está associada ao prejuízo da melhora funcional e possui correlação com baixos valores de PImáx em pacientes críticos.

A técnica de estimulação diafragmática elétrica transcutânea

Condutas voltadas para prevenção ou tratamento da DD são importantes na tentativa de minimizar eventuais danos ao paciente crítico. No âmbito da reabilitação pulmonar ambulatorial, foram demonstrados efeitos positivos com a utilização da eletroterapia, especificamente através da técnica de estimulação diafragmática elétrica transcutânea (EDET) em pacientes com doença pulmonar obstrutiva crônica (DPOC) (CANCELLIERO et al., 2013). Esta técnica consiste no posicionamento de eletrodos sobre a pele, em locais próximos aos pontos motores do diafragma, transmitindo uma corrente intermitente e gerando potenciais de ação capazes de produzir contrações musculares (CANCELLIERO et al., 2012). Consideram-se dois equipamentos diferentes de eletroestimulação para utilização da EDET em mulheres: o Dualpex (modelo Phrenics) e o Dualpex 961; ambos os equipamentos demonstram efeitos positivos na força muscular respiratória (PImáx). Quanto ao segundo equipamento, foi utilizado modo de estimulação elétrica funcional (FES), com corrente bifásica, pulsada e simétrica. Porém, na literatura, não há ainda evidências acerca dos efeitos dessa terapia no IED de pacientes críticos idosos, ou ainda que avaliassem a repercussão da EDET no tempo de ventilação mecânica e de internação hospitalar dessa população.

Justificativa

O período prolongado de internação acarreta uma série de despesas hospitalares, governamentais e para os familiares dos pacientes envolvidos. Estas despesas incluem medicamentos de variados tipos, energia elétrica, oxigênio, acessórios como tubo orotraqueal, sondas de aspiração e filtros trocadores de calor e umidade, além dos recursos humanos. O tempo de ventilação mecânica é uma variável diretamente proporcional ao tempo de internação hospitalar, e sua redução é eficaz na atenuação dos custos com a assistência, bem como na minimização dos danos ao paciente.

Há uma grande possibilidade de o paciente crítico desenvolver fraqueza muscular, deformidades nas articulações de membros superiores e inferiores, infecções hospitalares e diversas outras limitações, enquanto estiver restrito ao leito. Deste modo, é importante que recursos terapêuticos sejam constantemente inseridos na área de terapia intensiva para encurtar o processo de desmame da ventilação mecânica, tendo como consequência uma aceleração da alta hospitalar. A espessura e força muscular do diafragma, de acordo com a literatura, são de suma importância para determinar, em conjunto com outras variáveis e índices, o sucesso ou insucesso do desmame ventilatório. Portanto, o tratamento dos pacientes sob VMI deve considerar a otimização destas variáveis referentes ao músculo em questão.

Tendo em vista a necessidade de novos recursos para otimizar o desmame ventilatório, a escassez de evidências sobre o uso da EDET e sua influência na força muscular respiratória e espessura diafragmática em pacientes críticos, novas pesquisas são necessárias. Além do baixo custo, a EDET é uma técnica que possui boa praticidade. A implementação da mesma poderá proporcionar um menor tempo de ventilação mecânica e de internação através da melhora da força muscular do diafragma, caso o recrutamento precoce de unidades motoras esteja associado à melhora da PImáx e do FED.

1 **OBJETIVOS**

1.1 **Objetivo geral**

Investigar a influência da EDET na hemodinâmica, tempo de ventilação mecânica, força muscular respiratória e espessura do diafragma de pacientes críticos idosos em UTI.

1.2 **Objetivos específicos**

Os objetivos específicos são:

a) avaliar o impacto da EDET na força muscular respiratória de pacientes críticos idosos;
b) avaliar a fração de espessamento do diafragma após a EDET;
c) avaliar o tempo de ventilação mecânica dos participantes da pesquisa após a intervenção proposta; e
d) avaliar a resposta hemodinâmica da EDET.

2 **HIPÓTESES DO ESTUDO**

H0 - Não haverá diferença estatisticamente significativa entre as médias dos grupos estudados em relação à variável FED ($p > 0,05$).

H1 - Haverá diferença estatisticamente significativa entre as médias dos grupos estudados em relação à variável FED ($p < 0,05$).

H0 - Não haverá diferença estatisticamente significativa entre as médias dos grupos estudados em relação à variável tempo de ventilação mecânica ($p > 0,05$).

H1 - Haverá diferença estatisticamente significativa entre as médias dos grupos estudados em relação à variável tempo de ventilação mecânica ($p > 0,05$).

H0 - Não haverá diferença estatisticamente significativa entre as médias dos grupos estudados em relação à hemodinâmica ($p > 0,05$).

H1 - Haverá diferença estatisticamente significativa entre as médias dos grupos estudados em relação à hemodinâmica ($p < 0,05$).

3 **MÉTODOS**

3.1 **Delineamento do estudo e recrutamento**

Tratou-se de um estudo de natureza experimental, de tipologia ensaio clínico controlado e randomizado.

Esse estudo foi previamente aprovado pelo Comitê de Ética em Pesquisa da Faculdade de Ciências Médicas e da Saúde de Juiz de Fora (MG) sob o número CAAE: 87664318.2.0000.5103 (ANEXO). Por se tratar de um ensaio clínico, o protocolo foi cadastrado também no *Clinical Trials* sob o número NCT04565002.

Todos os participantes da pesquisa foram submetidos à avaliação da força muscular respiratória (manovacuometria) e da espessura do diafragma (USG_D), e apenas os pacientes do GE foram expostos a uma intervenção através da utilização da EDET.

3.2 **Amostra**

A amostra foi composta por participantes de ambos os sexos, com idade ≥ 60 anos, que foram submetidos à VMI. Os participantes da pesquisa foram divididos em grupo controle (GC) e grupo experimental (GE) e realizaram as mesmas etapas de avaliação, durante o teste de respiração espontânea após o desmame da ventilação mecânica, sendo apenas o GE submetido à EDET. Os detalhes da intervenção serão expostos posteriormente.

O cálculo do tamanho da amostra foi feito no software MedCalc 8.2 (MedCalc Software Mariakerke, Bélgica). Uma vez que o desfecho principal foi avaliar a influência da EDET no tempo de ventilação mecânica, força muscular respiratória e espessura do diafragma de pacientes críticos idosos, tomou-se como base a variável "espessura diafragmática", sendo o valor médio utilizado para o cálculo baseado em estudos anteriores (FERRARI et al., 2014; GOLIGHER et al., 2015). Então, considerando $\alpha = 5\%$, $\beta = 30\%$ e intervalo de confiança de 95% igual a ± 5%, o tamanho da amostra mínimo obtido foi de 20 participantes em cada grupo. Ajustando-se para possíveis perdas da ordem de 10%, calculou-se a amostra em 22 participantes em cada grupo.

3.2.1 Local de realização do estudo e recrutamento

O presente estudo contou com indivíduos provenientes do Hospital e Maternidade Therezinha de Jesus e Hospital Monte Sinai, na cidade de Juiz de Fora (MG).

A aplicação dos testes aconteceu nas UTI adulto desses hospitais.

3.3 **Critérios de inclusão e exclusão**

3.3.1 Critérios de inclusão

Foram incluídos na presente pesquisa os indivíduos que se encaixaram nos seguintes critérios:

a) Pacientes com idade superior a 60 anos;
b) Pacientes que permaneceram em VMI por no mínimo 24 horas.

3.3.2 Critérios de exclusão

Foram excluídos da presente pesquisa os indivíduos que se encaixaram nos seguintes critérios:

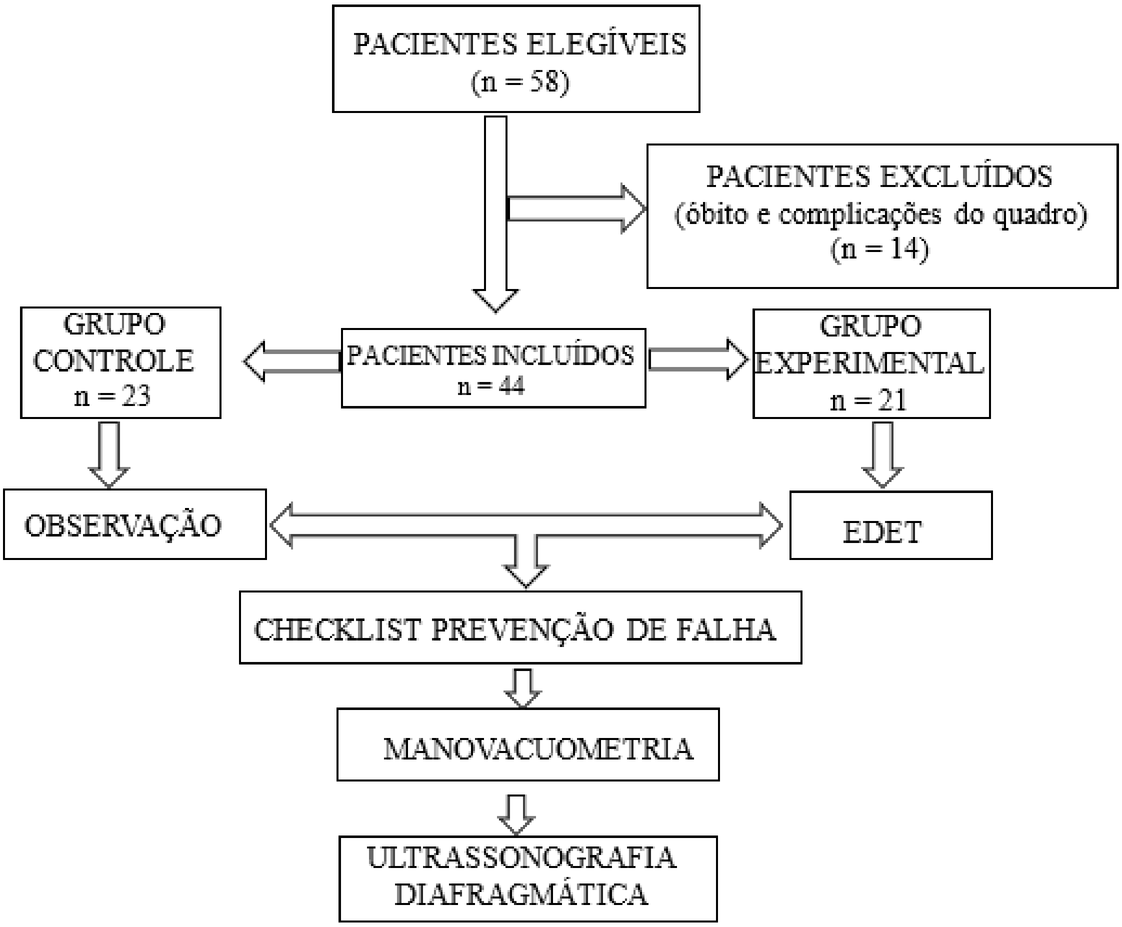
a) pacientes com doenças e/ou lesões neurológicas graves que impedissem a evolução do desmame ventilatório;
b) pacientes com cicatriz cirúrgica recente e/ou lesões abertas nas regiões de posicionamento dos eletrodos;

c) pacientes com instabilidade hemodinâmica grave (frequência cardíaca > 140 batimentos/minuto, pressão arterial < 65 mmHg ou > 120 mmHg, saturação periférica de oxigênio < 86% com fração inspirada de oxigênio ≥ 60%) que não foi resolvida imediatamente e gerou perda do prazo de 24 horas estabelecido no estudo;
d) pacientes em assincronia com o ventilador mecânico, que não foi resolvida imediatamente com ajustes ventilatórios necessários, levando à "quebra do protocolo" proposto no presente estudo;
e) pacientes com hipoglicemia (glicemia < 60 mg/dL);
f) pacientes com marca-passo cardíaco;
g) pacientes com pneumotórax não drenado;
h) pacientes em uso de drogas vasoativas em dose ascendente;
i) pacientes submetidos ao uso de bloqueadores neuromusculares durante a intervenção; e
j) pacientes que eram usuários crônicos de corticoides.

3.4 **Procedimentos/metodologia proposta**

A avaliação dos participantes da pesquisa aconteceu nas UTI Adulto (I e II) do Hospital e Maternidade Therezinha de Jesus e Hospital Monte Sinai – Juiz de Fora (MG). Os procedimentos seguiram a ordem exposta a seguir (Figura 1).

Figura 1 – Fluxograma da coleta de dados. EDET = Estimulação Diafragmática Elétrica Transcutânea



Fonte: O autor, 2023.

3.4.1 Distribuição dos participantes, avaliação e intervenção

Os participantes da pesquisa foram divididos em dois grupos, seus responsáveis assinaram o Termo de Consentimento Livre e Esclarecido (APÊNDICE A) conforme exposto anteriormente, sendo alocados através da ferramenta virtual *research randomizer* em GC ou GE, as intervenções foram realizadas pela equipe de fisioterapia e, as avaliações propostas, pelos pesquisadores. Foi utilizado o prontuário eletrônico (RMSaúde) institucional para coleta dos dados gerais (incluindo nome completo, sexo, idade, comorbidades, tempo de internação, tempo de ventilação mecânica, medicações e intercorrências). Os parâmetros hemodinâmicos e ventilatórios na avaliação e intervenção foram obtidos à beira do leito e nos prontuários, através da análise do ventilador mecânico, do monitor do paciente e do *software* RMSaúde. Posteriormente, esses dados foram registrados em uma ficha clínica (APÊNDICE B). Os participantes da pesquisa foram submetidos à avaliação da FED através da USG_D, bem como da força muscular respiratória, através da manovacuometria, imediatamente após o desmame ventilatório, já em processo de teste de respiração espontânea, em modo assistido com pressão de suporte em 7cmH_2O e pressão expiratória positiva final em 5cmH_2O. É válido ressaltar que o desmame e extubação foram realizados seguindo um *checklist* institucional (APÊNDICE C) para maior segurança do paciente.

O GE, imediatamente após o período de 24 horas em VMI, foi submetido à EDET, duas vezes ao dia, com intervalo de seis horas entre as terapias para não conflitar com outras condutas da equipe multiprofissional. Inicialmente, a mesma foi realizada com o paciente em modo ventilatório assisto-controlado e bem adaptado à ventilação. O parâmetro de sensibilidade foi ajustado no valor necessário para que as contrações produzidas pela estimulação elétrica não disparassem o ventilador mecânico, evitando episódios de assincronia. Após a suspensão de fármacos com efeito sedativo (como, por exemplo, benzodiazepínicos e opioides endógenos) e retomado o *drive* ventilatório, a EDET continuou a ser empregada nos pacientes do GE até a extubação, em modo ventilatório espontâneo, seguindo o mesmo protocolo, porém com a sensibilidade reajustada aos valores padronizados para prevenção de fadiga muscular. Os procedimentos serão detalhados a seguir.

3.4.2 <u>Ultrassonografia diafragmática</u>

Durante a realização da ultrassonografia, os pacientes permaneceram em posição supina. Utilizou-se o transdutor linear para avaliar as estruturas superficiais e o transdutor cardíaco para avaliar as estruturas profundas. Há uma ampla variação de técnicas a serem empregadas, porém a avaliação de oito zonas é prática e rápida para ser realizada na avaliação de emergência e em pacientes em UTI. A avaliação de oito zonas consiste na varredura de quatro áreas por hemitórax, a saber: as zonas 1 e 2, que indicam respectivamente a parede torácica anterior superior e a anterior inferior; e as zonas 3 e 4, que indicam a parede torácica lateral superior e a lateral inferior, respectivamente (GARGANI, 2014; VOLPICELLI et al., 2006).

O equipamento utilizado para realização de todos os exames de ultrassonografia pulmonar foi o GE LogiqE (Logiq-E GE 2014, Contagem, MG, Brasil), do Setor de Ultrassonografia do Hospital e Maternidade Therezinha de Jesus, Juiz de Fora (MG).

3.4.3 Avaliação da força muscular respiratória

De acordo com a American Thoracic Society (2002), o protocolo adequado para se obter as medidas referentes à força muscular respiratória deve respeitar as seguintes características: a) ambiente com temperatura aproximada de 21ºC; b) calibração prévia do manovacuômetro; c) paciente em postura sentada (cabeceira elevada em 90°); e d) execução de uma inspiração máxima partindo do volume residual (VR) para alcance da capacidade pulmonar total (CPT). O procedimento foi refeito por mais duas vezes, com intervalo de dois minutos entre as repetições (prevenção de fadiga muscular) e as medidas de PImáx consideradas foram as maiores registradas. O equipamento utilizado foi da marca M120 - Murenas, São Paulo, Brasil, com escala de 4 cmH_2O, com variação de +/- 120 cmH_2O.

3.4.4 Estimulação Diafragmática Elétrica Transcutânea

O protocolo da EDET foi iniciado 24h após a intubação orotraqueal e composto pelos seguintes parâmetros: a) frequência de 30 Hz; b) largura de pulso de 0,4 ms; c) frequência respiratória de 15 incursões respiratórias/minuto; d) tempo de sustentação de 1 s; e) tempo de subida de 1 s; f) tempo de descida de 2 s; e g) tempo sem estímulo de 2 s (GEDDES et al., 1990). Foi utilizado o equipamento (Dualpex 961, modo FES, Quark®, São Paulo, Brasil). O posicionamento dos eletrodos foi realizado de acordo com estudo de Cancelliero et al. (2012), que propôs o posicionamento de dois eletrodos na região paraxifoidea direita e esquerda, e outros dois na direção da linha média axilar, sobre o sétimo espaço intercostal, também dos lados direito e esquerdo. A duração do procedimento foi de 30 minutos, duas vezes ao dia, com intervalo de seis horas entre as aplicações, até que o paciente passasse pelo processo de extubação (CANCELLIERO et al., 2012). Enquanto o participante não possuísse nível de consciência, não estivesse em modo ventilatório assistido e sem o uso de fármacos com efeito sedativo, a sensibilidade do ventilador foi ajustada de maneira que não disparasse o equipamento, para evitar episódios de assincronia. Imediatamente após a recuperação do nível de consciência, retomada do *drive* ventilatório e suspensão das drogas sedativas, o paciente durante a EDET foi estimulado a inspirar após a percepção da chegada da corrente elétrica, em modo espontâneo, e com a sensibilidade ajustada nos valores basais.

3.4.5 Análise dos dados

Com objetivo de verificar a distribuição dos dados, foi realizado o teste de Shapiro-Wilk. Diante de uma distribuição paramétrica, a diferença entre as médias das variáveis contínuas entre os grupos experimental e controle foi avaliada por meio do teste *t*. As variáveis com distribuição não paramétrica foram analisadas por meio do teste de Mann-Whitney. O software usado foi o SPSS 22. Considerou-se significância estatística um valor de $p < 0,05$.

4 RESULTADOS E DISCUSSÃO

A seguir, serão apresentados dois artigos produzidos como resultados dos trabalhos desenvolvidos na elaboração da presente Tese. O primeiro foi publicado na revista *Rehabilitation Research and Practice* em dezembro de 2021, com base nos dados parciais do estudo. O segundo foi submetido à revista Physiotherapy Research International em março de 2023, com base nas informações finais obtidas pelo estudo.

4.1 Artigo 1 – Rehabilitation research and practice immediate hemodynamic responses of transcutaneous electrical diaphragmatic stimulation in critically ill elderly patients

Rehabilitation Research and Practice Immediate Hemodynamic Responses of Transcutaneous Electrical Diaphragmatic Stimulation in Critically Ill Elderly Patients

Short title: Transcutaneous diaphragmatic stimulation in critically ill elderly

Hebert Olímpio Júnior,[1] Gustavo Bittencourt Camilo,[1,2] Aline Priori Fioritto,[3] Agnaldo José Lopes,[1,4,5]

[1]*Medical Sciences Post-Graduation Program, School of Medical Sciences, State University of Rio de Janeiro (UERJ), Rio de Janeiro, Brazil*
[2]*Faculty of Medical and Health Sciences of Juiz de Fora (SUPREMA), Minas Gerais, Brazil*
[3]*Federal University of Juiz de Fora (UFJF), Juiz de Fora, Minas Gerais, Brazil*
[4]*Rehabilitation Sciences Post-Graduation Program, Augusto Motta University Center (UNISUAM), Rio de Janeiro, Brazil*
[5]*Local Development Post-Graduation Program, Augusto Motta University Center (UNISUAM), Rio de Janeiro, Brazil*

ORCID numbers and email addresses:

Hebert Olímpio Júnior: ORCID: https://orcid.org/0000-0002-1533-0964. E-mail: hebertojr@hotmail.com
Gustavo Bittencourt Camilo: ORCID: https://orcid.org/0000-0001-7387-8381. E-mail: gustavoscamilo@gmail.com
Aline Priori Fioritto: ORCID: https://orcid.org/0000-0001-7106-7876. E-mail: aline.priori.fioritto@gmail.com

Agnaldo José Lopes: ORCID: https://orcid.org/0000-0001-8598-4878. E-mail: agnaldolopes.uerj@gmail.com
Correspondence should be addressed to Agnaldo J. Lopes; agnaldolopes.uerj@gmail.com

ABSTRACT

Background. Critically ill patients admitted to intensive care units (ICUs) may develop diaphragmatic dysfunction, especially when artificial airways are used. Positive effects have been observed when using the transcutaneous electrical diaphragmatic stimulation (TEDS) technique in in different clinical conditions. However, no study has evaluated the safety of TEDS in patients admitted to ICUs. This study aimed to evaluate the influence of TEDS on the hemodynamic and vital parameters of critically ill elderly patients under invasive mechanical ventilation (IMV). *Methods.* Forty-seven patients aged > 60 years under IMV were subjected to evaluation of hemodynamic variables before and after TEDS. The procedure lasted 30 minutes and was performed one time. *Results.* The sample consisted of 33 men and 14 women, with a mean age of 69.9 ± 7.64 years. The mean systolic blood pressure pre-TEDS and post-TEDS was 126.6 ± 23.7 and 122.9 ± 25.9, respectively (p = 0.467). The mean diastolic blood pressure pre-TEDS and post-TEDS was 71.1 ± 12.2 and 67.7 ± 14.2, respectively (p = 0.223). There were no significant differences in mean arterial pressure or heart rate between the pre-TEDS and post-TEDS time points (p = 0.335 and p = 0.846, respectively). *Conclusion.* Our findings suggest that TEDS does not promote clinically relevant impacts in hemodynamic or vital parameters in critically ill elderly patients. These findings point to a possible safety in the application of the TEDS in this population.

1 INTRODUCTION

Critically ill patients admitted to intensive care units (ICUs) are prone to develop muscle weakness, especially when they use artificial airways. The factors associated with this outcome are bed confinement, use of drugs with sedative effects or neuromuscular blockers, and exposure to invasive mechanical ventilation (IMV) [1]. The clinical condition known as ICU-acquired weakness (ICU-AW) is defined as a syndrome that is not explained by any etiology other than ICU hospitalization and is associated with lowered quality of life [2].

The elderly population has a greater tendency for the manifestation of comorbidities, which contributes to hospital admissions. Polyneuropathy and myopathy related to intensive care are common conditions in them, generating a worse prognosis of ICU-AW [3, 4]. The respiratory muscles are among the most affected: the muscle fibers can atrophy due to oxidative stress, activation of the ubiquitin-proteasome pathway, and a decrease in the number of myofibrils [5–7]. The muscles affected by IMV in the general population and especially in the elderly population include the diaphragm; when specific atrophy of the muscle fibers of the diaphragm is observed, the change is known as diaphragmatic dysfunction [8]. Controlling the factors that increase the risk of ICU-AW is key to preventing its development. Some 25-50% of subjects receiving ventilatory support have muscle weakness, and of this group, 85-95% persist with neuromuscular impairment for 2-5 years [9]. Considering the progression of diaphragmatic dysfunction, which is one manifestation of ICU-AW, consequences such as increased duration of IMV, increased risk of respiratory complications, and prolonged hospital stay may be observed if no specific intervention is performed [10,11].

In the context of outpatient pulmonary rehabilitation, positive effects have been observed when using the transcutaneous electrical diaphragmatic stimulation (TEDS) technique in patients with chronic obstructive pulmonary disease (COPD) [12]. This technique consists of placing electrodes on the skin in locations near the motor points of the diaphragm, transmitting an intermittent current, and generating action potentials capable of producing muscle contractions [13, 14]. Studies that have evaluated the safety of neuromuscular electrical stimulation (NES) have suggested that it does not alter the stability of vital parameters such as heart rate (HR) and blood pressure (BP) [15, 16]. However, no study has evaluated the safety of TEDS in patients admitted to the ICU. Considering the practicality of the procedure, its low cost, the importance of applying new therapeutic modalities in the context of diaphragmatic dysfunction, and the scarcity of evidence on this topic in the ICU context, the objective of the present study was to evaluate the influence of TEDS on hemodynamic and vital parameters of critically ill elderly patients.

2 **MATERIALS AND METHODS**

2.1 **Study design and Participants**

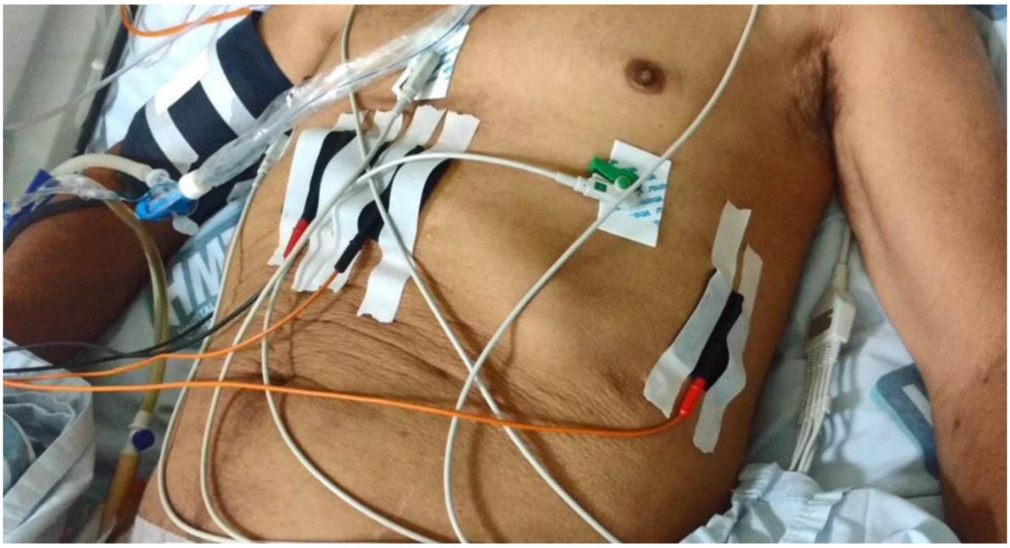
This is an experimental study that evaluated 47 patients (of 71 eligible) aged ≥ 60 years who underwent IMV at the Therezinha de Jesus Hospital and Maternity Hospital and at the Monte Sinai Hospital, both located in Juiz de Fora, Brazil. All participants underwent hemodynamic evaluation before and immediately after TEDS application. They underwent the same evaluation steps, and the variables systolic BP (SBP), diastolic BP (DBP), mean arterial pressure (MAP), and HR were measured immediately before and after the intervention. Patients with the following characteristics were excluded: recent surgical scar and/or open lesion in the regions where the electrodes would be placed, severe hemodynamic instability (HR > 140 bpm, MAP < 65 mmHg or > 120 mmHg, peripheral oxygen saturation < 86% with fraction of inspired oxygen ≥ 60%), patient–ventilator asynchrony not reversible with adjustments or optimization of sedation, hypoglycemia < 60 mg/dL, presence of a cardiac pacemaker, untreated pneumothorax, and use of increasing doses of vasoactive drugs.

This study was approved by the Research Ethics Committee of the Faculty of Medical and Health Sciences of Juiz de Fora (SUPREMA) under number 2.739.692 and all patients approved and consented in participating of this study. This study was registered with the ClinicalTrials.gov Identifier code NCT04565002.

2.2 **Intervention**

The intervention was performed with the patient in assist-control ventilatory mode. The sensitivity parameter was adjusted to the value required for the contractions produced by the electrical stimulation not to trigger the mechanical ventilator, thus avoiding episodes of asynchrony. The following parameters were used: frequency of 30 Hz, pulse width of 0.4 ms, respiratory rate (RR) of 15 irpm, hold time of 1 s, rise time of 1 s, fall time of 2 s, and time without stimulation 2 s [13]. Phrenic electrostimulation equipment (Dualpex 961, Quark, SP, Brazil) was used. The electrodes were positioned according to Cancelliero et al. [14], who proposed the placement of two electrodes in the right and left paraxiphoid regions and two others in the direction of the axillary midline, on the seventh intercostal space, on the right and left sides. The positioning of the TEDS electrodes is shown in Figure 1. The diaphragm stimulation lasted 30 minutes [12].

Figure 1 – Positioning of electrodes during transcutaneous electrical diaphragmatic stimulation



2.3 **Data Analysis**

The distribution of the measured outcome variables was evaluated by the Shapiro-Wilk test. The results are expressed as the mean (SD) or frequency (percentage). The difference between the mean of a continuous variable before and after intervention was evaluated by paired t-test. The significance level adopted was $p < 0.05$. Data analysis was performed using IBM SPSS Statistics 23 software.

3 **RESULTS**

Of the 71 patients who participated in the present study, 24 were excluded for the following reasons: interruption for a medical procedure ($n = 5$), intense psychomotor agitation ($n = 12$), and patient–ventilator asynchrony ($n = 7$). Thus, the sample consisted of 47 patients, 33 male, with a mean age of 69.9 ± 7.64 years. The main clinical conditions that led to ICU admission were heart disease, lung disease, and sepsis. The characteristics of the sample, including demographic and anthropometric data and the admission conditions, are shown in Table 1.

Table 1 – Characteristics of the studied sample

Variables	Values
Demographic Data	
Age (years)	69.9 ± 7.64
Gender (male)	33 (70.2%)
Body Composition	
Weight (kg)	64.6 ± 9.87
Height (cm)	166.5 ± 6.85
Clinical conditions of hospitalization	
Cardiac diseases	
Acute heart failure	6 (12.8%)
Acute myocardial infarction	4 (8.51%)
Lung diseases	
COPD exacerbation	5 (10.6%)
Asthma exacerbation	5 (10.6%)
Neurological diseases	
Stroke	3 (6.38%)
Spinal cord injury	3 (6.38%)
Sepsis	9 (19.2%)
Postoperative state after cardiac surgery	7 (14.9%)
Postoperative state after abdominal surgery	5 (10.6%)

Results expressed as means ± SD or number (%).

The mean value of SBP pre-TEDS was 126.6 ± 23.7 mmHg, whereas the value post-TEDS was 122.9 ± 25.9 mmHg (p = 0.467). Mean DBP was 71.1 ± 12.2 mmHg before the procedure and 67.7 ± 14.2 mmHg after intervention (p = 0.223). The comparisons between the pre-TEDS and post-TEDS values are shown in Table 2.

Table 2 – Differences between the systolic blood pressure, diastolic blood pressure, mean arterial pressure and heart rate when comparing the moments before and after the intervention

Variables	Before TEDS	After TEDS	***p*-value**
SBP	126.6 ± 23.7	122.9 ± 25.9	0.467
DBP	71.1 ± 12.2	67.7 ± 14.2	0.223
MAP	90.2 ± 16.7	86.7 ± 18.8	0.335
HR	92.8 ± 18.9	93.5 ± 19.2	0.846

Results expressed as means ± SD. SBP: systolic blood pressure; DBP: dyastolic blood pressure; MAP: mean arterial pressure; HR: heart rate; TEDS: transcutaneous electrical diaphragmatic stimulation.

Power analysis was conducted using G*power version 3.1. Considering a type-I error of 5%, a minimal correlation between measurements of 0.5, a two-tailed paired test, and the observed means ± SD (before and after TEDS), the actual statistical power to detect the observed effects were 80% (SBP), 80.2% (DBP), 80% (MAP), and 80% (HR).

4 **DISCUSSION**

This is the first study to evaluate the influence of TEDS on the hemodynamic and vital parameters of critically ill elderly patients. The main finding was that there was no significant change in hemodynamic parameters in the sample from before to after the application of TEDS, which suggests the intervention is safe.

NES is a safe technique as long as it is correctly applied by a trained professional [17–20]. Evaluating patients with COPD, Akar et al. [18] observed a reduction in HR in the postintervention period, suggesting that the use of NES did not generate cardiac overload in the patients evaluated. Iwatsu et al. [19] followed 61 patients in the postoperative period of cardiac surgery to study the safety of NES by evaluating hemodynamic parameters and the presence of arrhythmias. These authors did not observe changes in the evaluated parameters, which suggests that NES does not increase cardiac workload and is a safe intervention in these patients. In the present study, there was no statistically and clinically relevant difference in HR when comparing pre- and post-TEDS moments. Even considering that the increase in transpulmonary pressure caused by IMV and muscle contractions affects cardiac output, right ventricular afterload and left ventricular preload, the TEDS in our study was not able to change HR. This can be explained at least in part by the fact that we have adjusted the sensitivity of the mechanical ventilator, preventing its triggering [21].

One of the concerns with the use of TEDS is the occurrence of adverse effects, including skin reactions. Evaluating critically ill patients, Segers et al. [20] did not observe a significant change in the studied variables (BP, HR and RR), and only hyperemia occurred in 50% of the patients immediately after the removal of the electrodes, which gradually disappeared. Our study did not find adverse events related to TEDS in the integumentary system, although the procedure lasted a short time. Also regarding concerns about side effects, Parry et al. [22] used some parameters as safety cut-offs to determine when to start or stop NES. These authors did not observe serious adverse effects, corroborating the findings of the present study that used some of their cut-off points.

Although there are still few studies on TEDS, this technique has been used in the clinical practice of intensive physical therapy because it has shown promise in improving respiratory muscle strength [23–26]. Even with the physiological decline of the respiratory system resulting from aging, training with TEDS can be an effective tool in respiratory physiotherapy, promoting an increase in diaphragm muscle strength in elderly people [25]. The present study showed that TEDS did not significantly alter the hemodynamic parameters of this population, which reinforces its applicability in the ICU, given the influence of the procedure on the motor units of the diaphragm that produce involuntary stimuli to the muscle and prevent autophagy and disuse atrophy. A recent systematic review [27] showed that the application of TEDS promotes an increase in respiratory muscle strength in individuals with COPD, elderly individuals, healthy women, and patients in the postoperative period of myocardial revascularization surgery.

Interestingly, a recent study conducted by Duarte et al. [28] suggest that TEDS influences the duration of IMV as well as the length of stay in ICU in patients with spinal cord injury (SCI). Unlike the retrospective case series evaluated by these authors (n = 10), our study is an experimental clinical trial that evaluated the influence of TEDS on the immediate hemodynamic responses to determine the safety of the procedure in critically ill elderly (and not just in patients with SCI). Additionally, Duarte et al. [28] proposed the comparison between the TEDS and the standard weaning protocol in neurological patients who were already able to voluntarily contract their respiratory muscles. On the contrary, we analysed the application of TEDS in patients initially without ventilatory drive, which allows the emergence of new evidence to assess the impact of TEDS earlier. This is important because critical patients newly admitted to the ICU are submitted to the administration of sedoanalgesia, which justifies the decrease in the ventilatory drive and contributes to ICU-AW [29].

Immobility associated with IMV is one of the main factors involved in the development of ICU-AW and is a predictor of mortality, especially in the elderly population. Muscle strength can be lost at a rate of 10-15% per week of disuse. The combination of 18-69 hours of diaphragm inactivity and IMV is associated with marked atrophy of both slow- and fast-twitch fibers [30]. Kress et al. [30] suggest that increased proteolysis, which is responsible for fiber atrophy, can be attenuated and thus improve the outcomes of this specific population. These data demonstrate the importance of measures to prevent the consequences of inactivity, such as the intervention proposed in our study. We believe that ICU-AW-preventive measures in elderly patients, such as TEDS, can become part of the routine of ICUs to forestall unfavorable outcomes in this population.

The main limitations were the fact that the procedure was applied only once, the lack of a control group, and the lack of assessment of the effect of the technique on the diaphragm muscle strength. Although no significant difference was found in the variables studied before and after the procedure, the small sample and the different clinical conditions of hospitalization should be highlighted; these are limiting factors for predicting the safety of the TEDS in critically ill elderly patients. In addition, given our use of a single evaluation step, it was not possible to identify the medium- or long-term effects of the intervention. Despite these limitations, we believe that this study can serve as a starting point for controlled and randomized clinical trials that can deepen our knowledge about TEDS.

5. **CONCLUSIONS**

TEDS did not promote clinically relevant impacts in hemodynamic or vital parameters when comparing the pre- and postintervention time points in critically ill elderly patients. These findings point to a possible safety in the application of the TEDS in this population.

FUNDING STATEMENT

This study was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) [grant numbers 407138/2018-8 and 302215/2019-0], the Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ) [grant numbers #E-26/202.679/2018 and #E-26/010.002124/2019], and the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) [grant number Finance Code 001].

REFERENCES

1. Stevens RD, Marshall SA, Cornblath DR, et al., A framework for diagnosing and classifying intensive care unit-acquired weakness. Critical Care Medicine. 2009;37(10): 299–308.

2. Anekwe DE, Biswas S, Bussières A, Spahija J. Early rehabilitation reduces the likelihood of developing intensive care unit-acquired weakness: a systematic review and meta-analysis. Physiotherapy. 2020;107:1–10.

3. Dalton RE, Tripathi RS, Abel EE et al., Polyneuropathy and myopathy in the elderly. HSR Proceedings in Intensive Care and Cardiovascular Anesthesia. 2012; 4 (1):15–9.

4. Latronico N, Bolton C. Critical illness polyneuropathy and myopathy: a major cause of muscle weakness and paralysis. The Lancet Neurology. 2011; 10(10)931–41.

5. Levine S, Nguyen T, Taylor N, et al. Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans. The New England Journal of Medicine. 2008; 358(13): 1327–35.

6. Hussain SN, Mofarrahi M, Sigala I et al. Mechanical ventilation-induced diaphragm disuse in humans triggers autophagy. American Journal of Respiratory and Critical Care Medicine. 2010; 182(11):1377–86.

7. Van den Berg, M, Hoojiman PE, Beishuizen A, et al. Diaphragm atrofy and weakness in the absence of mitochondrial dysfunction in critically ill. American Journal of Respiratory and Critical Care Medicine. 2017; 196 (12):1544–58.

8. Desai SV, Law TJ, Needham DM., Long-term complications of critical care. Critical Care Medicine. 2011;39(2):371–9.

9. Radell PJ, Remahl S, Nichols DG, Eriksson LI. Effects of prolonged mechanical ventilation and inactivity on piglet diaphragm function. Intensive Care Medicine. 2002;28(3): 358–64.

10. Sassoon CS, Caiozzo VJ, Manka A, Sieck GC. Altered diaphragm contractile properties with controlled mechanical ventilation. Journal of Applied Physiology. 2002;92(6):.2585–95.

11. Matamis D, Soilemezi E, Tsagourias M, Akoumianaki E, Dimassi S, Boroli F et al. Sonographic evaluation of the diaphragm in critically ill patients: technique and clinical applications. Intensive Care Medicine. 2013; 39(5):801–810.

12. Cancelliero KM, Ike D, Pantoni CBF, Mendes RG, Borghi-Silva A, Costa D. Acute effects of transcutaneous electrical diaphragmatic stimulation on respiratory pattern in COPD patients: cross-sectional and comparative clinical trial. Brazilian Journal of Physical Therapy. 2013;17(6):547–55.

13. Geddes LA, Voorhees WD, Bouland JD. Optimum stimulus frequency for contracting the inspiratory muscle with chest-surface electrodes to produce artificial respiration. Annals of Biomedical Engineering. 1990;18(1):103–8.

14. Cancelliero KM, Ike D, Sampaio LMM, Santos VLA, Stirbulov R, Costa D, Transcutaneous electrical diaphragmatic stimulation (TEDS) for the respiratory muscle strengthening: randomized and controlled clinical study. Fisioterapia e Pesquisa.2012;19(4):303–8.

15. Carvalho VO, Roque JM, Bocchi EA, Ciolac EG, Guimarães GV. Hemodynamic response in one session of strength exercise with and without electrostimulation in heart failure patients: a randomized controlled trial. Cardiology Journal. 2011;18(1):39–46.

16. Gerovasili V, Tripodaki E, Karatzano E et al. Short-term systemic effect of electrical muscle stimulation in critically ill patients. Chest. 2009;136(5):1249–56.

17. Sachetti A, Carpes MF, Dias AS, Sbruzzi G. Safety of neuromuscular electrical stimulation among critically ill patients: systematic review. Revista Brasileira de Terapia Intensiva. 2018;30(2):219–25.

18. Akar O; Günay E, Ulasli SS et al., “Efficacy of neuromuscular electrical stimulation in patients with COPD followed in intensive care unit. Clinical Respiratory Journal. 2017;11 (6):743–50.

19. Iwatsu K, Yamada S, Iida Y et al. Feasibility of neuromuscular electrical stimulation immediately after cardiovascular surgery. Archives of Physical Medicine and Rehabilitation. 2015;96(1):63–8.

20. Segers J, Hermans G, Bruyninckx F, Meyfroidt G, Langer D, Gosselink R. Feasibility of neuromuscular electrical stimulation in critically ill patients. Journal of Critical Care. 2014; 29(6):1082–8.

21. Sassoon CS. Triggering of the ventilator in patient-ventilator interactions. Respiratory Care. 2011;56(1):39–51.

22. Parry SM, Berney S, Warrillow S et al. Functional electrical stimulation with cycling in the critically ill: a pilot case-matched control study. Journal of Critical Care, 2014;29(4): 695.

23. Maynard LG, Barreto AS, Santana-Filho VJ, Cerqueira Neto ML, Dias DPM, Silva-Júnior VM. Effects of transcutaneous electrical diaphragmatic stimulation on the cardiac autonomic balance in healthy individuals: a randomized clinical trial. Fisioterapia e Pesquisa. 2016;23(3):248–56

24. Tanaka S., Masuda T, Kamiya k et al. A single session of neuromuscular electrical stimulation enhances vascular endothelial function and peripheral blood circulation in patients with acute myocardial infarction. International Heart Journal. 2016; 57(6):676–681.

25. Santos LA, BorgiBJR, Daister JLN, Pazzinotto-Forti EM. Diaphragmatic effects of the transcutaneous electrical stimulation on the pulmonary function. Revista Brasileira de Geriatria e Gerontologia. 2013;16(3):495–502.

26. Cerqueira TCF, Cerqueira Neto ML, Carvalho AJG et al. Neuromuscular electrical stimulation on hemodynamic and respiratory response in patients submitted to cardiac surgery: pilot randomized clinical trial. International Journal of Cardiovascular Sciences. 2019;32(5): 483–489.

27. Ferreira LL, Mello JRC, Brito MVC, Cavenaghi OM. Effectiveness of transcutaneous electrical diaphragmatic stimulation on respiratory muscle strength, lung volumes and capacities: a systematic review. Medicina. 2015;48(5): 491–500.

28. Duarte GL, Bethiol AL, Ratt LSR, Franco G, Moreno R, Tonella RM et al. Transcutaneous electrical diaphragmatic stimulation reduces the duration of invasive mechanical ventilation in patients with cervical spinal cord injury: retrospective case series. Spinal Cord Series and Cases. 2021;7(1):26.

29. Farhan H, Moreno-Duarte I, Latronico N, Zafonte R, Eikermann Met al. Acquired Muscle Weakness in the Surgical Intensive Care Unit: Nosology, Epidemiology, Diagnosis, and Prevention. Anesthesiology. 2016;124(1): 207–234.

30. Kress JP, Hall JB. ICU-acquired weakness and recovery from critical illness. The New England Journal of Medicine. 2014; 370(17):1626–1635.

4.2 **Artigo 2 - Effects of transcutaneous electrical diaphragmatic stimulation on respiratory muscle and the duration of mechanical ventilation in critically ill elderly patients: a randomized controlled clinical trial**

Effects of Transcutaneous Electrical Diaphragmatic Stimulation on Respiratory Muscle and the Duration of Mechanical Ventilation in Critically ill Elderly Patients: a Randomized Controlled Clinical Trial

Running Head: Transcutaneous diaphragmatic stimulation in critically ill elderly

Running Head: Transcutaneous diaphragmatic stimulation in critically ill elderly

Author names and affiliations:

Hebert Olímpio Júnior,[1] Gustavo Bittencourt Camilo,[1,2] Júlia Abrantes Marques,[3] Agnaldo José Lopes,[1,4]

[1]Post-Graduation Programme in Medical Sciences, School of Medical Sciences, Universidade do Estado do Rio de Janeiro (UERJ), Rio de Janeiro, Brazil

[2]Faculdade de Ciências Médicas e da Saúde de Juiz de Fora (SUPREMA), Minas Gerais, Brazil

[3]Fundação Presidente Antônio Carlos de Ubá, Minas Gerais, Brazil

[4]Rehabilitation Sciences Post-Graduation Programme, Centro Universitario Augusto Motta (UNISUAM), Rio de Janeiro, Brazil

E-mail: agnaldolopes.uerj@gmail.com

E-mail address of each author

Hebert Olímpio Júnior – hebertojr@hotmail.com

Gustavo Bittencourt Camilo – gustavoscamilo@gmail.com

Júlia Abrantes Marques – julia_abrantes18@hotmail.com

Agnaldo José Lopes – agnaldolopes.uerj@gmail.com

Correspondence: Agnaldo J. Lopes, Rehabilitation Sciences Post-Graduation Program, Augusto Motta University Centre (UNISUAM), Rua Dona Isabel, 94, Bonsucesso, 21032-060, Rio de Janeiro, Brazil. Tel. and fax: +55 21 21 2576 2030. E-mail address: agnaldolopes.uerj@gmail.com

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

FUNDING STATEMENT

The authors wish to thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico [CNPq; Grant number #301967/2022-9], Brazil, the Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro [FAPERJ; Grant numbers #E-26/211.024/2019, #E-26/211.187/2021, #E-26/211.104/2021, and #E-26/200.929/2022], Brazil, and the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior [CAPES, Finance Code 001, 88881.708719/2022-01, and 88887.708718/2022-00], Brazil.

CONFLICT OF INTEREST DISCLOSURE

The authors declare no conflict of interest.

ETHICS APPROVAL STATEMENT

This study was approved by the Research Ethics Committee of the Faculty of Medical and Health Sciences of Juiz de Fora (SUPREMA) under the number CAAE-87664318.2.0000.5103.

PATIENT CONSENT STATEMENT

All participants signed an informed consent form.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

Not applicable.

STUDY REGISTRATION

This study was registered with the ClinicalTrials.gov identifier code NCT04565002.

ABSTRACT

Background and Objectives: Elderly patients under invasive mechanical ventilation (IMV) are more susceptible to muscle weakness. In these individuals, there is diaphragmatic dysfunction (DD) with impairment in the biomechanical characteristics of the muscle due to disuse. Thus, interventions aimed at the management of DD are essential to alleviate this condition. In the out-of-hospital environment, there are benefits to transcutaneous electrical diaphragmatic stimulation (TEDS), which is an easy-to-apply and low-cost technique. We aimed to evaluate the influence of TEDS on respiratory muscle strength, diaphragm thickness (DT), and IMV time in critically ill elderly patients. **Methods:** This was a randomized controlled clinical trial in which patients were divided into an experimental group (EG) (*n*=21) and a control group (CG) (*n*=23). TEDS started 24 h after orotracheal intubation and lasted until the end of weaning. Both groups underwent the following assessments during the spontaneous breathing test after weaning from mechanical ventilation: measurement of respiratory muscle strength by pressure gauge, analysis of DT by lung ultrasound, and extubation failure prevention checklist. **Results:** There were 23 participants in the EG and 21 in the CG. The mean values of the diaphragmatic thickening index in the EG and CG participants were 99.13 ± 26.75 and 66.88 ± 31.77, respectively (p=0.001). The median value of maximum inspiratory pressure in EG and CG participants was 22 (17–28) and 18 (16–30) cmH_2O, respectively (p=0.005). The Tobin index and the integrative weaning index did not show a significant difference (p=0.584 and p=0.102, respectively). The duration of mechanical ventilation in the EG and CG was 6.28 ± 2.68 and 9.21 ± 2.76 days, respectively (p=0.001). **Conclusions:** TEDS shortened mechanical ventilation time, improved inspiratory muscle strength, and increased DT in critically ill elderly patients. TEDS may be a promising tool making DD milder and accelerating hospital discharge in this population.

Keywords: Ageing; Intensive care, Pulmonary rehabilitation, Musculoskeletal

1 INTRODUCTION

Patients undergoing invasive mechanical ventilation (IMV) are at high risk of developing muscle weakness in the first hours after orotracheal intubation, as they are exposed to several factors for muscle damage, including sedation, immobility, and controlled ventilation (Demoule et al., 2016). Elderly patients on IMV deserve attention because, as our life expectancy has gone up, the elderly population has considerably increased, resulting in a higher incidence of admissions of elderly people to intensive care units (ICUs) (Pacifico et al., 2022; Cederwall et al., 2021). Among the muscles affected by prolonged IMV, the diaphragm stands out because it shows a progressive reduction in its ability to generate tension by atrophy of the muscle fibers, causing diaphragm dysfunction (DD) (Radell et al., 2002).

Considering the progressive characteristics of DD, some consequences, such as increased time on IMV, increased risk of respiratory complications, and longer hospitalization, may be observed it is not counteracted (Sassoon et al., 1985; Matamis et al., 2013). One of the most recent indices to predict the outcome after weaning from ventilation is the integrative weaning index (IWI), which incorporates respiratory mechanics, oxygenation, and breathing pattern and has a sensitivity of 99% and specificity of 86% to predict the weaning outcome of patients on mechanical ventilation (Ebrahimabadi et al., 2017). This indicator may be a more objective index than conventional methods because it evaluates both the function of the cardiovascular system and respiratory compliance (Ebrahimabadi et al., 2017).

The evaluation of the degree of DD can be performed using instruments that measure inspiratory muscle strength, such as a pressure gauge, in addition to imaging tests that demonstrate the diaphragm thickness (DT), such as diaphragmatic ultrasound (DUS) (American Thoracic Society/European Respiratory Society, 2002; Umbrello et al., 2015). DUS has been increasingly incorporated into ICUs because it is a simple, safe, low-cost procedure that does not use ionizing radiation and provides relevant information on the respiratory system (Demi et al., 2014). The variable related to inspiratory muscle strength in manovacuometry is the maximum inspiratory pressure (MIP), while the DT is determined by DUS and represented by diaphragm thickness index (DTI), which contributes to the initial diagnosis of DD and is also relevant in the follow-up of diaphragm function during hospitalization and weaning (Ferrari et al., 2014; Kim et al., 2017). Low DTI is associated with impaired diaphragmatic function and is associated with low MIP values in critically ill patients (Goligher et al., 2015).

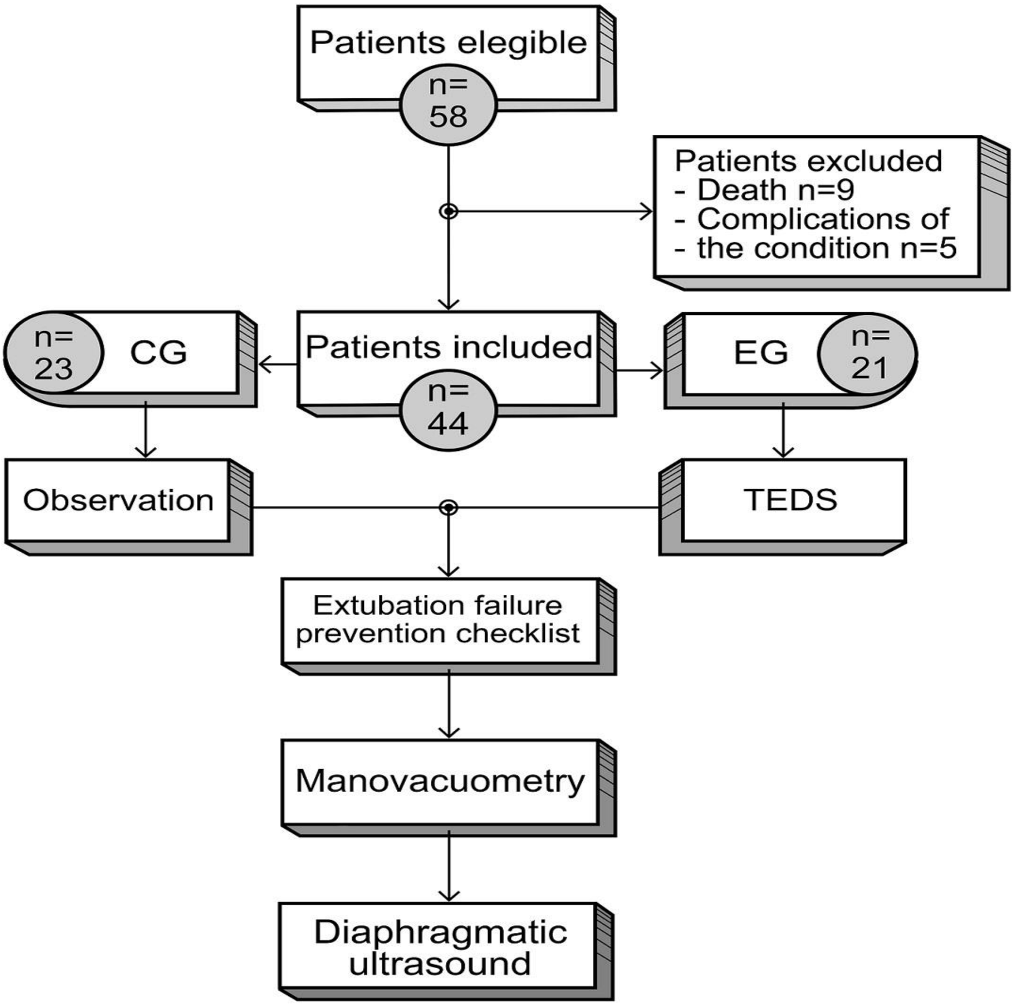
After obtaining the variables related to the function of the diaphragm, measures aimed at the prevention or treatment of DD are important to reduce any damage to critically ill patients. In the context of outpatient pulmonary rehabilitation, positive effects were demonstrated with the use of electrotherapy, specifically transcutaneous electrical diaphragmatic stimulation (TEDS), in patients with chronic obstructive pulmonary disease (COPD) (Cancelliero et al., 2013). This technique consists of placing electrodes on the skin near the motor points of the diaphragm, transmitting an intermittent current and generating action potentials capable of inducing muscle contractions (Cancelliero et al., 2012). However, there is still no evidence of the use of TEDS on the DTI of critically ill elderly patients or of the repercussions of TEDS on the duration of mechanical ventilation and hospital stay in this population. Given the practicality and low cost of TEDS, we aimed to evaluate the effect of TEDS on respiratory muscle strength, DT, and mechanical ventilation time in critically ill patients in the ICU.

2 MATERIALS AND METHODS

2.1. Study design, participants, and ethics

This was a randomized controlled trial with 44 patients (out of 58 eligible patients) admitted to the ICUs of Hospital e Maternidade Therezinha de Jesus and Hospital Monte Sinai, Juiz de Fora, Brazil. Patients of both sexes, aged ≥60 years, who were on IMV for at least 24 h were included. Exclusion criteria: severe neurological lesions that could prevent weaning from ventilation; recent surgical scar and/or open lesions in the regions where the electrodes were placed; severe hemodynamic instability; asynchrony with the mechanical ventilator; hypoglycemia; cardiac pacemaker; undrained pneumothorax; use of vasoactive drugs in ascending doses; use of neuromuscular blockers during the intervention; and chronic use of corticosteroids. The participants were allocated through a virtual research randomizer tool into an experimental group (EG) to undergo TEDS (n=22) and a control group (CG) (n=22). The two groups underwent the same evaluations during the spontaneous breathing test after weaning from IMV (Fig. 1).

Figure 1 – Data collection flowchart. Abbreviations: CG, control group; EG, experimental group; TEDS, transcutaneous electrical diaphragmatic stimulation



The protocol was approved by the research ethics committee of our institution under protocol number 2,739,692, and informed consent was obtained from legal representatives of the patients. The protocol was registered on ClinicalTrials.gov under the number NCT04565002.

The sample size needed was calculated using MedCalc 8.2 software (MedCalc Software Mariakerke, Belgium). The DTI variable was used as a basis, whose mean value used for the calculation was based on previous studies (Goligher et al., 2015; Ferrari et al., 2014). Therefore, considering $\alpha = 5\%$, $\beta = 30\%$, and a 95% confidence interval equal to $\pm 5\%$, the minimum sample size would be 20 participants in each group.

2.2 **Intervention**

TEDS was initiated immediately after the 24-hour period on IMV, twice a day, lasting 30 minutes with a 6-hour interval between applications. Initially, TEDS was performed with the patient in assisted-controlled ventilation and well adapted to ventilation. The sensitivity parameter was adjusted so that the contractions produced by electrical stimulation did not trigger the mechanical ventilator, thus preventing episodes of asynchrony. After discontinuation of sedative drugs and resumption of ventilatory drive, TEDS continued to be applied until extubation in spontaneous ventilatory mode, but with sensitivity readjusted to the standard values for the prevention of muscle fatigue. The TEDS protocol consisted of the following parameters: frequency of 30 Hz; pulse width of 0.4 ms; respiratory rate of 15 bpm; holding time of 1 sec; rise time of 1 sec; descent time of 2 sec; and time without stimulation of 2 sec (Geddes et al., 1990). Phrenics equipment (Dualpex 961, Quark®, São Paulo, Brazil) was used. Two electrodes were placed in the right and left paraxiphoid region, respectively, and another two electrodes were placed in the direction of the axillary midline over the seventh intercostal space, also on the right and left sides (Cancelliero et al., 2012).

2.2 **Measurements**

The hemodynamic and ventilatory parameters were obtained from the medical records and at the bedside by analyzing the mechanical ventilator and the patient monitor. We evaluated the Tobin index and the IWI, which is calculated from basic parameters such as lung capacity, arterial oxygen saturation (SaO_2), respiratory rate, and tidal volume.

The MIP measurement was performed using a pressure gauge (M120, Murenas, São Paulo, Brazil) following previous recommendations (American Thoracic Society/European Respiratory Society, 2002). The measurement was performed with the patient in a sitting position and with the headboard elevated by 90°. The patient performed a maximum inspiration starting from the residual volume until reaching the total lung capacity (TLC). The procedure was performed three times, with a 2-min interval between repetitions to prevent muscle fatigue, and the MIP measure considered was the highest recorded.

DUS was performed with portable equipment (Logiq- $_E$ GE 2014, Contagem, Brazil). During the examination, the patients remained in the supine position, and a linear transducer was used to evaluate the superficial structures and a cardiac transducer to evaluate the deep structures. Eight zones were evaluated, with scanning of four areas per hemithorax: zones 1 and 2 were the upper and lower anterior chest walls, respectively, and zones 3 and 4 were the upper and lower lateral chest walls (Volpicelli et al., 2012; Gargani et al., 2014). The DTI was calculated as the difference between DT at TLC (DT_{TLC}) and functional residual capacity (DT_{FRC}), divided by DT_{FRC} (Ferrari et al., 2014; Kim et al., 2017).

2.3 **Statistical analysis**

To verify the distribution of the data, the Shapiro–Wilk test was performed. The results are expressed as measures of central tendency and dispersion suitable for numerical data and as frequency and percentage for categorical data. Numerical variables were compared by Student's t test for independent samples or the Mann–Whitney test. Categorical variables were compared using the chi-squared test or Fisher's exact test. The software used was SPSS version 22, and the significance level was set at 0.05.

3 **RESULTS**

Of the 58 patients evaluated for inclusion, eight were excluded for the following reasons: death (*n*=9) and clinical complications such as respiratory failure and hemodynamic instability that were not reversed with short-term approaches (*n*=5). The sample therefore consisted of 44 patients, 28 of whom were female, with a mean age of 66 (60–79) years. The main clinical conditions that led to ICU admission were sepsis (*n*=12, 27.27%) and cardiovascular diseases (*n*=11, 25%).

Of the total sample, 21 and 23 participants were allocated to the EG and CG, respectively. The EG had 61.90% women, and the CG had 65.22% women (p = 0.82). The mean body weight of the EG and CG was 62.90 ± 10.66 and 62.73 kg ± 13.70, respectively (*p*=0.96). There was no significant difference between the two groups in the clinical conditions of hospitalization (Table 1).

Table 1 – Sample characteristics considering the experimental and control groups

Variable	**Experimental group (*n*=21)**	**Control group (*n*=23)**	***p*-value**
Demographic data			
Age (years)	69 (60–86)	66 (60–79)	0.96
Female/male	13/8	15/8	0.82
Body composition			
Weight (kg)	62.90 ± 10.66	62.73 ± 13.70	0.96
Clinical conditions of hospitalization			
Cardiovascular conditions	7 (33.33%)	4 (17.39%)	0.22
Respiratory conditions	4 (19.05%)	3 (13.04%)	0.44
Postoperative orthopedic surgeries	3 (14.29%)	2 (8.70%)	0.45
Postoperative abdominal surgeries	1 (4.76%)	2 (8.70%)	0.53
Hepatical cirrhosis	0 (0%)	3 (13.04%)	0.13
Exogenous intoxication	1 (4.76%)	2 (8.70%)	0.53
Sepsis	5 (23.81%)	7 (30.43%)	0.62

The values shown are the mean ± SD, median (minimum-maximum) or number (%)

DT, respiratory muscle strength, predictive indices of weaning, and duration of mechanical ventilation are compared between groups in Table 2. The mean DTI in the EG and CG participants was 99.13 ± 26.75 and 66.88 ± 31.77, respectively (*p*=0.001). The median MIP in the EG and CG participants was 22 (17–28) and 18 (16–30), respectively (*p* = 0.005). The Tobin index and IWI did not show significant differences (*p*=0.584 and *p* = 0.102). The duration of mechanical ventilation in the EG and CG was 6.28 ± 2.68 and 9.21 ± 2.76 days, respectively (p=0.001).

Table 2 – Comparisons between diaphragm thickness values, respiratory muscle strength, predictive weaning indexes and duration of mechanical ventilation between groups

Variable	**Experimental group (*n*=23)**	**Control group (*n*=21)**	***p*-value**
DTI	99.13 ± 26.75	66.88 ± 31.77	0.001
MIP (cm H_2O)	22 (17–28)	18 (16–30)	0.005
Tobin index	50.16 ± 16.89	53.21 ± 19.59	0.584
IWI	60.72 (58.46)	67.87 (52.63)	0.102
Duration of mechanical ventilation (days)	6.28 ± 2.68	9.21 ± 2.76	0.001

Abbreviations: DTI, diaphragm thickening index; MIP, maximum inspiratory pressure; IWI, integrative weaning index. The values shown are the mean ± SD and median (minimum-maximum).

4 DISCUSSION

In the present study, the main findings observed were that, after the application of TEDS in elderly patients on IMV, DTI and MIP increased. The Tobin and IWI predictive indices of weaning were not changed significantly by the application of TEDS. Furthermore, the duration of mechanical ventilation was significantly reduced by TEDS. To our knowledge, no studies have evaluated the application of TEDS in critically ill elderly individuals.

Critically ill patients who develop significant loss of DT have long stays in the ICU (Moury et al., 2019; Grassi et al., 2020). Grosu et al. (2017) found that patients on mechanical ventilation begin to develop diaphragmatic thinning soon after intubation, observed in 84% of individuals 72 h after initiation of mechanical ventilation. Soták et al. (2021) reported that ICU patients who received phrenic nerve stimulation during mechanical ventilation exhibited an increase in DT, whereas mechanically ventilated patients who did not receive stimulation experienced a corresponding decrease in thickness. These findings are in agreement with our results, as mechanical ventilation affects diaphragmatic function, resulting in atrophy, muscle damage, decreased strength, and dysfunction of diaphragmatic contraction. In the present study, DTI significantly increased after the application of TEDS. It is believed that external stimulation of the phrenic nerve through TEDS allows the involvement and recruitment of much larger muscle units of the diaphragm, leading to a more effective contraction than when the stimulus is induced without the resource, i.e., simply from the central nervous system. This rationale allows for the possibility of using TEDS for active diaphragmatic rehabilitation even in patients undergoing pressure support ventilation, i.e., those who are already in the process of weaning or who simply already have an indication for it.

MIP significantly improved after the application of TEDS. In line with our findings, Cancelliero et al. (2013) showed that TEDS promotes an increase in muscle strength in patients with COPD without interfering with spirometric parameters. Considering the muscle changes, the application of TEDS increases inspiratory muscle strength, possibly due to the relationship of changes in the muscle fiber type caused by electrical stimulation, with an increase in type II fibers and a reduction in type I fibers. Type II muscles are fast-twitch fibers that require firing and rigorous force and have a short duration. Bezerra et al. (2014) measured the MIP of elderly women with a manovacuometer before and after 12 weeks of yoga and saw a significant increase in MIP after the intervention. This effect may be an adaptation of the respiratory muscles to the training included in the program. In contrast, the population analyzed by Neder et al. (1999) presented MIP values below the predicted value, and age was the strongest negative correlate. The aging process is associated with a reduction in total, diaphragmatic, and respiratory accessory muscle mass, as well as a decline in work production for the same level of neural stimulation. With age, there is a slight reduction in TLC and a considerable increase in VR, resulting in lower MIP values.

We did not observe a significant change in the Tobin predictive weaning index after the application of TEDS. Cader et al. (2012) showed that the Tobin index has high sensitivity and low specificity, and even with successful extubation, the Tobin index was similar between our EG and CG. As a parameter for weaning from mechanical ventilation, Mantovani et al. (2007) found that the Tobin index is safe, well accepted by patients, and does not come with any complications, although their patients did not have previous respiratory failure or other serious conditions and were on mechanical ventilation because they underwent surgery under general anesthesia due to noninvasive disease. These authors reported that the Tobin index helped them perform extubation and predict clinical complications after extubation of patients undergoing general anesthesia.

We did not observe any significant change in IWI after the application of TEDS. Long-term intubation and mechanical ventilation increase the risk of morbidity and mortality due to complications such as ventilator-associated pneumonia and tracheal stenosis, which prolong ICU stays and increase health care costs. Therefore, efforts toward early identification of the appropriate time for weaning patients from mechanical ventilation are indicated to reduce exposure to these complications. El-Baradey et al. (2015) and Azeredo et al. (2017) analyzed the IWI's ability to predict failure or success in weaning in elderly ICU patients and noted that the measure was more accurate than all other indices they tested. Although there was no significant difference in IWI between the groups in our study, its application is important to support the extubation process. One of the reasons for this is the range of variables that have no direct relationship with the capacity for diaphragmatic contraction, such as SaO_2. Ebrahimabadi et al. (2017) and Huo et al. (2020) also used the IWI to predict the weaning outcome, and they concluded that their results and their proposed cutoff points were consistent and reliable, with high sensitivity and specificity.

Our study found a significantly shorter ventilation time after the application of TEDS. O'Rourke et al. (2020) showed that bilateral percutaneous placement of short-term, small-diameter multipolar electrical implants near the phrenic nerves in the neck region using ultrasound was a safe and feasible approach to stimulate the diaphragm. Stimulation of the phrenic nerve for 30 min per day at normal breathing settings for 8 months was shown to prevent atrophy of the diaphragm.

Duarte et al. (2021) trained patients' inspiratory muscles twice a day, 7 days a week, for a mean of 47 sessions per patient. Patients undergoing TEDS with a diagnosis of spinal cord injury spent considerably less time in the IMV and ICU than patients in the group that underwent a standard weaning protocol, which corroborates our findings. Additionally, it is necessary to consider that we evaluated elderly patients with comorbidities and clinical conditions different from those in the study by Duarte et al. (2021) and that the levels of muscle atrophy are also manifested differently. O'Rourke et al. (2020) and Duarte et al. (2021) suggest that muscle training through TEDS is a simple and low-cost intervention that leads to an increase in IPM, which is the gold standard for evaluating the strength of inspiratory muscles, especially the diaphragm. O'Rourke et al. (2020) observed an increase in tidal volumes as a consequence of phrenic nerve stimulation. These authors reported that the observed increase in DT resulting from TEDS strongly supports the efficacy of therapy to mitigate the development of ventilator-induced DD, as it may result in shorter weaning times and better measures of diaphragmatic strength.

4.1. **Study limitations**

The present study has some limitations. First, there was no separation of patients into subgroups by baseline conditions. The clinical conditions of mechanical ventilation are different when comparing a patient with sepsis and a patient in the postoperative period of orthopedic surgery, given that sepsis-induced acute lung injury is common in the ICU, with rapid deterioration and progression to discomfort syndrome respiratory disease and an extremely high mortality rate. Second, initial ultrasound was not performed to obtain a reference value of the diaphragm of each patient to make before-vs.-after-intervention comparisons. Third, IPM was not measured before the interventions to more accurately compare whether there was an increase in the inspiratory muscle strength of the EG patients as a result of the application of TEDS.

5 CONCLUSION AND IMPLICATIONS FOR PHYSIOTHERAPY PRACTICE

The application of TEDS causes an increase in the DT, in addition to improving inspiratory muscle strength and reducing the duration of mechanical ventilation. The IWI and Tobin weaning indices do not seem to be influenced by TEDS. Thus, the findings suggest that TEDS is a promising tool and support its use to mitigate the development of DD and accelerate hospital discharge in elderly patients on mechanical ventilation.

REFERENCES

American Thoracic Society/European Respiratory Society. ATS/ERS Statement on respiratory muscle training. *American Journal Critical Care Medicine*. 2002; *166*(4): 518-624. https://10.1164/rccm.166.4.518

Azeredo, L. M., Nemer, S. N., Barbas, C. S., Caldeira J. B., Noé, R., Guimarães B. L., … Caldas, C.P., (2015). The integrative weaning index in elderly ICU subjects. *Respiratory Care*, *62*(3), 333-339. https://10.4187/respcare.04524

Bezerra, L. A., Melo, H. F., Garay, A. P., Reis, V. M., Aidar, F. J., Bodas, A. R., … Oliveira, R.J. (2014). Do 12-week yoga program influence respiratory function of elderly women? *Journal of Human Kinetics*, *43*, 177-184. https://10.2478/hukin-2014-0103

Cader, S. A., Vale, R. G. S., Zamora, V. E., Costa, C. H., Dantas, E. H. M., (2012). Extubation process in bed-ridden elderly intensive care patients receiving inspiratory muscle training: a randomized clinical trial. *Clinical Interventions in Aging*, *7*, 437-443. https://10.2147/CIA.S36937

Cancelliero, K. M., Ike, D., Pantoni, C. B. F., Mendes, R. G., Borghi-Silva, A., & Costa, D., (2013). Acute effects of transcutaneous electrical diaphragmatic stimulation on respiratory pattern in COPD patients: cross-sectional and comparative clinical trial. *Brazilian Journal of Physical Therapy*, *17*(6), 547-555. https://10.1590/S1413-35552012005000121

Cancelliero, K. M., Ike, D., Sampaio, L. M. M., Santos, V. L. A., Stirbulov, R., & Costa, D. (2012). Estimulação diafragmática elétrica transcutânea (EDET) para fortalecimento muscular respiratório. *Brazilian Journal of Physical Therapy, 17*(6), 547-555. https://10.1590/S1809-29502012000400002
Cederwall, C.J., Naredi, S., Olausson, S., Rose, L., & Ringdal, M. (2021). Prevalence and use of intensive care beds in individuals on prolonged mechanical ventilation in Swedish ICUs. *Breath Care*, *66*(2), 300-306. https://10.4187/respcare.08117

Demi, L., Demi, M., Smargiassi, A., Inchingolo, R., Faita, F., & Soldati, G. (2014). Ultrasonography in lung pathologies: new perspectives. *Multidisciplinary Respiratory Medicine*, *9*(1), 27. https://10.1186/2049-6958-9-27

Demoule, A., Molinari, N., Jung, B., Prodanovic, H., Chanques, G., Matecki, S., … Jaber, S. (2016). Patterns of diaphragm function in critically ill patients receiving prolonged mechanical ventilation: a prospective longitudinal study. *Annals Intensive Care*, 6(1), 75. https://10.1186/s13613-016-0179-8

Duarte, G. L., Bethiol, A. L., Ratti, L. D. S. R., Franco, G. Moreno, R., Tonella, R. M., & Falcão, A. L. E. (2021). Transcutaneous electrical diaphragmatic stimulation reduces the duration of invasive mechanical ventilation in patients with cervical spinal cord injury: retrospective case series. *Spinal Cord Series and Cases*, *7*(1), 1-6. https://10.1038/s41394-021-00396-4

Ebrahimabadi, S., Moghadam, A. B., Vakili, M., Modanloo, M., & Khoddam, H. (2017). Studying the Power of the Integrative Weaning Index in Predicting the Success Rate of the Spontaneous Breathing Trial in Patients under Mechanical Ventilation. *Indian Journal of Critical Care Medicine*, *21*(8), 488-493. https://10.4103/ijccm.IJCCM_10_17

El-Baradey, G. F., El-Shmaa, N. S., & Ganna, S. A. (2015). Can integrative weaning index be a routine predictor for weaning success? *Indian Journal of Critical Care Medicine*, *19*(12), 703-707. https://10.4103/0972-5229.171352

Ferrari, G., De Filippi, G., Elia, F., Panero, F., Volpicelli, G., & Apra, F. (2014). Diaphragm ultrasound as a new index of discontinuation from mechanical ventilation. *Critical Ultrasound Journal*, *6*(1), 8. https://10.1186/2036-7902-6-8

Gargani, L., & Volpicelli, G., (2014). How I do it: lung ultrasound. *Cardiovascular Ultrasound, 12*(25), 1-10. https://10.1186/1476-7120-12-25

Geddes, L. A., Voorhees, W. D., & Bouland, J. D. (1990). Optimum stimulus frequency for contracting the inspiratory muscle with chest-surface electrodes to produce artificial respiration. *Annals of Biomedical Engineering*, *18*(1), 103-108. https://10.1007/BF02368420

Goligher, E. C., Fan, E., Herridge, M.S., Murray, A., Vorona, S., Brace, D., … Ferguson, N.D. (2015). Evolution of diaphragm thickness during mechanical ventilation: impact of inspiratory effort. *American Journal Respiratory Critical Care Medicine,* 192(9), 1080-1088. https://10.1164/rccm.201503-0620OC

Grassi, A., Ferlica, D., Lupieri, E., Calcinati, S., Francesconi, S., Sala, V., … Giacomo, B. (2020). Assisted mechanical ventilation promotes recovery of diaphragmatic thickness in critically ill patients: a prospective observational study. *Critical Care*, *24*(1), 1-12. https://10.1186/s13054-020-2761-6

Grosu, H. B., Ost, D. E., Lee, Y. I., Song, J., Li, L. Eden, E., … Rose, K. (2017). Diaphragm Muscle Thinning in Subjects Receiving Mechanical Ventilation and Its Effect on Extubation. *Respiratory Care*, *62*(7), 904-911. https://10.4187/respcare.05370

Huo, Y., Guo, S., Zhang, K., Zhang, T., Li, B., Zhang, Q., Hu, Z. (2020). A clinical study on the ability of the integrative weaning index to predict weaning from mechanical ventilation. *Annals of Palliative Medicine, 9*(5), 3162-3169. https://10.21037/apm-20-1335

Kim, W. Y., & Lim, C. M. (2017). Ventilator-Induced Diaphragmatic Dysfunction: Diagnosis and Role of Pharmacological Agents. *Respiratory Care*, *2*(11), 1485-1491. https://10.4187/respcare.05622

Mantovani, C., Zuliani, L. M., Sano, D. T., Waisberg, D. R., Silva, I. F., & Waisberg, J. (2007). Evaluating the use of the tobin index when weaning patients from mechanical ventilation after general anesthesia. *Revista Brasileira de Anestesiologia*, *57*(6), 592-605. https://10.1590/s0034-70942007000600002

Matamis, D., Soilemezi, E., Tsagourias, M., Akoumianaki, E., Dimassi, S., Boroli, F., … Brochard, L. (2013). Sonographic evaluation of the diaphragm in critically ill patients. Technique and clinical applications. *Intensive Care Medicine*, *192*(9), 1080-1088. https://10.1007/s00134-013-2823-1

Moury, P. H., Cuisiner, A., Durand, M., Bosson, J.L., Chavanon, O., Payen, J. F., … Albaladejo, P. (2019). Diaphragm thickening in cardiac surgery: a perioperative prospective ultrasound study. *Annals of Intensive Care, 9*(1), 1-11. https://10.1186/s13613-019-0521-z

Neder, J. A., Andreoni, S., Lerario, M. C., & Nery, L. E. (1999). Reference values for lung function tests II: maximal respiratory pressures and voluntary ventilation. *Brazilian Journal of Medical and Biological Research*, *32*(6), 719-727. https://10.1590/S0100-879X1999000600007

O'Rourke, J., Soták, M., Curleu, G.F., Doolan, A., Henlin, T, Mullins, G., … Ranieri, M.V. (2020). Initial Assessment of the Percutaneous Electrical Phrenic Nerve Stimulation System in Patients on Mechanical Ventilation. *Critical Care Medicine*, *48*(5), e362-e370. https://10.1097/CCM.0000000000004256

Pacifico, A. A. C. P., Feitosa, E. S. C., Parnaiba, A. L. S., Aquino, P. L., Cavalcante, A. A., Bezerra, T. S, … Carneiro, S. L. (2022). Descriptive and temporal analysis of the mortality rate and average hospital stay due to burns and corrosion in the elderly in Brazil between 2010 and 2019. *Revista Brasileira de Cirurgia Plastica*, *37*(2), 194-198. https://10.5935/2177-1235.2022RBCP0032

Radell, P. J., Remahl, S., Nichols, D. G., & Eriksson, L. I. (2002). Effects of prolonged mechanical ventilation and inactivity on piglet diaphragm function. *Intensive Care Medicine*, *28*(3), 358-364. https://10.1007/s00134-002-1207-8

Sassoon, C. S., Caiozzo, V. J., Manka, A., & Sieck, G. C. (1985). Altered diaphragm contractile properties with controlled mechanical ventilation. *Journal of Applied Physiology*, *92*(6), 2585-2595. https://10.1152/japplphysiol.01213.2001

Soták, M., Roubik, K., Henlin, T., & Tyll, T., (2021). Phrenic nerve stimulation prevents diaphragm atrophy in patients with respiratory failure on mechanical ventilation. *BMC Pulmonary Medicine*, *21*(1), 1-8. https://10.1186/s12890-021-01677-2

Volpicelli, G., Elbarbary, M., Blaivas, M., Lichtenstein, D.A., Mathis, G., Kirkpatrick, A.W., … Petrovic, T. (2012). International evidence-based recommendations for point-of-care lung ultrasound. *Intensive Care Medicine*, *38*(4), 577-591. https://10.1007/s00134-012-2513-4

Umbrello, M., Formenti, P., Longhi, D., Galimberti, A., Piva, I., Pezzi, A. Iapichino, G. (2015). Diaphragm ultrasound as indicator of respiratory effort in critically ill patients undergoing assisted mechanical ventilation: a pilot clinical study. *Critical Care*, *19*(1), 161. https://10.1186/s13054-015-0894-9

CONSIDERAÇÕES FINAIS

Inúmeras são as alterações no sistema respiratório de pacientes idosos submetidos à VMI. Dentre os músculos respiratórios afetados, destaca-se o diafragma por ser o principal músculo responsável pelo aumento do diâmetro céfalo-caudal da caixa torácica, o que permite a entrada de ar nos pulmões pela inspiração. Além das já estudadas modificações no sistema respiratório, os estudos evidenciaram alterações no IED e na Pimáx.

A EDET possibilitou a obtenção de resultados que evidenciaram sua importância na força muscular inspiratória e espessura do diafragma, com rigor metodológico até então não encontrado em outras evidências com tema semelhante. A partir desses achados, pode-se pensar em incluir a EDET na rotina de tratamento do paciente idoso crítico submetido à VMI, considerando também seu baixo risco hemodinâmico encontrado.

A EDET representa uma abordagem promissora para a manutenção das fibras do diafragma e pode oferecer uma opção futura para prevenir ou mesmo tratar a DD induzida pelo ventilador mecânico. No entanto, é possível reconhecer que esse recurso constitui apenas uma técnica no processo de tratamento, e que outras ferramentas devem ser exploradas em conjunto.

REFERÊNCIAS

AMERICAN THORACIC SOCIETY; EUROPEAN RESPIRATORY SOCIETY. Statement on respiratory muscle testing. *Am J Respir Crit Care Med*. 2002;166(4):518-624.

AZEREDO, L. M. et al.The Integrative Weaning Index in Elderly ICU Subjects. *Respir Care*., v.62, n.3, 333-339, 2017.

BALAHURA, A. M. et al. Pulmonary thromboembolism in an emergency hospital: Are our patients different? *Rom J Intern Med.*, v.55, n.4, p.237-244, 2017.

BEZERRA, L. A. et al.O programa de yoga de 12 semanas influencia a função respiratória das mulheres idosas? *J Hum Kinet*., v.43, p.177-84, 2014.

BOUZA, C.; MARTÍNEZ-ALÉS, G.; LÓPEZ-CUADRADO, T. Recent trends in invasive mechanical ventilation in the elderly: a population-based national study. *Age aging*., v.50, n.5, p.1607-1615, 2021.

CADER, S. A. et al. Extubation process in bed-ridden elderly intensive care patients receiving inspiratory muscle training: a randomized clinical trial. *Clin Interv Aging*., v.7, v.437-443, 2012.

CANCELLIERO, K. M. et al. Acute effects of transcutaneous electrical diaphragmatic stimulation on respiratory pattern in COPD patients: cross-sectional and comparative clinical trial. *Braz J Phys Ther*., v.17, n.6, p.547-55, 2013.

CANCELLIERO, K. M. et al. Estimulação diafragmática elétrica transcutânea (EDET) para fortalecimento muscular respiratório. *Fisioter Pesq*., v.19, n.4, p.303-308, 2012.

CEDERWALL, C. J. et al. Prevalence and use of intensive care beds in individuals on prolonged mechanical ventilation in Swedish ICUs. *Breath care*, v.66, n.2, .300-306, 2021.

DELERME, S.; RAY, P. Acute respiratory failure in the elderly: diagnosis and prognosis. *Age Ageing*, v.37, n.3, p.251-257, 2008.

DEMI, L. et al. Ultrasonography in lung pathologies: new perspectives. *Multidiscip Respir Med*., v.9, n.1, p.27, 2014.

DEMOULE, A. et al. Patterns of diaphragm function in critically ill patients receiving prolonged mechanical ventilation: a prospective longitudinal study. *Ann Intensive Care*, v.6, n.1, p.75, 2016.

DESAI, S. V.; LAW, T. J.; NEEDHAM, D. M. Long-term complications of critical care. *Crit Care Med*. v.39, n.2, p.371-379, 2011.

DUARTE, G. L. et al. Transcutaneous electrical diaphragmatic stimulation reduces the duration of invasive mechanical ventilation in patients with cervical spinal cord injury: retrospective case series. *Spinal Cord Ser Cases,* v.7, n.1, p. 1-6, 2021.

EBRAHIMABADI, S. et al, Studying the Power of the Integrative Weaning Index in Predicting the Success Rate of the Spontaneous Breathing Trial in Patients under Mechanical Ventilation. *Indian J Crit Care Med*., v. 21, n. 8, p.488-493, 2017.

EL-BARADEY, G. F.; EL-SHMAA, N. S.; GANNA, S.A. Can integrative weaning index be a routine predictor for weaning success? *Indian J Crit Care Med.*, v.19, n.12, p.703-707, 2015.

FERRARI, G. et al. Diaphragm ultrasound as a new index of discontinuation from mechanical ventilation. *Crit Ultrasound J*., v.6, n. 1, p.1-6, 2014.

FLATTET, Y. et al. Determining prognosis in acute exacerbation of COPD. *Int J Chron Obstruct Pulmon Dis*., n.12, p.467-475, 2017. DOI: 10.2147/COPD.S122382
GARGANI, L.; VOLPICELLI, G. How I do it: lung ultrasound. *Cardiovasc Ultrasound*, v.12, n.25, p.1-10, 2014.

GEDDES, L. A.; VOORHEES, W. D.; BOULAND, J. D. Optimum stimulus frequency for contracting the inspiratory muscle with chest-surface electrodes to produce artificial respiration. *Ann Biomed Eng*., v.18, n.1, p.103-108, 1990.

GOLIGHER, E. C. et al. Evolution of diaphragm thickness during mechanical ventilation: impact of inspiratory effort. *Am J Respir Crit Care Med*., v.192, n.9, p.1080-1088, 2015.

GRASSI, A. et al. Assisted mechanical ventilation promotes recovery of diaphragmatic thickness in critically ill patients: a prospective observational study. *Crit Care*. v.24, n.1, p.85, 2020.

GROSU, H. B. et al.Diaphragm Muscle Thinning in Subjects Receiving Mechanical Ventilation and Its Effect on Extubation. *Respir Care,* v.62, n.7, p.904-911, 2017.

HUGHES, L. D.; WITHAM, M. D. Causes and correlates of 30 day and 180 day readmission following discharge from a Medicine for the Elderly Rehabilitation unit. BMC Geriatr., v.18, n.1, p.197, 2018.

HUO, Y. A clinical study on the ability of the integrative weaning index to predict weaning from mechanical ventilation. *Ann Palliat Med*., v.9, n.5, p.3162-3169, 2020.

HUSSAIN, S. N. et al. Mechanical ventilation-induced diaphragm disuse in humans triggers autophagy. *Am J Respir Crit Care Med*., v.182, n.11, 1377-1386, 2010.

IBGE. *Conheça o Brasil – População:* Quantidade de homens e mulheres. 2019 Disponível em: https://educa.ibge.gov.br/jovens/conheca-o-brasil/populacao/18320-quantidade-de-homens-e-mulheres.html. Acesso em: 16 nov 2020.

KIM, W.Y, LIM CM. Ventilator-Induced Diaphragmatic Dysfunction: Diagnosis and Role of Pharmacological Agents. *Respir Care*, v.62, n.11, p.1485-1491, 2017.

LEVINE, S. et al. Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans. *N Engl J Med*., v.358, n.13, p.1327-1335, 2008

LI Q et al. Association between the severity of early acute kidney injury and subsequent hospital complications and 90-day mortality in geriatric patients receiving invasive mechanical ventilation. *Healthc Risk Management Policy,* v.15, p.793-804, 2022.

MOGHADAMNIA, M. T. et al. Ambient temperature and cardiovascular mortality: a systematic review and meta-analysis. *PeerJ.*, v.5, e3574, 2017. DOI 10.7717/peerj.3574

MANTOVANI, N. C. Evaluating the use of the tobin index when weaning patients from mechanical ventilation after general anesthesia. *Rev Bras Anestesiol*., v.57, n.6, p.592-605, 2007.

MATAMIS, D. et al. Sonographic evaluation of the diaphragm in critically ill patients. Technique and clinical applications. *Intensive Care Med*., v.39, n.5, p.801-810, 2013

MOURY, P. H. et al.Diaphragm thickening in cardiac surgery: a perioperative prospective ultrasound study. *Ann Intensive Care*, v.9, n.1, p.50, 2019.

NEDER, J. A. et al. Reference values for lung function tests II: maximal respiratory pressures and voluntary ventilation. *Braz J Med Biol Res.*, v.32, n.6, p.719-27, 1999.

NEMER, S.N. et al. A new integrative weaning index of discontinuation from mechanical ventilation. *Crit Care*., v.13, n.5, p.152, 2009.

NEMER, S.N. et al. A new integrative weaning index of discontinuation from mechanical ventilation. *Crit Care*., v.13, n.5, p.152, 2009.

O'ROURKE, J. et al. Initial Assessment of the Percutaneous Electrical Phrenic Nerve Stimulation System in Patients on Mechanical Ventilation. *Crit Care Med*., v.48, n.5, e362-e370, 2020.

PACÍFICO, A. A. C. P. et al. Análise descritiva e temporal da taxa de mortalidade e média de permanência hospitalar por queimaduras e corrosões em idosos no Brasil entre 2010 e 2019. *Rev. Bras. Cir Plást.* 2022;37(2):194-198.

RADELL, P. J. et al. Effects of prolonged mechanical ventilation and inactivity on piglet diaphragm function. *Intensive Care Med*., v.28, n.3, p.358-364, 2002.

SASSOON, C. S. et al. Altered diaphragm contractile properties with controlled mechanical ventilation. *J Appl Physiol*., v.92,n.6, p.2585-2595, 1985.

SANKAR, S. et al.Hospitalizisations related to systemic sclerosis and the impact of interstitial lung disease. Analysis of patients hospitalized at the University of Michigan, USA. *Clin Exp Rheumatol.*, v.39, 4, p. 43-51, 2021.

SILVA, J. B. et al. Perfil clínico de longevos em uma unidade de terapia intensiva. *Acta Paul Enferm*., v.31, n.1, p.39-45, 2018.

SOARES, A. M. M. et al. Causes for hospitalization of elderly individuals due to primary care sensitive conditions and its associated contextual factors. *Rev Assoc Med Bras (1992).* v.65, n.8, p.1086-1092, 2019.

SOTÁK, M. et al.Phrenic nerve stimulation prevents diaphragm atrophy in patients with respiratory failure on mechanical ventilation. *BMC Pulm Med*., v.21, n.1, p.314, 2021.

UMBRELLO, M. et al. Diaphragm ultrasound as indicator of respiratory effort in critically ill patients undergoing assisted mechanical ventilation: a pilot clinical study. *Crit Care*, v.19, n.1, p.161, 2015

VAN DEN BERG, M. et al. Diaphragm atrofy and weakness in the absence of mitochondrial dysfunction in critically ill. *Am J Respir Crit Care Med*., v. 92, n. 12, p.1544-1558, 2017.

VOLPICELLI, G. et al. Bedside lung ultrasound in the assessment of alveolar interstitial syndrome. *Am J Emerg Med*., v.24, n.6, p. 689-696, 2006.

VOLPICELLI G. et al. International evidence-based recommendations for point-of-care lung ultrasound. *Intensive Care Med*., v.38, n.4, p.577-591, 2012.

WONG, L. R. R.; CARVALHO, J. A.M. O rápido processo de envelhecimento populacional do Brasil: sérios desafios para as políticas públicas. *Rev Bras Estud Popul*., v.23, n.1, p.5-26, 2006.

ZHANG, W. et al. GPR43 regulation of mitochondrial damage to alleviate inflammatory reaction in sepsis. *Aging (Albany NY)*, v.13, n.18, p.22588-22610, 2021.

APÊNDICE A - Termo de Consentimento Livre e Esclarecido para Pesquisa

(Resolução nº466, de 10 de dezembro de 2012. Conselho Nacional de Saúde)

O senhor (a) está sendo convidado a permitir a participação, como responsável legal, do paciente ____, de um estudo denominado **"Efeito da estimulação diafragmática elétrica transcutânea na força muscular respiratória, na espessura do diafragma e no tempo de ventilação mecânica de pacientes críticos idosos"**, cujo objetivo é verificar se existe relação entre a aplicação de um estímulo elétrico sobre o principal músculo respiratório e o tempo em que o paciente permanece em uso do equipamento de respiração artificial (ventilador mecânico), analisando também a força do músculo após o procedimento e a sua espessura através de um exame de ultrassonografia. O projeto foi aprovado pelo Comitê de Ética da Faculdade de Ciências Médicas e da Saúde de Juiz de Fora (MG) sob o número CAAE: 87664318.2.0000.5103.

Existem poucos estudos sobre este assunto e este conhecimento é importante para que o fisioterapeuta e os outros profissionais da saúde possam traçar um melhor plano de tratamento para seus pacientes.

O participante da pesquisa será submetido a um estímulo elétrico na região torácica, para fazer com que o músculo seja ativado mesmo de forma não intencional, com objetivo de possivelmente preservar sua integridade ou minimizar a perda de massa. No momento em que a sedação for retirada para avaliação da possibilidade de desmame do equipamento de respiração artificial, serão avaliados espessura do músculo por meio da ultrassonografia, sua força através do acionamento de um botão no ventilador mecânico e o tempo em que o paciente permaneceu intubado, caso ele passe pelo desmame e extubação com sucesso. É importante ressaltar que os pacientes serão divididos em dois grupos: um que fará o procedimento exposto acima e outro que passará pelo protocolo padrão do hospital. Em ambos os casos, todo o suporte clínico será oferecido, a diferença está consistirá apenas em quem irá passar, ou não, pelo procedimento adicional de estimulação elétrica.

Através dos resultados desta pesquisa, o paciente poderá se beneficiar com a redução do tempo de ventilação mecânica e com um músculo respiratório eventualmente mais preparado para passar pelo processo de reabilitação. Esses dados serão divulgados em meios científicos, mantendo em sigilo seu nome e o nome do participante.

Entretanto, poderão existir riscos decorrentes do procedimento realizado no estudo, entre eles: instabilidade dos batimentos cardíacos, da pressão arterial e da respiração; interferências do estímulo elétrico sobre as informações contidas no monitor do paciente; conflito entre o que foi ajustado no ventilador mecânico e as reações do paciente. Caso isso aconteça a estimulação será interrompida imediatamente, com todo suporte clínico sendo prontamente oferecido.

Sua privacidade e a do paciente serão respeitadas, ou seja, os nomes e/ou quaisquer outros dados ou elementos que possam de qualquer forma permitir sua identificação, serão mantidos em sigilo. Será garantido o anonimato e sua privacidade. Caso o senhor(a) e/ ou o paciente tenham interesse, poderão ter acesso aos resultados da pesquisa posteriormente.

Caso queira, o senhor(a) poderá não permitir a participação do paciente no estudo, ou retirar seu consentimento a qualquer momento, sem precisar se explicar, não sofrendo qualquer prejuízo na assistência prestada pela equipe multiprofissional.

Em qualquer etapa do estudo, você poderá acessar o profissional responsável, Hebert Olímpio Júnior (UERJ), cujo contato se dará através do telefone: (32) 99130-1526. Caso haja alguma consideração ou dúvida sobre a ética da pesquisa, entre em contato como o Comitê de Ética em Pesquisa da Faculdade de Ciências Médicas e da Saúde de Juiz de Fora, que fica localizado na Alameda Salvaterra, nº 200, Salvaterra CEP 36.033-003 - Juiz de Fora – MG – telefone **(32) 2101-5000.**

Juiz de Fora, _____ de ________________ de_______

____

Nome e assinatura do responsável legal pelo paciente

____

Nome e assinatura do responsável por obter o consentimento

_____________________ _____________________

Testemunha Testemunha

APÊNDICE B – Variáveis Durante a Intervenção

Nome: ____Idade:______

Doença de Base:__________________________________Sexo:_____Altura:_______

Peso:________IMC:_______Dias com TOT:_______

Parâmetros ventilatórios:

(   ) Modo VCP: Pins:_____ Tins:_____FiO_2:____PEEP:______I:E:_______FR:_____

(   ) Modo VCV: Vt:_____Fluxo:______FiO_2:____PEEP:_____I:E:_______FR:_____

(   ) Modo VCP-VG: Vt:_____Tins:_____FiO_2:____PEEP:_____I:E______FR:_____

(   ) Modo PSV: Psup:_____FiO_2:_____PEEP:_____

Mecânica pulmonar (PRÉ-EDET):

Cst:_____Pva:_____Rva:_____Pplatô:_____P0,1:_____

Mecânica pulmonar (PÓS-EDET):

Cst:_____Pva:_____Rva:_____Pplatô:_____P0,1:_____

Hemodinâmica e sinais vitais (PRÉ-EDET):

PA:____________PAM:_______SpO_2:______FC:________T:_______

Hemodinâmica e sinais vitais (PÓS-EDET)

PA:_____________PAM:______SpO_2______FC:________T:_______

Medicamentos:

____

____

____

____

APÊNDICE C – Checklist de Prevenção de Falha de Extubação

Paciente: **Prontuário:** **Doença de Base:** **Balanço Hídrico:**	
Etapa 1: Problema	0 Ponto: Resolução do Problema que levou a intubação Ponto: Sem resolução do problema que levou a intubação
Etapa 2: Hemodinâmica	0 Ponto: Se o paciente estiver estável sem ou com DVA's em doses baixas Ponto: Se o paciente estiver estável com doses altas de DVA's ou instável hemodinamicamente
Etapa 3: Nível de Consciência	0 Ponto: Se glasgow = ou > 9T Ponto: Se glasgow < 9
Etapa 4: Respiratório	0 Ponto: Estar em PSV, com PS < ou = 12, PEEP < ou = 8 1 Ponto: Estar em PSV, com PS > 12, PEEP > 8, VC <6ml/kg com FR >30-35 0 Ponto: Se PaO2/FiO2 > 250 Ponto: Se PaO2/FiO2 < 250
Etapa 5: Força Muscular	0 Ponto: Pimax < -20 Ponto: Pimax > -20
Etapa 6: Imagem Pulmonar	0 Ponto: Sem alterações ou sem alterações relevantes 1 Ponto: Alterações reversíveis com VNI pós extubação Pontos: Apresenta alterações significativas
Etapa 7: Testes complementares	0 Ponto: Tobin < 104 ***[FR/VC(L)]*** 1 Ponto: Tobin >104
0 – 4 Pontos: Provável Sucesso **5 Pontos: Reavaliar possíveis complicações e agendar novo checlist**	**Resultado:**____ Observações:

– 10 Pontos: Provável Falha na extubação	
Etapa 8: Variáveis do Ventilador Mecânico	P 0,1: ______ PEEP: _____ FiO_2: ______ Pressão de Platô: ____ Pimax: _____ FR: ______ Vt: _______ IWI: ______
Etapa 9: Variáveis da Gasometria	PaO_2: ______ SpO_2: _______

APÊNDICE D – Artigo publicado

Hindawi
Rehabilitation Research and Practice
Volume 2021, Article ID 9091278, 5 pages
https://doi.org/10.1155/2021/9091278

Research Article

Immediate Hemodynamic Responses to Transcutaneous Electrical Diaphragmatic Stimulation in Critically Ill Elderly Patients

Hebert Olímpio Júnior,[1] **Gustavo Bittencourt Camilo**,[1,2] **Aline Priori Fioritto**,[3] **and Agnaldo José Lopes**[1,4,5]

[1] *Medical Sciences Post-Graduation Program, School of Medical Sciences, State University of Rio de Janeiro (UERJ), Rio de Janeiro, Brazil*
[2] *Faculty of Medical and Health Sciences of Juiz de Fora (SUPREMA), Minas Gerais, Brazil*
[3] *Federal University of Juiz de Fora (UFJF), Juiz de Fora, Minas Gerais, Brazil*
[4] *Rehabilitation Sciences Post-Graduation Program, Augusto Motta University Center (UNISUAM), Rio de Janeiro, Brazil*
[5] *Local Development Post-Graduation Program, Augusto Motta University Center (UNISUAM), Rio de Janeiro, Brazil*

Correspondence should be addressed to Agnaldo José Lopes; agnaldolopes.uerj@gmail.com

Received 30 June 2021; Revised 20 November 2021; Accepted 6 December 2021; Published 22 December 2021

Academic Editor: Jae-Young Lim

Background. Critically ill patients admitted to intensive care units (ICUs) may develop diaphragmatic dysfunction, especially when artificial airways are used. Positive effects have been observed when using the transcutaneous electrical diaphragmatic stimulation (TEDS) technique in different clinical conditions. However, no study has evaluated the safety of TEDS in patients admitted to ICUs. This study is aimed at evaluating the influence of TEDS on the hemodynamic and vital parameters of critically ill elderly patients under invasive mechanical ventilation (IMV). *Methods.* Forty-seven patients aged >60 years under IMV were evaluated for hemodynamic variables before and after TEDS. The procedure lasted 30 minutes and was performed once. *Results.* The sample consisted of 33 men and 14 women with a mean age of 69.9 ± 7.64 years. The mean systolic blood pressures pre-TEDS and post-TEDS were 126.6 ± 23.7 and 122.9 ± 25.9, respectively ($p = 0.467$). The mean diastolic blood pressures pre-TEDS and post-TEDS were 71.1 ± 12.2 and 67.7 ± 14.2, respectively ($p = 0.223$). No significant differences in the mean arterial pressure or heart rate were found between the pre-TEDS and post-TEDS time points ($p = 0.335$ and $p = 0.846$, respectively). *Conclusion.* Our findings suggest that TEDS does not have clinically relevant impacts on hemodynamic or vital parameters in critically ill elderly patients. These findings point to the possible safety of TEDS application in this population.

1. Introduction

Critically ill patients admitted to intensive care units (ICUs) are prone to develop muscle weakness, especially when they use artificial airways. The factors associated with this outcome are bed confinement, the use of drugs with sedative effects or neuromuscular blockers, and exposure to invasive mechanical ventilation (IMV) [1]. The clinical condition known as ICU-acquired weakness (ICU-AW) is defined as a syndrome that is not explained by any etiology other than ICU hospitalization and is associated with lowered quality of life [2].

The elderly population has a greater tendency to develop comorbidities, which contributes to hospital admissions. Polyneuropathy and myopathy related to intensive care are common conditions in these patients, generating a worse prognosis of ICU-AW [3, 4]. Respiratory muscles are among the most affected: muscle fibers can atrophy due to oxidative stress, activation of the ubiquitin-proteasome pathway, and a decrease in the number of myofibrils [5–7]. The muscles affected by IMV in the general population and especially in the elderly population include the diaphragm; when specific atrophy of the muscle fibers of the diaphragm is observed, the change is known as diaphragmatic dysfunction [8]. Controlling the factors that increase the risk of ICU-AW is key to preventing its development. Approximately 25-50% of subjects receiving ventilatory support have muscle weakness, and among this group, 85-95% experience neuromuscular impairment that persists for 2-5 years [9]. Considering the progression of diaphragmatic dysfunction, which is one manifestation of ICU-AW, consequences such as an increased IMV duration, an increased risk of respiratory complications, and a prolonged hospital stay may be observed if no specific intervention is performed [10, 11].

In the context of outpatient pulmonary rehabilitation, positive effects have been observed when using the transcutaneous electrical diaphragmatic stimulation (TEDS) technique in patients with chronic obstructive pulmonary disease (COPD) [12]. This technique consists of placing electrodes on the skin at locations near the motor points of the diaphragm, transmitting an intermittent current, and generating action potentials capable of producing muscle contractions [13, 14]. Studies evaluating the safety of neuromuscular electrical stimulation (NES) have suggested that it does not alter the stability of vital parameters such as heart rate (HR) and blood pressure (BP) [15, 16]. However, no study has evaluated the safety of TEDS in patients admitted to the ICU. Considering the practicality of the procedure, its low cost, the importance of applying new therapeutic modalities in the context of diaphragmatic dysfunction, and the scarcity of evidence on this topic in the ICU context, the objective of the present study was to evaluate the influence of TEDS on hemodynamic and vital parameters in critically ill elderly patients.

2. Materials and Methods

2.1. Study Design and Participants. This is an experimental study evaluating 47 patients (of 71 eligible) aged ≥60 years who underwent IMV at the Therezinha de Jesus Hospital and Maternity Hospital and at the Monte Sinai Hospital, both located in Juiz de Fora, Brazil. All participants underwent hemodynamic evaluations before and immediately after TEDS application. They underwent the same evaluation steps, and the variables systolic BP (SBP), diastolic BP (DBP), mean arterial pressure (MAP), and HR were measured immediately before and after the intervention. Patients with the following characteristics were excluded: a recent surgical scar and/or an open lesion in the regions where the electrodes would be placed, severe hemodynamic instability (HR > 140 bpm, MAP < 65 mmHg or>120 mmHg, peripheral oxygen saturation < 86% with a fraction of inspired oxygen ≥ 60%), patient–ventilator asynchrony not reversible with adjustments or optimization of sedation, hypoglycemia < 60 mg/dL, the presence of a cardiac pacemaker, untreated pneumothorax, and the use of increasing doses of vasoactive drugs.

This study was approved by the Research Ethics Committee of the Faculty of Medical and Health Sciences of Juiz de Fora (SUPREMA) under number 2.739.692, and all patients consented to participate in this study. This study was registered with the ClinicalTrials.gov identifier code NCT04565002.

2.2. Intervention. The intervention was performed with the patient in assist-control ventilatory mode. The sensitivity parameter was adjusted to the value required for the contractions produced by the electrical stimulation not to trigger the mechanical ventilator, thus avoiding episodes of asynchrony. The following parameters were used: a frequency of 30 Hz, a pulse width of 0.4 ms, a respiratory rate (RR) of 15 breaths per minute, a hold time of 1 s, a rise time of 1 s, a fall time of 2 s, and a time without stimulation of 2 s [13]. Phrenic electrostimulation equipment (Dualpex 961, Quark, SP, Brazil) was used. The electrodes were positioned according to Cancelliero et al. [14], who proposed the placement of two electrodes in the right and left paraxiphoid regions and another two in the direction of the axillary midline on the seventh intercostal space on the right and left sides. The positioning of the TEDS electrodes is shown in Figure 1. Diaphragm stimulation lasted 30 minutes [12].

2.3. Data Analysis. The distribution of the measured outcome variables was evaluated by the Shapiro-Wilk test. The results are expressed as the mean (standard deviation (SD)) or frequency (percentage). The difference between the mean of a continuous variable before and after the intervention was evaluated by a paired t-test. The significance level adopted was $p < 0.05$. The data analysis was performed using the IBM SPSS Statistics version 23.0 software (IBM Corp., Armonk, NY, USA).

3. Results

Of the 71 patients who participated in the present study, 24 were excluded for the following reasons: interruption of a medical procedure ($n = 5$), intense psychomotor agitation ($n = 12$), and patient–ventilator asynchrony ($n = 7$). Thus, the sample consisted of 47 patients, including 33 males, with a mean age of 69.9 ± 7.64 years. The main clinical conditions leading to ICU admission were heart disease, lung disease, and sepsis. The characteristics of the sample, including demographic and anthropometric data and admission conditions, are shown in Table 1.

The mean SBP pre-TEDS was 126.6 ± 23.7 mmHg, whereas the value post-TEDS was 122.9 ± 25.9 mmHg ($p = 0.467$). The mean DBP values were 71.1 ± 12.2 mmHg before the procedure and 67.7 ± 14.2 mmHg after the intervention ($p = 0.223$). The comparisons between the pre-TEDS and post-TEDS values are shown in Table 2.

Power analysis was conducted using G∗power version 3.1. Considering a type-I error of 5%, a minimal correlation between measurements of 0.5, a two-tailed paired test, and the observed means ± SD (before and after TEDS), the actual statistical powers to detect the observed effects were 80% (SBP), 80.2% (DBP), 80% (MAP), and 80% (HR).

4. Discussion

This is the first study to evaluate the influence of TEDS on the hemodynamic and vital parameters of critically ill elderly patients. The main finding was no significant change in

Figure 1: Positioning of the electrodes during transcutaneous electrical diaphragmatic stimulation.

Table 1: Characteristics of the studied sample.

Variables	Values
Demographic data	
Age (years)	69.9 ± 7.64
Sex (male)	33 (70.2%)
Body composition	
Weight (kg)	64.6 ± 9.87
Height (cm)	166.5 ± 6.85
Clinical conditions requiring hospitalization	
Cardiac diseases	
Acute heart failure	6 (12.8%)
Acute myocardial infarction	4 (8.51%)
Lung diseases	
COPD exacerbation	5 (10.6%)
Asthma exacerbation	5 (10.6%)
Neurological diseases	
Stroke	3 (6.38%)
Spinal cord injury	3 (6.38%)
Sepsis	9 (19.2%)
Postoperative state after cardiac surgery	7 (14.9%)
Postoperative state after abdominal surgery	5 (10.6%)

Results expressed as the means ± SD or number (%).

Table 2: Differences between systolic blood pressure, diastolic blood pressure, mean arterial pressure, and heart rate from before to after the intervention.

Variables	Before TEDS	After TEDS	p value
SBP	126.6 ± 23.7	122.9 ± 25.9	0.467
DBP	71.1 ± 12.2	67.7 ± 14.2	0.223
MAP	90.2 ± 16.7	86.7 ± 18.8	0.335
HR	92.8 ± 18.9	93.5 ± 19.2	0.846

Results expressed as the means ± SD. SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; HR: heart rate; TEDS: transcutaneous electrical diaphragmatic stimulation.

hemodynamic parameters in the sample from before to after TEDS application, suggesting that the intervention is safe.

NES is a safe technique when correctly applied by a trained professional [17–20]. When evaluating patients with COPD, Akar et al. [18] observed a reduction in HR in the postintervention period, suggesting that the use of NES did not generate cardiac overload in the patients evaluated. Iwatsu et al. [19] followed 61 patients in the postoperative period of cardiac surgery to study the safety of NES by evaluating hemodynamic parameters and the presence of arrhythmias. These authors did not observe changes in the evaluated parameters, suggesting that NES does not increase cardiac workload and is a safe intervention in these patients. In the present study, no statistically and clinically relevant difference in HR was noted when comparing pre- and post-TEDS time points. Even considering that the increase in transpulmonary pressure caused by IMV and muscle contractions affects cardiac output, right ventricular afterload, and left ventricular preload, TEDS did not change HR in our study, which can be at least partly explained by our adjustment of the sensitivity of the mechanical ventilator, thus preventing its triggering [21].

One of the concerns with the use of TEDS is the occurrence of adverse effects, including skin reactions. When evaluating critically ill patients, Segers et al. [20] did not observe a significant change in the studied variables (BP, HR, and RR), and only hyperemia occurred in 50% of the patients immediately after removal of the electrodes, which gradually disappeared. Our study did not find adverse events related to TEDS in the integumentary system, although the procedure lasted a short time. Additionally, regarding concerns about side effects, Parry et al. [22] used some parameters as safety cutoffs to determine when to start or stop NES. These authors did not observe serious adverse effects, corroborating the findings of the present study, which used some of their cutoff points.

Although few studies on TEDS have been published to date, this technique has been used in clinical practice in intensive physical therapy because it has shown promise for improving respiratory muscle strength [23–26]. Even with the physiological decline of the respiratory system resulting from aging, training with TEDS can be an effective tool in respiratory physiotherapy by promoting an increase in diaphragm muscle strength in elderly people [25]. The present study showed that TEDS did not significantly alter the hemodynamic parameters of this population, which reinforces its applicability in the ICU given the influence of the procedure on the motor units of the diaphragm that produce involuntary stimulation of the muscle and prevent autophagy and disuse atrophy. A recent systematic review [27] showed that the application of TEDS promotes an increase in respiratory muscle strength in individuals with COPD, elderly individuals, healthy women, and patients in the postoperative period of myocardial revascularization surgery.

Interestingly, a recent study conducted by Duarte et al. [28] suggested that TEDS influences the duration of IMV as well as the length of stay in the ICU in patients with spinal cord injury (SCI). Unlike the retrospective case series evaluated by these authors ($n = 10$), our study is an experimental clinical trial evaluating the influence of TEDS on immediate hemodynamic responses to determine the safety of the procedure in critically ill elderly individuals (not only patients with SCI). Additionally, Duarte et al. [28] proposed a comparison between TEDS and the standard weaning protocol in neurological patients who were already able to voluntarily contract their respiratory muscles. In contrast, we analyzed the application of TEDS in patients initially without ventilatory drive, thus allowing identification of new evidence to assess the impact of TEDS earlier, which is important because critical patients newly admitted to the ICU receive sedative and analgesic agents, justifying the decrease in the ventilatory drive and contributing to ICU-AW [29].

Immobility associated with IMV is one of the main factors involved in the development of ICU-AW and is a predictor of mortality, especially in the elderly population. Muscle strength can be lost at a rate of 10-15% per week of disuse. The combination of 18-69 hours of diaphragm inactivity and IMV is associated with marked atrophy of both slow- and fast-twitch fibers [30]. Kress and Hall [30] suggested that increased proteolysis, which is responsible for fiber atrophy, can be attenuated and thus improve the outcomes of this specific population. These data demonstrate the importance of measures to prevent the consequences of inactivity, such as the intervention proposed in our study. We believe that ICU-AW-preventive measures in elderly patients, such as TEDS, can become part of the routine of ICUs to forestall unfavorable outcomes in this population.

The main limitations were the fact that the procedure was applied only once, the lack of a control group, and the lack of assessment of the effect of the technique on the diaphragm muscle strength. Although no significant difference was found in the variables studied before and after the procedure, the small sample size and the different clinical conditions of hospitalization should be highlighted; these are limiting factors for predicting the safety of TEDS in critically ill elderly patients. In addition, given our use of a single evaluation step, the medium- or long-term effects of the intervention could not be identified. Despite these limitations, we believe that this study can serve as a starting point for controlled and randomized clinical trials that can deepen our knowledge about TEDS.

5. Conclusions

TEDS did not have clinically relevant impacts on hemodynamic or vital parameters when comparing the pre- and postintervention time points in critically ill elderly patients. These findings point to the possible safety of TEDS application in this population.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest.

Acknowledgments

This study was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (grant numbers 407138/2018-8 and 302215/2019-0), the Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ) (grant numbers #E-26/202.679/2018 and #E-26/010.002124/2019), and the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) (grant number Finance Code 001).

References

[1] R. D. Stevens, S. A. Marshall, D. R. Cornblath et al., "A framework for diagnosing and classifying intensive care unit-acquired weakness," *Critical Care Medicine*, vol. 37, Supplement 10, pp. S299–S308, 2009.

[2] D. E. Anekwe, S. Biswas, A. Bussières, and J. Spahija, "Early rehabilitation reduces the likelihood of developing intensive care unit- acquired weakness: a systematic review and meta-analysis," *Physiotherapy*, vol. 107, pp. 1–10, 2020.

[3] R. E. Dalton, R. S. Tripathi, E. E. Abel et al., "Polyneuropathy and myopathy in the elderly," *HSR Proceedings in Intensive Care and Cardiovascular Anesthesia*, vol. 4, no. 1, pp. 15–19, 2012.

[4] N. Latronico and C. Bolton, "Critical illness polyneuropathy and myopathy: a major cause of muscle weakness and paralysis," *The Lancet Neurology*, vol. 10, no. 10, pp. 931–941, 2011.

[5] S. Levine, T. Nguyen, N. Taylor et al., "Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans," *The New England Journal of Medicine*, vol. 358, no. 13, pp. 1327–1335, 2008.

[6] S. N. Hussain, M. Mofarrahi, I. Sigala et al., "Mechanical ventilation-induced diaphragm disuse in humans triggers autophagy," *American Journal of Respiratory and Critical Care Medicine*, vol. 182, no. 11, pp. 1377–1386, 2010.

[7] M. van den Berg, P. E. Hooijman, A. Beishuizen et al., "Diaphragm Atrophy and weakness in the absence of

mitochondrial dysfunction in the critically ill," *American Journal of Respiratory and Critical Care Medicine*, vol. 196, no. 12, pp. 1544–1558, 2017.

[8] S. V. Desai, T. J. Law, and D. M. Needham, "Long-term complications of critical care," *Critical Care Medicine*, vol. 39, no. 2, pp. 371–379, 2011.

[9] P. J. Radell, S. Remahl, D. G. Nichols, and L. I. Eriksson, "Effects of prolonged mechanical ventilation and inactivity on piglet diaphragm function," *Intensive Care Medicine*, vol. 28, no. 3, pp. 358–364, 2002.

[10] C. S. Sassoon, V. J. Caiozzo, A. Manka, and G. C. Sieck, "Altered diaphragm contractile properties with controlled mechanical ventilation," *Journal of Applied Physiology*, vol. 92, no. 6, pp. 2585–2595, 2002.

[11] D. Matamis, E. Soilemezi, M. Tsagourias et al., "Sonographic evaluation of the diaphragm in critically ill patients: technique and clinical applications," *Intensive Care Medicine*, vol. 39, no. 5, pp. 801–810, 2013.

[12] K. M. Cancelliero, D. Ike, C. B. F. Pantoni, R. G. Mendes, A. Borghi-Silva, and D. Costa, "Acute effects of transcutaneous electrical diaphragmatic stimulation on respiratory pattern in COPD patients: cross-sectional and comparative clinical trial," *Brazilian Journal of Physical Therapy*, vol. 17, no. 6, pp. 547–555, 2013.

[13] L. A. Geddes, W. D. Voorhees, and J. D. Bouland, "Optimum stimulus frequency for contracting the inspiratory muscles with chest-surface electrodes to produce artificial respiration," *Annals of Biomedical Engineering*, vol. 18, no. 1, pp. 103–108, 1990.

[14] K. M. Cancelliero, D. Ike, L. M. M. Sampaio, V. L. A. Santos, R. Stirbulov, and D. Costa, "Estimulação diafragmática elétrica transcutânea (EDET) para fortalecimento muscular respiratório: estudo clínico controlado e randomizado," *Fisioterapia e Pesquisa*, vol. 19, no. 4, pp. 303–308, 2012.

[15] V. O. Carvalho, J. M. Roque, E. A. Bocchi, E. G. Ciolac, and G. V. Guimarães, "Hemodynamic response in one session of strength exercise with and without electrostimulation in heart failure patients: a randomized controlled trial," *Cardiology Journal*, vol. 18, no. 1, pp. 39–46, 2011.

[16] V. Gerovasili, E. Tripodaki, E. Karatzanos et al., "Short-term systemic effect of electrical muscle stimulation in critically ill patients," *Chest*, vol. 136, no. 5, pp. 1249–1256, 2009.

[17] A. Sachetti, M. F. Carpes, A. S. Dias, and G. Sbruzzi, "Safety of neuromuscular electrical stimulation among critically ill patients: systematic review," *Revista Brasileira de Terapia Intensiva*, vol. 30, no. 2, pp. 219–225, 2018.

[18] O. Akar, E. Günay, S. Sarinc Ulasli et al., "Efficacy of neuromuscular electrical stimulation in patients with COPD followed in intensive care unit," *Clinical Respiratory Journal*, vol. 11, no. 6, pp. 743–750, 2017.

[19] K. Iwatsu, S. Yamada, Y. Iida et al., "Feasibility of neuromuscular electrical stimulation immediately after cardiovascular surgery," *Archives of Physical Medicine and Rehabilitation*, vol. 96, no. 1, pp. 63–68, 2015.

[20] J. Segers, G. Hermans, F. Bruyninckx, G. Meyfroidt, D. Langer, and R. Gosselink, "Feasibility of neuromuscular electrical stimulation in critically ill patients," *Journal of Critical Care*, vol. 29, no. 6, pp. 1082–1088, 2014.

[21] C. S. Sassoon, "Triggering of the ventilator in patient-ventilator interactions," *Respiratory Care*, vol. 56, no. 1, pp. 39–51, 2011.

[22] S. M. Parry, S. Berney, S. Warrillow et al., "Functional electrical stimulation with cycling in the critically ill: a pilot case-matched control study," *Journal of Critical Care*, vol. 29, no. 4, pp. 695.e1–695.e7, 2014.

[23] L. G. Maynard, A. S. Barreto, V. J. Santana-Filho, M. L. Cerqueira Neto, D. P. M. Dias, and V. M. Silva-Júnior, "Effects of transcutaneous electrical diaphragmatic stimulation on the cardiac autonomic balance in healthy individuals: a randomized clinical trial," *Fisioterapia e Pesquisa*, vol. 23, no. 3, pp. 248–256, 2016.

[24] S. Tanaka, T. Masuda, K. Kamiya et al., "A single session of neuromuscular electrical stimulation enhances vascular endothelial function and peripheral blood circulation in patients with acute myocardial infarction," *International Heart Journal*, vol. 57, no. 6, pp. 676–681, 2016.

[25] L. A. Santos, J. R. Borgi, J. L. N. Daister, and E. M. Pazzinotto-Forti, "Efeitos da estimulação diafragmática elétrica transcutânea na função pulmonar em idosos," *Revista Brasileira de Geriatria e Gerontologia*, vol. 16, no. 3, pp. 495–502, 2013.

[26] T. C. Cerqueira, M. L. Cerqueira, A. J. Carvalho et al., "Neuromuscular electrical stimulation on hemodynamic and respiratory response in patients submitted to cardiac surgery: pilot randomized clinical trial," *International Journal of Cardiovascular Sciences*, vol. 32, no. 5, pp. 483–489, 2019.

[27] L. L. Ferreira, J. R. C. Mello, M. V. C. Brito, and O. M. Cavenaghi, "Efetividade da estimulação diafragmática elétrica transcutânea na força muscular respiratória, volumes e capacidades pulmonares: revisão sistemática," *Medicina (Ribeirão Preto)*, vol. 48, no. 5, pp. 491–500, 2015.

[28] G. L. Duarte, A. L. Bethiol, L. S. R. Ratti et al., "Transcutaneous electrical diaphragmatic stimulation reduces the duration of invasive mechanical ventilation in patients with cervical spinal cord injury: retrospective case series," *Spinal Cord Series And Cases*, vol. 7, no. 1, p. 26, 2021.

[29] H. Farhan, I. Moreno-Duarte, N. Latronico, R. Zafonte, and M. Eikermann, "Acquired muscle weakness in the surgical intensive care Unit," *Anesthesiology*, vol. 124, no. 1, pp. 207–234, 2016.

[30] J. P. Kress and J. B. Hall, "ICU-acquired weakness and recovery from critical illness," *The New England Journal of Medicine*, vol. 370, no. 17, pp. 1626–1635, 2014.

APÊNDICE E – Comprovante de Submissão do segundo artigo

Fwd: Manuscript submitted to Physiotherapy Research International

De: Agnaldo Lopes
agnaldolopes.uerj@gmail.com
Para: Hebert Olímpio Júnior
hebertojr@hotmail.com
Enviado: sábado, 11 de março 19:03

---------- Forwarded message ---------
De: **Physiotherapy Research International**
<no-reply@atyponrex.com>
Date: sáb., 11 de mar. de 2023 às 19:02
Subject: Manuscript submitted to Physiotherapy Research International
To: Agnaldo Lopes
<agnaldolopes.uerj@gmail.com>

Dear Agnaldo Lopes,

Your manuscript entitled "EFFECTS OF TRANSCUTANEOUS ELECTRICAL DIAPHRAGMATIC STIMULATION ON RESPIRATORY MUSCLE AND THE DURATION OF MECHANICAL VENTILATION IN CRITICALLY ILL ELDERLY PATIENTS: A RANDOMIZED CONTROLLED CLINICAL TRIAL" has been successfully submitted online and is being delivered to the Editorial Office of *Physiotherapy Research International* for consideration.

You will receive a follow-up email with further instructions from our electronic editorial office platform, ScholarOne Manuscripts, typically within one business day. That message will confirm that the Editorial Office has received your submission and will provide your Manuscript ID.

Thank you for submitting your manuscript to *Physiotherapy Research International*

Sincerely,
The Editorial Staff at Physiotherapy Research International

By submitting a manuscript to or reviewing for this publication, your name, email address, and affiliation, and other contact details the publication might require, will be used for the regular operations of the publication, including, when necessary, sharing with the publisher (Wiley) and partners for production and publication. The publication and the publisher recognize the importance of protecting the personal information collected from users in the operation of these services and have practices in place to ensure that steps are taken to maintain the security, integrity, and privacy of the personal data collected and processed. You can learn more by reading our data protection policy. In case you don't want to be contacted by this publication again, please send an email to priproofs@wiley.com.

ANEXO – Parecer Consubstanciado

FACULDADE DE CIÊNCIAS MÉDICAS E DA SAÚDE DE JUIZ DE

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: EFEITO DA ESTIMULAÇÃO DIAFRAGMÁTICA ELÉTRICA TRANSCUTÂNEA NA FORÇA MUSCULAR RESPIRATÓRIA, ESPESSURA DO DIAFRAGMA E NO TEMPO DE VENTILAÇÃO MECÂNICA DE PACIENTES CRÍTICOS IDOSOS.

Pesquisador: Hebert Olímpio Júnior

Área Temática:

Versão: 2

CAAE: 87664318.2.0000.5103

Instituição Proponente: Universidade do Estado do Rio de Janeiro - UERJ

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 2.739.692

Apresentação do Projeto:

Projeto já apresentado anteriormente, avaliado, com parecer de ajustar o cronograma.

Objetivo da Pesquisa:

Projeto já apresentado anteriormente, avaliado, com parecer de ajustar o cronograma.

Avaliação dos Riscos e Benefícios:

Projeto já apresentado anteriormente, avaliado, com parecer de ajustar o cronograma.

Comentários e Considerações sobre a Pesquisa:

Projeto já apresentado anteriormente, avaliado, com parecer de ajustar o cronograma.

Considerações sobre os Termos de apresentação obrigatória:

Coleta de dados iniciando em junho 2018, consequentemente após esse parecer. Consideramos adequado o cronograma.

Recomendações:

Sem recomendações

Conclusões ou Pendências e Lista de Inadequações:

Sem pendências ou inadequações

Considerações Finais a critério do CEP:

Endereço: BR 040, Km 796
Bairro: Salvaterra **CEP:** 36.045-410
UF: MG **Município:** JUIZ DE FORA
Telefone: (32)2101-5015 **Fax:** (32)2101-5043 **E-mail:** cep@suprema.edu.br

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1072601.pdf	22/05/2018 09:55:47		Aceito
Projeto Detalhado / Brochura Investigador	projeto_hebert_cepcep.docx	22/05/2018 09:55:21	Hebert Olimpio Júnior	Aceito
Parecer Anterior	PB_PARECER_CONSUBSTANCIADO_CEP_2620303.pdf	22/05/2018 09:51:14	Hebert Olimpio Júnior	Aceito
Outros	Tcud.pdf	06/02/2018 10:50:13	Hebert Olimpio Júnior	Aceito
Declaração de Instituição e Infraestrutura	declaracao_infraestrutura_preenchida.png	06/02/2018 10:46:56	Hebert Olimpio Júnior	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	JustificativaTCLE.pdf	05/02/2018 18:29:40	Hebert Olimpio Júnior	Aceito
Folha de Rosto	FOLHA_ROSTO.docx	05/02/2018 18:24:14	Hebert Olimpio Júnior	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

JUIZ DE FORA, 27 de Junho de 2018

Assinado por:
Soraida Sozzi Miguel
(Coordenador)