HUMBERTO SILVA

# PERFIL DE ATIVIDADE FÍSICA NA VIDA DIÁRIA E SEUS FATORES DETERMINANTES EM PACIENTES COM DOENÇA INTERSTICIAL PULMONAR

Londrina
2019

HUMBERTO SILVA

# PERFIL DE ATIVIDADE FÍSICA NA VIDA DIÁRIA E SEUS FATORES DETERMINANTES EM PACIENTES COM DOENÇA INTERSTICIAL PULMONAR

Dissertação apresentada ao Programa de Pós-Graduação em Ciências da Reabilitação (Programa Associado entre Universidade Estadual de Londrina [UEL] e Universidade Norte do Paraná [UNOPAR]), como requisito parcial à obtenção do título de Mestre em Ciências da Reabilitação.

Orientador: Prof. Dr. Carlos Augusto Marçal Camillo

Londrina
2019

Ficha de identificação da obra elaborada pelo autor, através do Programa de Geração Automática do Sistema de Bibliotecas da UEL

Silva, Humberto.
Perfil de atividade física na vida diária e seus fatores determinantes em pacientes com doença intersticial pulmonar / Humberto Silva. - Londrina, 2019.
65 f. : il.

Orientador: Carlos Augusto Marçal Camillo.
dissertação) - Universidade Estadual de Londrina, Centro de Ciências da Saúde, Programa de Pós-Graduação em Ciências da Reabilitação, 2019.
Inclui bibliografia.

1. Atividade física - . 2. Doenças intersticiais pulmonares - . I. Camillo, Carlos Augusto Marçal. II. Universidade Estadual de Londrina. Centro de Ciências da Saúde. Programa de Pós-Graduação em Ciências da Reabilitação. III. Título.

HUMBERTO SILVA

# PERFIL DE ATIVIDADE FÍSICA NA VIDA DIÁRIA E SEUS FATORES DETERMINANTES EM PACIENTES COM DOENÇA INTERSTICIAL PULMONAR

Dissertação apresentada ao Programa de Pós-Graduação em Ciências da Reabilitação (Programa Associado entre Universidade Estadual de Londrina [UEL] e Universidade Norte do Paraná [UNOPAR]), como requisito parcial à obtenção do título de Mestre em Ciências da Reabilitação.

**BANCA EXAMINADORA**

_____

Orientador: Prof. Dr. Carlos Augusto Marçal Camillo
Universidade Norte do Paraná - UNOPAR

_____

Prof. Dr. Celso Ricardo Fernandes Carvalho
Universidade de São Paulo - USP

_____

Prof. Dr. Fabio de Oliveira Pitta
Universidade Estadual de Londrina - UEL

Londrina, 07 de maio de 2019.

**Dedicatória**

Dedico esta dissertação a todos, familiares, amigos e pacientes que contribuiram e possibilitaram a realização deste trabalho.

“A vida é breve, a ocasião fugaz, a experiência é vacilante e o julgamento é difícil.”

Hipócrates

## AGRADECIMENTOS

Gostaria de agradecer a Deus primeiramente, pois sem dúvida, Ele tem me guiado e aberto portas desde o dia em que escolhi a Fisioterapia. Tornando possível alcançar meus objetivos e sonhos, e, ao mesmo tempo ajudando ao próximo, seja transmitindo conhecimento ou na assistência direta ao paciente.

Agradeço também a minha família, eles com certeza são presentes de Deus em minha vida. Minha mãe e meu pai sempre fizeram de tudo para que eu tivesse uma boa educação, me incentivaram e deram suporte em todos os momentos que precisei. Eles são meu porto-seguro e espero um dia poder retribuir tudo que fizeram por mim. Agradeço a minha irmã que sempre estava disposta a me ouvir e conversar e me apoiou em todas as decisões que tomei. Também a minha esposa, que foi minha companheira e parceira nesta trajetória e teve paciência e lidou com algumas coisas de casa sozinha quando não pude ajudar. A minha filha quero agradecer pelos momentos em que ela me proporcionou de alegria. Mesmo sem saber de nada, ela muitas vezes salvava meu dia só com um sorriso e fazia com que eu me lembrasse o porquê eu estava fazendo isso e me dava mais forças para seguir. Além de agradecê-la tenho que pedir desculpas também, pelos momentos em que fui ausente neste período, espero que entenda que é apenas uma fase e que estou fazendo isso pela nossa família.

Além disso, existem aquelas pessoas que apesar de não serem consanguíneos, formam nossa família. Este é o caso com Wagner, Ana, Jéssica, Darlly, amigos que me acompanham desde a residência. Assim como em qualquer família já tivemos momentos de desentendimentos, mas os momentos de alegria e companheirismo superam tudo isso. Obrigado pelo apoio, pelos conselhos, pelas risadas, entre outros momentos. Agradeço também aos amigos e colegas de

laboratório (LFIP/CEPPOS), todos eles de alguma forma contribuiram para realização do mestrado, direta ou indiretamente, e com certeza os momentos de pausa para o café foram importantes nesta fase. Agradeço aos colegas de trabalho do Hospital Evangélico e do Hospital Universitário, que sempre que possível se desdobravam para tentar trocar ou assumir meus plantões para que eu pudesse conduzir e concluir o mestrado. Agradeço também aos pacientes que se dispuseram a participar do estudo, sem eles este trabalho não seria possível.

Gostaria de agradecer ao professor Fabio e a professora Nidia, por terem me recebido de braços abertos em seu laboratório e ter possibilitado a realização do mestrado. E por último , mas não menos importante, agradeço ao meu orientador professor Carlos, o Guto. Ele foi destemido quando aceitou me orientar sem nem ao menos me conhecer. Recebi isso como um voto de confiança e busquei fazer o meu melhor, mas é claro que cometi muitas falhas e as vezes desapontei neste trajeto, peço desculpas por esses momentos. Agradeço por cada momento em que ele sentou comigo para discutir o projeto, para ensinar sobre pesquisa, análise estatisca, enfim, por todo momento de aprendizado que ele me proporcionou. Além de orientador, ele foi um amigo, me ajudando e abrindo as portas para que eu realize meus sonhos. Obrigado por todos tudo, desde os puxões de orelha e broncas até os cafés e conversas aleatórias.

Obrigado a todos de coração. Amo muito todos vocês.

SILVA, Humberto. **Perfil de atividade física na vida diária e seus fatores determinantes em pacientes com doença intersticial pulmonar.** 2019. 69 f. Dissertação de mestrado (Programa de Pós-Graduação em Ciências da Reabilitação – Programa Associado UEL – UNOPAR) – Universidade Estadual de Londrina, Londrina, 2019.

## RESUMO

**Introdução**: Os fatores que podem influenciar a atividade física de vida diária (AFVD), não foram totalmente investigadas em pacientes com doença intersticial pulmonar (DIP). **Objetivos**: Esta dissertação de mestrado teve como objetivo caracterizar a AFVD e investigar a relação entre a AFVD e outros desfechos (capacidade de exercício, função pulmonar, sono) em pacientes com DIP. Além disso, investigar os eventuais fatores determinantes da AFVD nessa população. **Métodos**: Foram recrutados pacientes com diagnóstico de DIP e indivíduos aparentemente saudáveis (grupo controle). Os indivíduos foram submetidos à avaliação da função pulmonar, capacidade de exercício, força muscular respiratória e periférica, atividade física, sono, dispneia e qualidade de vida relacionada à saúde. AFVD e medidas de sono foram avaliadas usando um monitor de atividade (Actigraph®, wGT3x-BT) em sua cintura por seis dias consecutivos, durante 24 horas. Resultados: Em comparação ao grupo controle, os pacientes com DIP apresentaram menor número de passos (5055 ± 2089 vs 8159 ± 3283 passos / dia, p = 0,0002), menor tempo gasto em atividade moderada a vigorosa (8 - 16 ] vs 30 [15 - 47] min / dia, p <0,0001) e menor tempo na postura em pé (290 ± 87 vs 392 ± 65 min, p = 0,0003), e mais tempo gasto na posição deitada (288 ± 91 vs 197 ± 66 min, p = 0,0003). Além disso, os pacientes apresentaram duração significativamente maior do tempo de sono durante o dia (56 ± 108 vs 6 ± 19 min, p = 0,01). Os modelos de regressão identificaram a função pulmonar (capacidade de difusão do monóxido de carbono, DLCO) e a duração do sono à noite e durante o dia para explicar parcialmente os passos diários, o tempo em atividades leves e o tempo em atividades moderadas a vigorosas. (0,26 <r2 <0,58; p <0,05 para todos). Conclusão: Pacientes com DIP apresentam menores níveis de atividade física quando comparados a indivíduos saudáveis do grupo. A atividade física diária é influenciada negativamente por pior função pulmonar e maior duração do sono (tanto à noite quanto durante o dia).

**Palavras-chave:** Doenças pulmonares intersticiais. atividade física. Sono.

SILVA, Humberto. **Perfil de atividade física na vida diária e seus fatores determinantes em pacientes com doença intersticial pulmonar.** 2019. 69 p. Dissertação de mestrado (Programa de Pós-Graduação em Ciências da Reabilitação – Programa Associado UEL – UNOPAR) – Universidade Estadual de Londrina, Londrina, 2019.

## ABSTRACT

**Background:** The factors that could influence daily physical activity (DPA) is not fully investigated in patients with interstitial lung disease (ILD). Objectives: This dissertation aimed to characterize DPA and investigate the relationship between DPA and other outcomes (exercise capacity, lung function, sleep) in patients with ILD. In addition, we investigate the possible determinants of DPA in this population. Methods: Patients diagnosed with ILD and apparently healthy individuals (control group) were recruited. The subjects were submitted to evaluation of lung function, exercise capacity, respiratory and peripheral muscle strength, physical activity, sleep, dyspnea and health related quality of life. DPA and sleep measurements were assessed using an activity monitor (Actigraph®, wGT3x-BT) at their waist for six consecutive days for 24 hours. Results: In comparison to the control group, patients with ILD had a lower number of steps (5055 ± 2089 vs 8159 ± 3283 steps / day, p = 0.0002), less time spent in moderate to vigorous activity (8-16) vs 30 [15-47] min / day, p <0.0001) and shorter time in standing posture (290 ± 87 vs 392 ± 65 min, p = 0.0003) 91 vs. 197 ± 66 min, p = 0.0003). In addition, the patients had significantly longer duration of daytime sleep (56 ± 108 vs 6 ± 19 min, p = 0.01). The regression models identified lung function (diffusion capacity of carbon monoxide, DLCO) and sleep duration at night and during the day to partially explain daily steps, time in light activities and time in moderate to vigorous activities . (0.26 <r2 <0.58, p <0.05 for all). Conclusion: Patients with ILD have a worse profile of physical activity when compared to healthy individuals in the group. Daily physical activity is negatively influenced by poorer lung function and longer sleep duration (both at night and during the day).

**Keywords:** Interstitial lung disease. Sleep. physical activity.

## LISTA DE FIGURAS

### CONTEXTUALIZAÇÃO



### ARTIGO

## LISTA DE TABELAS

## LISTA DE ABREVIAÇÕES

| | |
|---|---|
| ACSM | American College of Sports and Medicine |
| AFVD | Atividade física de vida diária |
| AVD | Atividade de vida diária |
| DIP | Doença intersticial pulmonar |
| DPOC | Doença pulmonar obstrutiva crônica |
| $VE/VO_2$ | Relação entre volume minuto e consumo de oxigênio |
| 6MWT | six-minute walk test |
| BMI | body mass index |
| COPD | chronic obstructive pulmonary disease |
| DLCO | diffusion capacity of carbon monoxide |
| DPA | daily physical activity |
| FEV1 | forced expiratory volume on the first second |
| FVC | forced vital capacity |
| HG | handgrip |
| HRQoL | health-related quality of life |
| ILD | interstitial lung disease |
| IPF | idiopathic pulmonary fibrosis |
| MEP | maximal expiratory pressure |
| MIP | maximal inspiratory pressure |
| MRC | Medical Research Council Scale |
| MVIC | maximal voluntary isometric contraction |
| MVPA | moderate-to-vigorous physical activity |
| MVV | maximal voluntary ventilation |
| QF | quadriceps force |
| SAS | Statistical Analysis System |
| SF-36 | Medical Outcomes Health Survey Short-Form 36-item |
| TCAR | Tomografia computadorizada de alta resolução |
| TLC | total lung capacity |

**SUMÁRIO**

## 1. INTRODUÇÃO

As doenças intersticiais pulmonares (DIP) são um grupo de doenças que apresentam características clínicas semelhantes, como inflamação alveolar crônica, fibrose difusa do parênquima pulmonar e, como consequência, déficit nas trocas gasosas (1–3). Embora a causa primária da maioria das DIPs ser pulmonar, as manifestações não se restringem ao sistema respiratório e resultam em manifestações extrapulmonares. Dentre essas manifestações, os pacientes geralmente apresentam intolerância ao exercício, disfunção muscular e baixos níveis de atividade física de vida diária (AFVD) (3).

Os níveis de AFVD têm se mostrado como um importante desfecho para pacientes com doenças respiratórias crônicas. Na doença respiratória obstrutiva crônica (DPOC), este desfecho aparece como um dos pontos principais para o conhecido ciclo vicioso da doença (i.e. dispneia – inatividade – descondicionamento físico) (4). Além disso, baixos níveis de AFVD estão associados com mortalidade, tanto em DPOC, quanto em DIP (5,6). Desde meados da última década há estudos investigando os níveis de AFVD em pacientes com DPOC (5,7–10). Em contrapartida, a avaliação da AFVD em pacientes com DIP ainda é relativamente recente com apenas poucos estudos publicados sobre o tema (6,11–14). As evidências disponíveis em pacientes com DIP se restringem a descrição de um número menor de passos/dia (independentemente da doença intersticial de base) em comparação com indivíduos saudáveis (11,12,15). Outros aspectos dos níveis de AFVD como tempo gasto em diferentes posturas e tempo gasto em atividades de diferentes intensidades estão diretamente relacionados com pior prognóstico em pacientes com DPOC (5,10). Apesar da semelhança na redução do número de passos entre pacientes com DIP e DPOC (10,16), ainda não há estudos investigando se o comportamento dos níveis de AFVD em DIP são similarmente menores que os de indivíduos saudáveis. Tampouco há informação na literatura sobre eventuais fatores que podem estar relacionados com piores níveis de AFVD em DIP.

Nesta dissertação será apresentado um trabalho desenvolvido durante o mestrado com o objetivo de caracterizar a AFVD de pacientes com DIP além de investigar a relação de outros desfechos clínicos (e.g, capacidade de exercício, força muscular, sintomas e qualidade/quantidade de sono) com a AFVD.

# 2. CONTEXTUALIZAÇÃO

## *2.1. Doenças Intersticiais Pulmonares (DIP)*

Doença intersticial pulmonar (DIP) é um termo genérico para um grupo de mais de 200 doenças diferentes que apresentam uma variação considerável em termos de curso clínico, tratamento e prognóstico(1–3). De modo a identificar o diagnóstico, é necessária uma avaliação clínica inicial onde são identificadas características de doença sistêmica (por exemplo, doença do tecido conjuntivo) ou fatores ambientais que possam desencadear a DIP (2,17). Estes fatores ambientais incluem: drogas pneumotóxicas, radioterapia, exposições ocupacionais (e.g. asbestose) ou alérgenos (e.g. pneumonite de hipersensibilidade) (2). Todas as DIPs são caracterizadas por inflamação e fibrose de magnitude variável.

Para avaliação inicial e diagnóstico das DIP, a radiografia do tórax é frequentemente a primeira investigação radiológica e, embora raramente seja suficiente para fazer um diagnóstico confiável diferencial entre as diferentes patologias, a radiografia pode desempenhar um papel no estabelecimento da gravidade e progressão da doença (2,3). Já a tomografia computadorizada de alta resolução (TCAR) do tórax revolucionou o diagnóstico e a classificação da DIP e, em muitos casos, elimina a necessidade de procedimentos diagnósticos invasivos (2,3,18). No entanto, a qualidade das imagens depende do protocolo utilizado. As características e padrões encontrados na TCAR variam de acordo com a patologia, o que auxilia no diagnóstico. Os principais padrões encontrados são: padrão reticular (bronquiectasias), padrão de vidro fosco e faveolamento (fibrose pulmonar idiopática [FPI]) e padrão nodular (sarcoidose) (2,3,18).

Além dos exames de imagem, outros exames complementares são importantes para avaliar a gravidade da doença e auxiliar no manejo clínico destes pacientes. Dentre estes exames podemos incluir os testes laboratoriais (hemograma, gasometria arterial, fatores autoimunes), testes de função pulmonar, incluindo a medida de difusão de monóxido de carbono (DLCO) e medida de saturação periférica de oxigênio (SpO2) no esforço (2,3).

*2.2. Comprometimento Pulmonar*

A maioria das DIP apresentam um padrão comum de anormalidade fisiológica, com um distúrbio ventilatório restritivo (19,20). Vários mecanismos, como a perda de volume, redução da distensibilidade alveolar e/ou do tamanho alveolar e aumento da tensão superficial devido a anormalidades do surfactante, podem afetar a mecânica pulmonar nas DIP (3). Consequentemente, as DIP estão associadas à contração da curva estática pressão-volume, reduzindo assim o volume pulmonar e a complacência pulmonar e aumentando a pressão de recuo pulmonar ao longo da amplitude da capacidade inspiratória (19,20).

Como resultado dessas alterações, os volumes pulmonares estáticos são tipicamente reduzidos (3,19,20). Porém a redução dos volumes pulmonares não acontece de forma uniforme (3,19,20). As mudanças na capacidade vital (CV) são geralmente maiores que na capacidade residual funcional (CRF) no volume residual (VR) (3,19,20). A CPT é geralmente menos afetada pelo recuo da parede torácica normal ou quase normal e pela preservação da função muscular inspiratória na maioria dos pacientes (3). O volume residual (VR) geralmente está preservado na maioria dos casos (3,19,20). Assim, a capacidade pulmonar total (CPT) é geralmente menos reduzida que a CV e a relação VR/CPT podem ser estar aumentadas nas DIP (3,19,20).

O mecanismo pelo qual a CRF e o VR podem ser preservados ainda não está claro, porém, isto pode ser uma consequência do fechamento prematuro de pequenas vias aéreas e aprisionamento aéreo ou de alterações císticas no parênquima pulmonar (19). Embora estas pequenas vias aéreas possam ser estreitadas por fibrose ou infiltrados inflamatórios, as vias aéreas de maior calibre são geralmente preservadas (19). Isto faz com que o volume expiratório (volume expiratório forçado no primeiro segundo [VEF1]) corrigido pelo fluxo aéreo (VEF1/CVF) apresentem valores normais (19).

A capacidade de difusão (DLCO) é reduzida em pacientes com DIP, e representa o teste mais sensível da função respiratória por estar diretamente relacionado com a capacidade de troca gasosa (3,19). A redução dos volumes pulmonares e a má distribuição do gás inspirado podem contribuir para a redução da DLCO. Tanto o distúrbio entre a relação ventilação/perfusão quanto o bloqueio alvéolo-capilar são atualmente considerados como os dois fatores determinantes relevantes da troca gasosa anormal nas DIP (3,19). Devido a isto, os pacientes

ambulatoriais com DIP, podem apresentar na gasometria arterial uma hipoxemia em repouso e, especialmente, no exercício (3).

*2.3. Comprometimento sistêmico nas Doenças Intersticiais Pulmonares.*

Além dos comprometimentos pulmonares e sinais clínicos descritos acima, pacientes com DIP comumente apresentam uma série de complicações sistêmicas que afetam diretamente o estado geral de saúde. A queixa principal de pacientes com DIP costuma ser dispneia, que piora com a realização de atividades físicas, como andar longas distâncias ou subir escadas (3). Nos casos mais avançados, a dispneia pode estar presente durante a realização de atividades de vida diária (AVD), por exemplo, tomar banho ou se vestir(3). Além da dispneia, estes pacientes apresentam tosse, mas geralmente sem presença de secreção (3).

Pacientes com DIP apresentam limitação da tolerância ao exercício. As causas da limitação são multifatoriais e estão geralmente associadas à sensação de dispneia e/ou fadiga muscular dos membros inferiores. Os mecanismos primários da limitação ao exercício nestes pacientes podem ser pulmonares, hemodinâmicos ou musculares (21–23). A figura 1 exemplifica a interação entre esses fatores. Em suma, durante o esforço, a relação entre ventilação e consumo de oxigênio ($VE/VO_2$) é aumentada. Ou seja, para uma determinada taxa metabólica o volume minuto é maior que o observado em indivíduos saudáveis (21). Ao mesmo tempo, o gasto energético por ciclo respiratório é elevado devido ao aumento da pressão de recolhimento estático dos pulmões e consequente maior atividade muscular inspiratória (21). A destruição do leito vascular por fibrose parenquimatosa progressiva, vasoconstrição hipóxica e volumes pulmonares reduzidos contribuem para o aumento da resistência vascular pulmonar na DIP (21,23–25). Esta limitação circulatória resultante da destruição capilar pulmonar e da vasoconstrição hipóxica, leva à hipertensão pulmonar e à disfunção cardíaca, também desempenhando importante papel na limitação do exercício (21,23,24). Além disso, o volume de ejeção está relativamente reduzido nos pacientes com DIP (26). Consequentemente, estes pacientes geralmente apresentam valores de frequência cardíaca acima do normal em níveis submáximos de exercício (26). Por fim, disfunção muscular periférica também é um importante contribuinte para a intolerância ao exercício em pacientes com DIP, já que a força e resistência muscular do quadríceps se

mostraram diminuídas nesta população (29–30). Embora ainda não tenham sido encontradas evidências de relação causal em DIP, vários fatores já foram estabelecidos como agentes causais da disfunção muscular, como: hipoxemia crônica, estresse inflamatório e oxidativo, uso de corticosteroides, inatividade física e desnutrição (29). Esses fatores podem exercer um efeito prejudicial sobre a função muscular, de forma que a hipoxemia de repouso e/ou ao esforço associado com o aumento do trabalho respiratório torna os músculos respiratórios e periféricos mais propensos à fadiga (22,30–33).

*2.4. O impacto da doença nas atividades físicas de vida diária*

Uma consequência comum da disfunção muscular e aumento da presença de sintomas observadas nesse grupo de pacientes é a redução dos níveis de atividade física na vida diária (AFVD). A inatividade física leva ao descondicionamento muscular e a um ciclo vicioso de piora da capacidade de exercício e aumento dos sintomas (4). A recomendação do American College of Sports and Medicine (ACSM) é de que indivíduos adultos devem atingir um gasto energético, durante a atividade física, de pelo menos 450 MET/semana (34) para que se obtenha benefícios na saúde e seja considerado ativo. Porém, pacientes com DPI frequentemente adotam um estilo de vida sedentário, que pode exercer efeitos prejudiciais no estado geral de saúde (3).

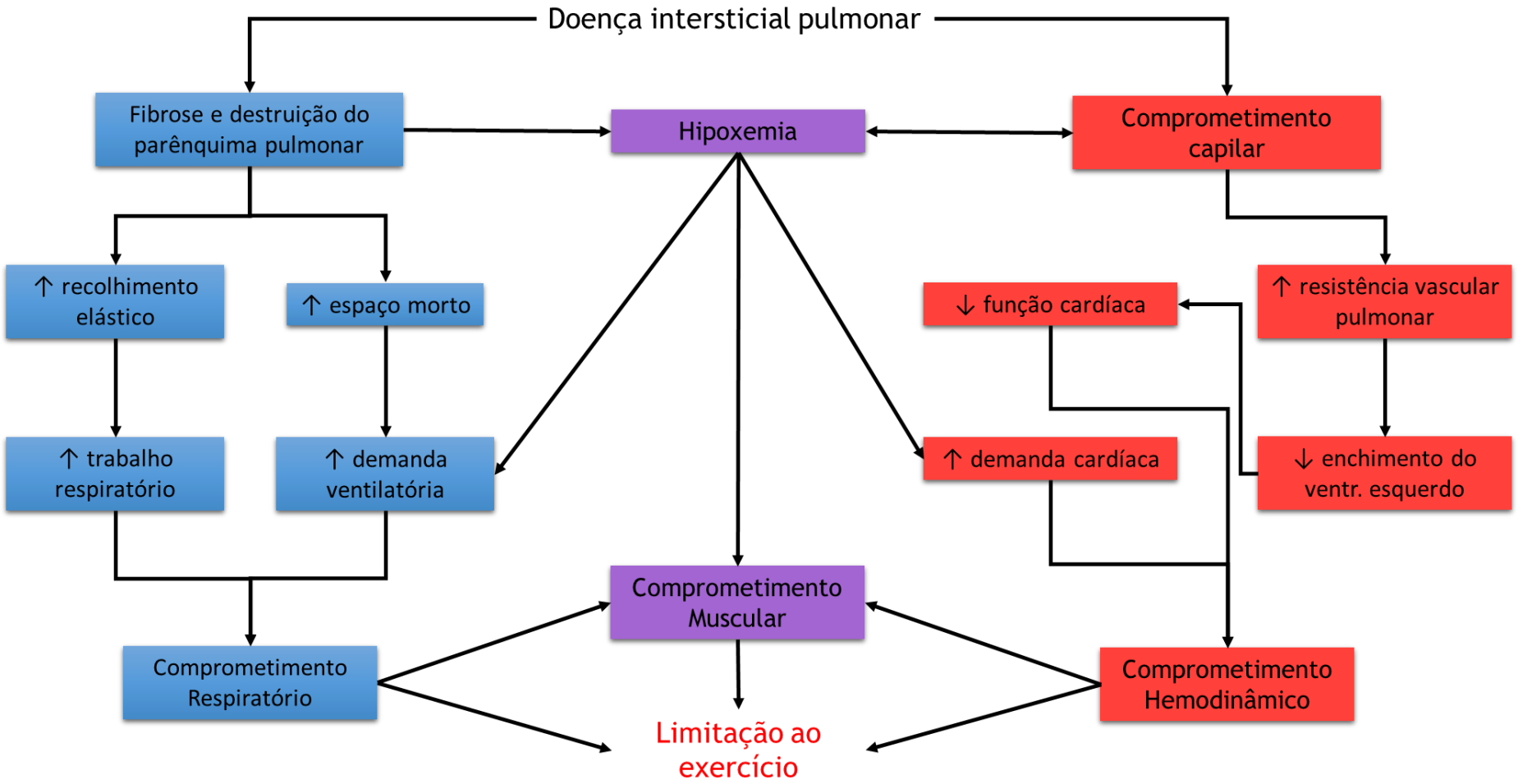
A AFVD é um parâmetro clínico significativo e está relacionado com mortalidade em pacientes com fibrose pulmonar idiopática (FPI) (6,12,35). Além disso, neste mesmo grupo de doentes, a AFVD apresenta correlação com capacidade de exercício (36). Estudos prévios que avaliaram a atividade física de vida diária (AFVD) em DIP demonstraram que há uma redução nos níveis de AFVD em comparação com indivíduos saudáveis (15). Os estudos reportam principalmente a redução no número de passos destes pacientes comparados com controles saudáveis (11,12,15,36). A AFVD, porém, é composta por outros aspectos como o gasto energético, tempo e intensidade durante atividades, além de tempo gasto em diferentes posturas (5). Estes desfechos, que são comumente captados por meio de monitores de atividade física (5), foram pouco investigados até o momento.

Mais recentemente, o sono tem surgido como um fator que também pode influenciar nos níveis de AFVD (37). A incidência de comorbidades relacionada ao

sono em pacientes com DIP é alta (38,39) e pacientes com doenças respiratórias crônicas geralmente apresentam uma qualidade do sono ruim (40). O sono dos pacientes com DIP, assim como a AFVD, pode ser avaliada de forma subjetiva ou objetiva. Existem questionários que permitem avaliar a qualidade do sono e o grau de sonolência diurna (41–44). O método “padrão ouro” para avaliação do sono é a polissonografia. Por se tratar de uma avaliação que necessita de treinamento e colaboração do paciente, o uso de outros dispositivos mais simples, como os acelerômetros, tem sido difundido para auxiliar na avaliação do sono (45). Comparada à polissonografia, o uso destes dispositivos ainda apresenta limitações, principalmente relacionadas ao local do corpo a ser utilizado, sendo que o uso no punho parece ser o mais adequado (46). Para pacientes com doença pulmonar obstrutiva crônica (DPOC) já foi demonstrado a relação entre o sono e a AFVD (47), porém esta relação ainda não foi investigada em DIP.

Diante de todas as repercussões apresentadas, pulmonares e sistêmicas, causadas pela DIP, e, levando em conta a semelhança na redução da AFVD entre pacientes com DIP e DPOC, torna-se importante investigar se os níveis de AFVD em DIP são similarmente menores que os de indivíduos saudáveis. Além disso, há também a necessidade em investigar eventuais fatores que podem estar relacionados com piores níveis de AFVD em DIP. Portanto, o estudo que compõe esta dissertação faz-se importante para tentar elucidar estas questões e permitir uma melhor caracterização da AFVD desta população. Desta forma, em estudos futuros poderão ser realizadas intervenções mais direcionadas à melhorar este desfecho.

*Figura 1 - Relação entre fatores que contribuem para limitação do exercício em pacientes com doença intersticial pulmonar.*




Fonte: O próprio autor.

## 3. ARTIGO ORIGINAL

***Artigo original formatado de acordo com as normas do periódico Respiratory Medicine; Fator de Impacto: 3.23; Qualis: A2***

# PROFILE OF PHYSICAL ACTIVITY AND ITS DETERMINANTS IN INTERSTITIAL LUNG DISEASE

Humberto Silva, PT[1,2]; Leandro Cruz Mantoani, PT PhD[1]; Wagner Florentin Aguiar, PT[1]; Aline Ferreira Lima Gonçalves, PT[1]; Thatielle Garcia da Silva, PT[1]; Marcos Ribeiro, MD PhD[2,3]; Vanessa Suziane Probst, PT, PhD[1]; Fabio Pitta, PT PhD[1,2]; Carlos Augusto Camillo, PT PhD[1,2,4].

[1]Post-graduation programme in Rehabilitation Sciences, Centre of Research and Post-graduation, Londrina State University, Londrina, Brazil.
[2]Laboratory of research in respiratory physiotherapy (LFIP), Physiotherapy Department, Londrina State University, Robert Koch Avenue 60, Postal code 86038-350, Londrina, Brazil.
[3]Department of Pneumology, Londrina State University, Londrina, Brazil.
[4]Department of Rehabilitation Sciences, University Pitágoras UNOPAR, Londrina, Brazil.

**Corresponding Author:**
Carlos Augusto Camillo, PhD
Centro de Pesquisa e Pós-Graduação - Unidade Piza
Rua Marselha, 519 - Parque Residencial Joaquim Toledo Piza, 86041-140 - Londrina, Paraná, Brasil.
E-mail: carlos.a.camillo@outlook.com

**Running title:** Characteristics and determinants of physical activity in ILD

**Abbreviation List:**

6MWT: Six-minute walk test

BMI: Body-mass index

COPD: Chronic obstructive pulmonary disease

$D_LCO$: Diffusion capacity of the lung for carbon monoxide

DPA: Daily physical activity

$FEV_1$: Forced expiratory volume on the first second

FVC: Forced vital capacity

HG: Handgrip force

HRQoL: Health-related quality of life

ILD: Interstitial lung disease

IPF: Idiopathic pulmonary fibrosis

MEP: Maximal expiratory pressure

MIP: Maximal inspiratory pressure

MRC: Medical Research Council Scale

MVIC: Maximal voluntary isometric contraction

MVPA: Moderate-to-vigorous physical activity

MVV: Maximal voluntary ventilation

QF: Quadriceps force

SF-36: Medical Outcomes Health Survey Short-Form 36-item

TLC: Total lung capacity

***ABSTRACT***

**Background:** The factors that could influence daily physical activity (DPA) is not fully investigated in patients with interstitial lung disease (ILD). **Aims:** To characterize DPA and to investigate the relationship between DPA and clinical outcomes as well as to identify determinants of DPA. **Methods:** Patients with diagnosis of ILD and apparently healthy subjects were recruited (Control group). Subjects underwent evaluations of pulmonary function, exercise capacity, respiratory and peripheral muscle strength, physical activity, sleep, dyspnoea and health-related quality of life. DPA and sleep measures were assessed using an activity monitor (Actigraph®, wGT3x-BT) on their waist for six consecutive days, during 24 hours. **Results:** In comparison with the control group, patients with ILD presented lower number of steps (5055 ± 2089 vs 8159 ± 3283 steps/day, p = 0.0002), less time spent in moderate-to-vigorous activity (8 [3 – 16] vs 30 [15 – 47] min/day, p<0.0001) and in standing position (290 ± 87 vs 392 ± 65 min, p=0.0003), and more time spent in lying position (288 ± 91 vs 197 ± 66 min, p=0.0003). Additionally, patients presented significantly larger duration of sleep time during the day (56 ± 108 vs 6 ± 19 min, p=0.01). Regression models identified lung function (diffusion capacity of carbon monoxide, $D_LCO$) and sleep duration at night and during the day to partially explain daily steps, time in light activities and time in moderate to vigorous activities. ($0.26<r^2<0.58$; p<0.05 for all). **Conclusion:** Patients with ILD present a lower levels of physical activity compared to a group healthy subjects. Daily physical activity is negatively influenced by worse lung function and longer sleep duration (both at night and during the day).

**Keywords:** Interstitial lung disease, sleep, physical activity

## Introduction



Daily physical activity (DPA) has been the focus of many studies in respiratory chronic diseases in the last years. Inactivity in daily life presents a major health issue and is consistently described as both cause and consequence of different chronic diseases (e.g., obesity, cardiovascular disease, diabetes, cancer)[1]. Moreover, physical inactivity is responsible for a substantial economic burden worldwide[2].

Patients with interstitial lung disease (ILD) present extrapulmonary manifestations, such as exercise intolerance, muscle dysfunction, and lower levels of daily life participation [3,4]. The reduced daily levels of physical activity is a known feature in respiratory patients [5]. Inactivity is also one of the key-factors of the vicious cycle of chronic respiratory diseases (including ILD). Reduced daily activities due to symptoms of dyspnoea induce a muscle dysfunction that in turn worsens the exercise capacity increasing symptoms of dyspnoea during activities of even lower intensities [5–7]. The downward spiral of symptom-induced inactivity may eventually lead to worse prognosis, as reported in patients with idiopathic pulmonary fibrosis (IPF) [8,9].

Although there is some preliminary evidence of a reduced number of daily steps in patients with different ILD [10–12]. Other domains of DPA such as time spent in different body positions, intensity of activities and sedentary time remain to be unveiled in this group of patients. DPA has a multidimensional approach and may be influenced by many factors, such as environmental, social, climatic and behavioural factors [5]. Recently, the measurements of nocturnal sleep appear as a factor that could impact DPA of patients with chronic obstructive pulmonary disease (COPD) [13]. In spite of the high prevalence of sleep disturbances [14] the relationship between DPA and sleep measurements in patients with ILD, remains unclear.

This study aimed to characterize the different domains of DPA in patients with ILD and to investigate the relationship between DPA and different clinical outcomes

including sleep measures. Moreover, potential determinants of DPA in this population were investigated. We hypothesized that patients with ILD are less active than a group of apparently healthy subjects and that sleep plays a role on daily activity levels in subjects with ILD.

## Methods

This was a cross-sectional study performed at the University Hospital of the Londrina State University (Londrina, Brazil). This study is part of a larger ongoing trial (BELIEVE-ILD) which was approved by the local ethic committee of the institution (#2.484.871). All subjects provided a written consent prior to their participation in the study. Patients with diagnosis of interstitial lung disease according to international guidelines [15,16] were included if they had stable clinical condition (absence of exacerbations) for at least 1 month prior the recruitment and if they did not present any clinical condition that could interfere on the assessments (e.g. musculoskeletal limitations, severe or unstable cardiovascular disease and neuromuscular disease). A group of apparently healthy subjects were recruited as a control group. Participants in the control group would be excluded from the study if presented any evidence of lung disease which was unknown prior to the inclusion. Only participants in both groups with valid data of the primary outcome were included in the statistical treatment.

After the inclusion, patients performed a set of evaluations including complete pulmonary function, exercise capacity, respiratory and peripheral muscle strength, daily physical activity, sleep measures, symptoms and health-related quality of life. Details of the tests are described below.

Lung function was assessed using pre and post bronchodilator spirometry, whole-body plethysmography and diffusion capacity of carbon monoxide ($D_LCO$) (Vmax, CareFusion®) according to international guidelines [17–20]. Obtained values were compared to normative data of the Brazilian population [21–23].

Exercise capacity was evaluated by the 6-minute walk test (6MWT). The test was performed twice, and the highest values used for the analysis. The adopted protocol followed international guidelines for field tests [24]. Obtained values were compared to normative data [25].

Respiratory muscle strength was assessed by the maximal respiratory pressures (inspiratory [MIP] and expiratory [MEP]) using a digital manometer (MVD300®, Globalmed, Brazil). The test was performed according to the international guidelines [26,27] and obtained values compared to normative data [28].

Peripheral muscle strength was assessed by handgrip and quadriceps force. The handgrip force of the dominant member was evaluated with a hand dynamometer [29]. (SH1001, Saehan Corporation, Korea). Quadriceps force was assessed by the maximal voluntary isometric contraction (MVIC) of the dominant limb using a strain gauge (EMG System®, Brazil) attached to a stationary multigym device (CRW 1000, CRW, Brazil) [2930].

Symptoms of dyspnoea were assessed by the Medical Research Council (MRC) scale [31] and Health-Related Quality of Life (HRQoL) by the Medical Outcomes Health Survey Short-Form 36-item (SF-36) [32].

*DPA and sleep assessment*

Subjects were instructed to wear an activity monitor (Actigraph®, wGT3x-BT) on their waist for six consecutive days, during 24 hours, including sleeping time. This activity monitor is validated in other patients with respiratory diseases as a reliable

method to assess DPA [33,34]. The device measures wearing time and records continuous DPA, daily steps, time spent in different postures (lying, sitting and standing), daily energy expenditure, time spent in different intensities (sedentary, light, moderate to vigorous) and duration of the sleep. DPA assessment was considered valid if the subject wore the monitor for at least 8 hours/day for at least 4 days [35]. DPA and sleep measurements data were analysed by the software ActiLife® (Actigraph).

*Statistical analysis*

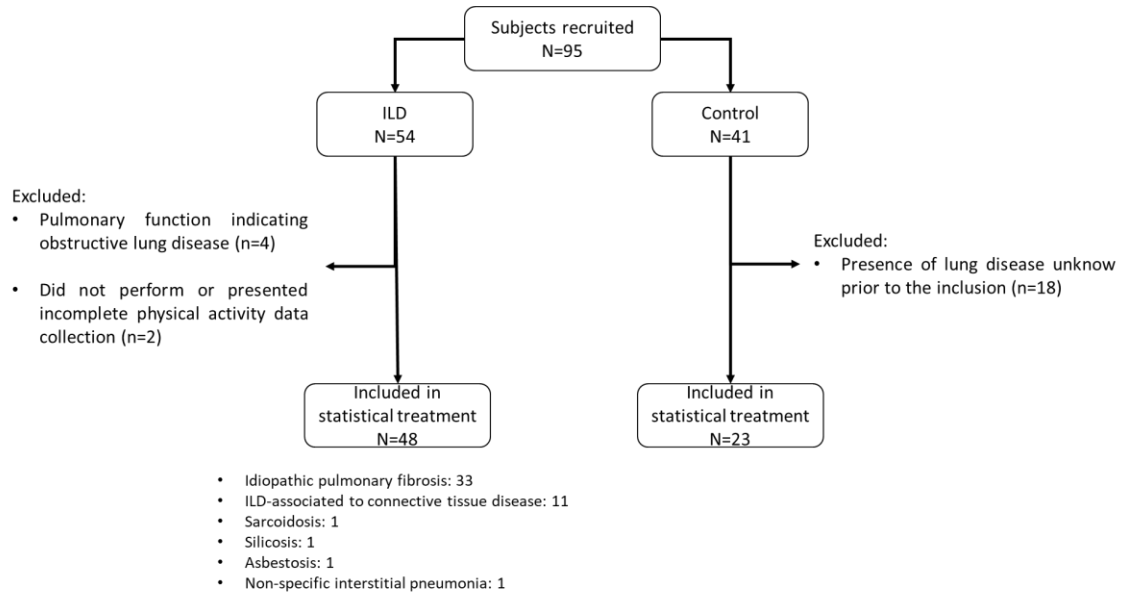
Normality of data was verified using the Shapiro-Wilk test. Data was expressed as mean ± standard deviation or median [interquartile range] according to its distribution. Comparisons of outcomes between ILD patients and the control group were done using the unpaired t tests or its equivalent non-parametric test (Mann-Whitney). Correlations between DPA variables and all other clinical outcomes were done were done using Pearson's or Spearman's coefficient correlation according to the distribution of the data. Specifically, the relation between sleep measurements and DPA in patients with ILD were done as follows: 1- correlations between the weekly average of the duration of sleep at night and the weekly average of DPA variables was done using Pearson or Spearman's coefficient as mentioned above; 2- correlations between the duration of sleep at night and DPA variables of the very following day were done using a day-by-day analysis with the generalized estimating equations. In patients with ILD, variables presenting significant correlation with DPA outcomes were included in a stepwise linear multiple regression model to identify variables that could explain DPA. In the presence of collinearity in the model, only the variable with the highest significant correlation coefficient was retained in the model.

All statistical tests were performed using Statistical Analysis System (SAS®) Studio 9.4. Statistical significance was set at $p < 0.05$.

## Results

Ninety-five participants were recruited and evaluated for inclusion. Of these, seventy-one (ILD=48 and Control=23) were included in the final analysis of the study (Figure 1).

*Figure 1 - Flowchart of recruitment and inclusion of the subjects in the study.*




*ILD: interstitial lung disease.*

Characteristics of all participants are described in **Table 1**. As expected, patients with ILD presented worse: lung function, exercise capacity, muscle strength and HRQoL compared to the control group.

**Table 1. Characteristics of studied subjects**

| Outcomes | ILD (n=48) | CONTROL (n=23) | p value |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Age, years | 61 ± 11 | 58 ± 9 | 0.22 |
| Sex, Male (%) | 20 (42) | 9 (39) | 0.83 |
| BMI, kg/m$^2$ | 27.9 ± 4.8 | 26.9 ± 5.1 | 0.32 |
| Comorbidities, n | 3 [1 – 5] | 2 [1 -3] | 0.02 |
| ***Pulmonary function*** | | | |
| FVC, L | 2.47 ± 0.75 | 3.73 ± 1.09 | <0.0001 |
| $FEV_1$, L | 2.03 ± 0.59 | 2.98 ± 0.80 | <0.0001 |
| FVC, % of predicted | 74 ± 18 | 100 ± 11 | <0.0001 |
| $FEV_1$, % | 77 ± 19 | 101 ± 11 | <0.0001 |
| FEV1/FVC | 82 ± 5 | 80 ± 4 | 0.08 |
| MVV, L | 95 ± 31 | 129 ± 38 | 0.0007 |
| MVV, % of predicted | 82 ± 21 | 99 ± 13 | <0.0001 |
| TLC, L | 4.61 ± 1.73 | 6.15 ± 1.76 | 0.0003 |
| TLC, % | 86 ± 31 | 99 ± 13 | 0.0006 |
| $D_LCO$, mL/mmHg/min | 12.9 ± 5.4 | 24.4 ± 6.1 | <0.0001 |
| $D_LCO$, % | 49 ± 20 | 85 ± 11 | <0.0001 |
| ***Exercise capacity*** | | | |
| 6MWT, m | 470 ± 97 | 588 ± 78 | <0.0001 |
| 6MWT, % of predicted | 87 ± 16 | 109 ± 11 | <0.0001 |
| ***Peripheral muscle strength*** | | | |
| QF, N | 358 ± 155 | 451 ± 175 | 0.01 |
| HG, kgf | 26 ± 10 | 32 ± 12 | 0.05 |
| ***Respiratory muscle strength*** | | | |
| MIP, cmH2O | 89 ± 37 | 109 ± 32 | 0.02 |
| MEP, cmH20 | 104 ± 34 | 130 ± 47 | 0.03 |
| MIP, % of predicted | 98 ± 34 | 116 ± 25 | 0.01 |
| MEP, % of predicted | 111 ± 30 | 137 ± 47 | 0.02 |
| ***Health-related quality of life (SF-36)*** | | | |
| Physical functioning, % of impact | 35 [25-60] | 75 [65-85] | <0.0001 |
| Physical role, % of impact | 25 [0-100] | 100 [100-100] | <0.0001 |
| Pain index, % of impact | 51 [36-62] | 61 [51-72] | 0.006 |
| General health perceptions, % of impact | 47 [32-57] | 67 [57-72] | <0.0001 |
| Vitality, % of impact | 60 [45-70] | 75 [60-80] | <0.001 |
| Social functioning, % of impact | 33 [0-100] | 88 [63-100] | 0.01 |
| Emotional role, % of impact | 63 [50 -100] | 100 [67-100] | 0.001 |
| Mental health index, % of impact | 68 [56-76] | 76 [64-84] | 0.03 |

BMI: body mass index; FVC: forced vital capacity; $FEV_1$: forced expiratory volume on the first second; MVV: maximal voluntary ventilation; TLC: total lung capacity; DLCO: diffusion capacity of carbon monoxide; 6MWT: six-minute walk test; QF: quadriceps force; HG: handgrip; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure, SF-36: Medical Outcomes Health Survey Short-Form 36-item.

Patients with ILD were less active in daily life compared to controls, presenting lower number of steps (5055 ± 2089 vs 8159 ± 3283 steps/day, p = 0.0002) and less time spent in moderate-to-vigorous physical activity (MVPA – 8 [3 – 16] vs 30 [15 – 47] min/day, p<0.0001) (**Table 2; Figure 2**).

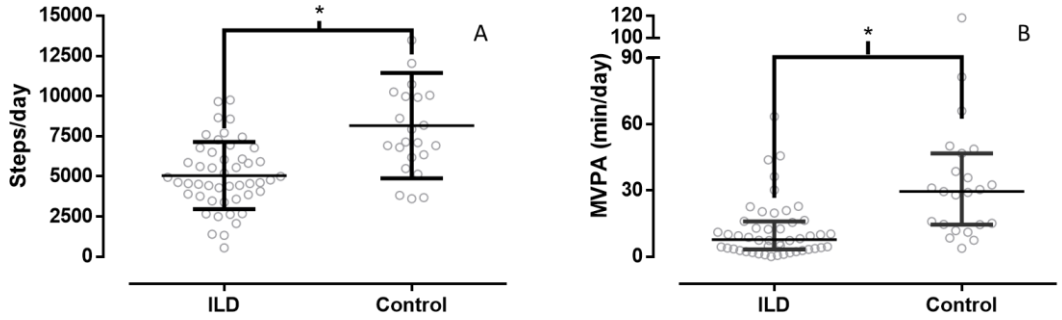
**Table 2. Comparisons of daily physical activity and sedentarism variables between groups**

| VARIABLE | ILD (n=48) | CONTROL (n=23) | p value |
|---|---|---|---|
| Steps, n/day | 5055 ± 2089 | 8159 ± 3283 | 0.0002 |

| | | | |
|---|---|---|---|
| Sedentary activity, min/day | 777 [712 - 897] | 785 [721 - 937] | 0.48 |
| Sedentary activity, %/day | 72 [66 – 77] | 67 [64 – 75] | 0.17 |
| Light activity, min/day | 311 [243 - 355] | 342 [293 - 362] | 0.15 |
| Light activity, %/day | 28 [21 - 34] | 30 [23 – 32] | 0.47 |
| MVPA, min/day | 8 [3 - 16] | 30 [15 - 47] | <0.0001 |
| MVPA, %/day | 0.6 [0.3 - 1.2] | 2.5 [1.3 – 3.9] | <0.0001 |
| Lying, min/day | 288 ± 91 | 197 ± 66 | 0.0003 |
| Sitting, min/day | 467 ± 108 | 452 ± 91 | 0.62 |
| Standing, min/day | 290 ± 87 | 392 ± 65 | 0.0003 |

MVPA: moderate-to-vigorous physical activity. %/day : time spent corrected by wearing time.

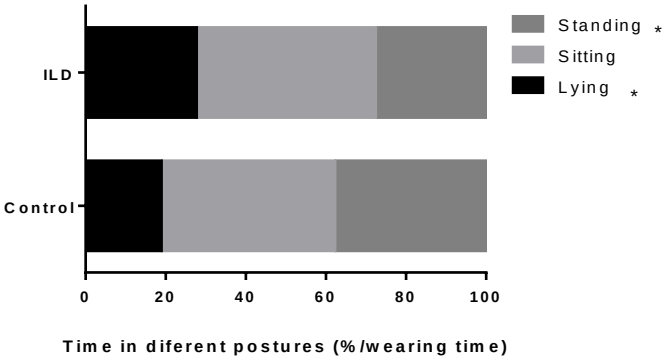
Figure 2 - Comparison of mean steps/day (A) and moderate to vigorous physical activity (B) between groups.




ILD: interstitial lung disease. MVPA: moderate to vigorous physical activity. *p<0.05.

No differences were found in time spent in sedentary and light activities between groups. Patients with ILD spent more time in lying position (288 ± 91 vs 197 ± 66 min, p=0.0003) and less time in standing position (290 ± 87 vs 392 ± 65 min, p=0.0003) compared to controls (**Table 2**). When adjusted the time in different postures by the wearing time, the difference of time in standing and lying position remained (Figure 3).

Figure 3 - Time spent in different postures adjusted by wearing time.




*ILD: interstitial lung disease. *p<0.05*

There were no differences regarding the time spent sleeping during the night (521 ± 101 vs 523 ± 97 min, p=0.98) between ILD and control subjects, respectively. However, patients with ILD spent significantly (p=0.01) more time sleeping during the day (56±108min) in comparison with the control group (6±19min).

In patients with ILD, significant correlations were found between daily steps and: $D_LCO$ (r=0.38, p=0.01), handgrip force (r=0.38, p=0.008), 6MWT (r=0.40, p=0.006) and MRC (r=-0.36, p=0.01). Time spent in light activities (min/day) correlated with 6MWT (r=0.30, p=0.04). Additionally, the time spent in MVPA (min/day) correlated with: $D_LCO$ (r=0.47, p=0.002), handgrip force (r=0.49, p=0.0004), quadriceps force (r=0.38, p=0.008), 6MWT (r=0.39, p=0.009) and MRC (r=-0.40, p=0.007).

When analysed as weekly average, duration of sleep at night correlated with steps counts (r=-0.52, p=0.0002), time spent in light activities (r=-0.61, p<0.0001) and MVPA (r=-0.42, p=0.002). Day-by-day correlation analysis (using generalized estimating equations) was done using a total of 241 nights in ILD. There was a significant correlation between duration of sleep at night and the time spent in light activities in the following's day (r= -0.35, p<0.0001).

Finally, regression models (Table 3) showed that the $D_LCO$, duration of sleep at night and during the day partially explained variations in daily step counts ($R^2$ = 0.49, p<0.0001), whilst time spent in light activities was partially explained by the duration of sleep at night and during the day ($R^2$ = 0.58, p<0.0001), and the time spent in MVPA was partially explained by the $D_LCO$ ($R^2$ = 0.26, p=0.001).

**Table 3. Factors associated with daily physical activity in interstitial lung disease (univariate and multivariate linear regressions).**

| **Model** | Variable | Univariate | | Multivariate | |
|---|---|---|---|---|---|
| ***Steps/day*** | | $R^2$ | p value | $R^2$ | p value |
| | Day sleep (min/day) | 0.24 | 0.0005 | 0.27 | 0.0008 |
| | DLCO (mL/mmHg/min) | 0.14 | 0.01 | 0.41 | 0.006 |
| | Night sleep (min/day) | 0.24 | 0.0005 | 0.49 | 0.03 |
| | 6MWT (m) | 0.16 | 0.006 | 0.53 | 0.11 |
| ***Light activity*** | | | | | |
| | 6MWT (m) | 0.09 | 0.04 | - | - |
| | Night sleep (min/day) | 0.39 | <0.0001 | 0.45 | <0.0001 |
| | Day sleep (min/day) | 0.25 | 0.0003 | 0.58 | 0.0013 |
| ***MVPA*** | | | | | |
| | Night sleep (min/day) | 0.24 | 0.0005 | - | - |
| | Day sleep (min/day) | 0.24 | 0.0005 | - | - |
| | DLCO (mL/mmHg/min) | 0.14 | 0.01 | 0.26 | 0.001 |
| | 6MWT (m) | 0.16 | 0.006 | 0.33 | 0.07 |

DLCO: diffusion capacity of carbon monoxide; 6MWT: six-minute walk test.

## DISCUSSION

Patients with ILD present worse daily physical activity profile compared with apparently healthy subjects, showing lower number of steps, less time spent in MVPA and in standing position, and more daily time spent lying. Longer sleep durations influence negatively the time spent in light activities and the number of steps specially if this pattern is consistently repeated along the week.

Previous studies showed an inactive profile of patients with ILD [9–12,36–38]. Typical findings comprise reduction of daily steps [9–12,39] and reduction of intensity of daily activities [10,36]. Our study confirms these findings and add to the discussion that

patients with ILD also spend more time in sedentary behaviour (i.e. higher time spent in lying position and sleeping during the day). This is particularly important as both inactivity and sedentarism have been linked with negative outcomes in other respiratory diseases [40,41]. Interestingly, the behaviour observed in our patients do not appear to be a novelty considering respiratory diseases. Studies in other respiratory chronic diseases, such as COPD, have vastly pointed global reductions in daily physical activities [5]. Similar to our findings, Pitta et al. [42] reported that patients spent more time lying and less time standing on daily life when compared to healthy elderly subjects.

Previous studies investigating the association between the number of steps and other clinical outcomes demonstrated a moderate correlation with $D_LCO$ [12] and 6MWT [10,12,43]. Our study found a similar correlation with DLCO (r= 0.49) and with 6MWT (r=0.35). In addition, this is the first study that investigated possible relation with other variables of DPA different than number of daily steps (i.e. time in different postures and in different physical activity intensities) with clinical outcomes.

A recent study in in patients with COPD investigated the association between nocturnal sleep measures and DPA [13]. They found an inverse correlation between the number of steps performed during the day and the number of sleeping bouts and the minutes spent awake after the sleep onset. In addition, it was reported that patients who slept > 480 minutes/night walked less in the following day [13]. The sleep analyses in our study showed a correlation between the duration of the sleep at night and number of steps, time spent in light and MVPA on following day, showing that sleep disturbances are likely to be a common affecting factor of DPA in respiratory diseases.

A reduction in lung diffusion capacity and prolonged sleep duration at night were associated with different DPA outcomes. This is not particularly surprising as a reduction in $D_LCO$ implies the use of a less efficient metabolic pathway (i.e. anaerobic metabolism) to generate energy for daily tasks. In fact, physiological variables, such as those of pulmonary function, directly impact the activities that require greater effort. A novelty of this study is the association of a prolonged sleep duration at night and worse DPA in the following day. At first, this finding may seem counterintuitive, as longer nights of sleep are related to better overall health status. Longer nights, however, do not necessarily mean “better nights”. There is evidence that prolonged sleep duration at night in both respiratory patients and healthy subjects are related to worse overall health status [13,44]. Albeit our findings do not allow to extrapolate on the quality of the sleep, it is likely that sleep quality is also impaired in this group of patients. Future studies need to confirm whether both duration and quality of sleep play a role on the amount of DPA in ILD.

This study has some limitations and therefore our results need to be interpreted with caution. There was a disbalance between the number patients with different diagnosis in our study. Although this is in line with previous investigations [45],the extrapolation of our results to the population of patients with ILD may be inadequate. The instrument chosen to assess sleep measurements is widely used in other populations [13,46]. The sleep analysis provided by the Actigraph® is highly reliable when the device is used on the wrist (and not on the waist as in the present study). Albeit we acknowledge this as a limitation to interpret sleep data, the duration of sleep recorded from the device in our study is somewhat in line with previous investigations using both actigraph [46] and other devices [13] in other studies. To

mitigate misinterpretation of the data, all data related to quality of sleep from the Actigraph was not included in the present investigation.

In conclusion, patients with ILD present a worse physical activity profile compared to a group healthy subjects. Daily physical activity is negatively influenced by worse lung function and longer sleep duration (both at night and during the day).

**REFERENCES**


1. Lee IM, Shiroma EJ, Lobelo F, et al. Effect of physical inactivity on major non-communicable diseases worldwide: An analysis of burden of disease and life expectancy. *Lancet* 2012;380(9838):219–229.
2. Ding D, Lawson KD, Kolbe-alexander TL, et al. The economic burden of physical inactivity : a global analysis of major non-communicable diseases. *Lancet* 2012;388(10051):1311–1324.
3. Vogiatzis I, Zakynthinos G, Andrianopoulos V. Mechanisms of Physical Activity Limitation in Chronic Lung Diseases. *Pulm Med* 2012;
4. Kozu R, Jenkins S, Senjyu H. Evaluation of activity limitation in patients with idiopathic pulmonary fibrosis grouped according to medical research council dyspnea grade. In: Archives of Physical Medicine and Rehabilitation. 2014.
5. Watz H, Pitta F, Rochester CL, et al. An official European Respiratory Society statement on physical activity in COPD. *Eur Respir J* 2014;44(6):1521–1537.
6. Ramon MA, Riet G Ter, Carsin A-E, et al. The dyspnoea-inactivity vicious circle in COPD: Development and external validation of a conceptual model. *Eur Respir J* 2018;1800079.
7. Holland AE. Exercise limitation in interstitial lung disease - mechanisms, significance and therapeutic options. *Chron Respir Dis* 2010;7(2):101–111.
8. Vainshelboim B, Kramer MR, Izhakian S, Lima RM, Oliveira J. Physical Activity and Exertional Desaturation Are Associated with Mortality in Idiopathic Pulmonary Fibrosis. *J Clin Med* 2016;5(8):1–11.
9. Bahmer T, Kirsten A-M, Waschki B, et al. Prognosis and longitudinal changes of physical activity in idiopathic pulmonary fibrosis. *BMC Pulm Med*

2017;17(1):104.

10. Nakayama MA, Bando MA, Araki KOJI, et al. Physical activity in patients with idiopathic pulmonary fibrosis. *Respirology* 2015;20:640–646.
11. Dale MT, McKeough ZJ, Munoz PA, Corte P, Bye PT, Alison JA. Physical activity in people with asbestos related pleural disease and dust-related interstitial lung disease: an observational study. *BMC Pulm Med* 2013;13:1–12.
12. Wallaert B, Monge E, Rouzic O Le, Wémeau-Stervinou L, Salleron J, Grosbois JM. Physical activity in daily life of patients with fibrotic idiopathic interstitial pneumonia. *Chest* 2013;144(5):1652–1658.
13. Spina G, Spruit MA, Alison J, et al. Analysis of nocturnal actigraphic sleep measures in patients with COPD and their association with daytime physical activity. *Thorax* 2017;72(8):694–701.
14. Mavroudi M, Papakosta D, Kontakiotis T, et al. Sleep disorders and health-related quality of life in patients with interstitial lung disease. *Sleep Breath* 2018;22:393–400.
15. Meyer KC. Diagnosis and management of interstitial lung diseases. *Transl Respir Med* 2014;2(4).
16. Antoniou KM, Margaritopoulos GA, Tomassetti S, Bonella F, Costabel U, Poletti V. Interstitial lung disease. *Eur Respir Rev* 2014;23:40–54.
17. Chetta A, Marangio E, Olivieri D. Pulmonary function testing in interstitial lung diseases. *Respiration* 2004;71(3):209–213.
18. Macintyre N, Crapo RO, Viegi G, et al. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. *Eur Respir J* 2005;26(4):720–735.
19. Wanger J, Clausen JL, Coates A, et al. Standardisation of the measurement of lung volumes. *Eur Respir J* 2005;26(3):511–522.
20. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. *Eur Respir J* 2005;26(2):319–338.
21. Neder J a, Andreoni S, Peres C, Nery LE. Reference values for lung function tests. III. Carbon monoxide diffusing capacity (transfer factor). *Braz J Med Biol Res* 1999;32(6):729–37.
22. Pereira CA de C, Sato T, Rodrigues SC. New reference values for forced spirometry in white adults in Brazil. *J Bras Pneumol* 2007;33(4):397–406.
23. Crapo RO, Morris AH. Standardized single breath normal values for carbon

monoxide diffusing capacity. *Am Rev Respir Dis* 1981;123(2):185–189.

24. Holland AE, Spruit MA, Troosters T, et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J* 2014;44(6):1428–46.
25. Britto RR, Probst VS, Dornelas De Andrade AF, et al. Reference equations for the six-minute walk distance based on a Brazilian multicenter study. *Brazilian J Phys Ther* 2013;17(6):556–563.
26. Black LF, Hyatt RE. Maximal respiratory pressures: normal values and relationship to age and sex. *Am Rev Respir Dis* 1969;99:696–702.
27. Grassino AE, Moxham J, Aldrich TK, et al. American Thoracic Society / European Respiratory Society ATS / ERS Statement on Respiratory Muscle Testing. *Am J Respir Crit Care Med* 2002;166:518–624.
28. Neder JA, Andreoni S, Lerario MC, Nery LE. Reference values for lung function tests. II. Maximal respiratory pressures and voluntary ventilation. *Brazilian J Med Biol Res* 1999;32(6):719–727.
29. Robles PG, Mathur S, Janaudis-Ferreira T, Dolmage TE, Goldstein RS, Brooks D. Measurement of Peripheral Muscle Strength in Individuals With Chronic Obstructive Pulmonary Disease: a sistematic review. *J Cardiopulm Rehabil Prev* 2011;31:11–24.
30. Hopkinson NS, Tennant RC, Dayer MJ, et al. A prospective study of decline in fat free mass and skeletal muscle strength in chronic obstructive pulmonary disease. *Respir Res* 2007;8:25.
31. Bestall JC., Paul EA., Garrod R., Garnham R., Jones PW., Wedzicha JA. Usefulness of the Medical Research Council ( MRC ) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* 1999;54:581–586.
32. Ware JE, Sherbourne CD. The MOS 36-Item Short-Form Health Survey ( SF-36 ) I . Conceptual Framework and Item Selection. *Med Care* 1992;30(6):473–483.
33. Rabinovich RA, Louvaris Z, Raste Y, et al. Validity of physical activity monitors during daily life in patients with COPD. *Eur Respir J* 2013;42(5).
34. Remoortel H Van, Raste Y, Louvaris Z, et al. Validity of six activity monitors in chronic obstructive pulmonary disease: A comparison with indirect calorimetry. *PLoS One* 2012;7(6):1–11.

35. Demeyer H, Burtin C, Remoortel H Van, et al. Standardizing the analysis of physical activity in patients with COPD following a pulmonary rehabilitation program. *Chest* 2014;146(2):318–327.
36. Atkins C, Baxter M, Jones A, Wilson A. Measuring sedentary behaviors in patients with idiopathic pulmonary fibrosis using wrist-worn accelerometers. *Clin Respir J* 2016;12:746–753.
37. Bahmer T, Waschki B. Physical Activity and Fatigue in Patients with Sarcoidosis. 2018;18–26.
38. Vainshelboim B, Izhakian S. Lifestyle Behaviors and Clinical Outcomes in Idiopathic Pulmonary Fibrosis. 2018;49100:27–34.
39. Bahmer T, Kirsten A-M, Waschki B, et al. Clinical Correlates of Reduced Physical Activity in Idiopathic Pulmonary Fibrosis. *Respiration* 2016;91(6):497–502.
40. Furlanetto KC, Donária L, Schneider LP, et al. Sedentary Behavior Is an Independent Predictor of Mortality in Subjects With COPD. *Respir Care* 2017;62(5):579–587.
41. Waschki B, Kirsten A, Holz O, et al. Physical activity is the strongest predictor of all-cause mortality in patients with COPD: a prospective cohort study. *Chest* 2011;140(2):331–342.
42. Pitta F, Troosters T, Spruit MA, Probst VS, Decramer M, Gosselink R. Characteristics of Physical Activities in Daily Life in Chronic Obstructive Pulmonary Disease. 2005;171:972–977.
43. Bahmer T, Kirsten A. Clinical Correlates of Reduced Physical Activity in Idiopathic Pulmonary Fibrosis. 2016;497–502.
44. Goldman SE, Stone KL, Ancoli-Israel S, et al. Poor sleep is associated with poorer physical performance and greater functional limitations in older women. *Sleep* 2007;30(10):1317–1324.
45. Mikolasch TA, Garthwaite HS, Porter JC. Update in diagnosis and management of interstitial lung disease. *Clin Med (Northfield Il)* 2017;17(2):146–53.
46. Slater JA, Botsis T, Walsh J, King S, Straker LM, Eastwood PR. Assessing sleep using hip and wrist actigraphy. *Sleep Biol Rhythms* 2015;13(2):172–180.

## 4. CONCLUSÃO GERAL

Podemos concluir que pacientes com DPI apresentam um pior perfil de atividade física, ou seja, são mais inativos que indivíduos saudáveis da mesma idade. A atividade física na vida diária é um fator impotante e que está relacionada com outros desfechos clínicos, o que demonstra a necessidade de estudos com intervenções direcionadas à AFVD nesta população. Interessantemente, verificamos que, em pacientes com DIP, a AFVD pode ser influenciado pela noite anterior de sono. Nossos achados destacam que dormir por um período prolongado em uma noite não tem um grande impacto na AFVD do dia seguinte. No entanto, quando isso ocorre repetidamente (por exemplo, 4 vezes/semana), pode prejudicar significativamente os níveis de AFVD desta população.

## 5. REFERÊNCIAS


1. Meyer KC. Diagnosis and management of interstitial lung diseases. Transl Respir Med. 2014;2(4).
2. Mikolasch TA, Garthwaite HS, Porter JC. Update in diagnosis and management of interstitial lung disease. Clin Med (Northfield Il). 2017;17(2):146–53.
3. Rubin AS, Santana AN da C, Costa AN, Baldi BG, Pereira CA de C, Carvalho CRR, et al. Diretrizes de Doenças Pulmonares Intersticiais da Sociedade Brasileira de Pneumologia e Tisiologia. J Bras Pneumol. 2012;38(Supl 2):S1–133.
4. Ramon MA, Ter Riet G, Carsin A-E, Gimeno-Santos E, Agustí A, Antó JM, et al. The dyspnoea-inactivity vicious circle in COPD: Development and external validation of a conceptual model. Eur Respir J. 2018;1800079.
5. Watz H, Pitta F, Rochester CL, Garcia-Aymerich J, ZuWallack R, Troosters T, et al. An official European Respiratory Society statement on physical activity in COPD. Eur Respir J. 2014;44(6):1521–37.
6. Bahmer T, Kirsten A-M, Waschki B, Rabe KF, Magnussen H, Kirsten D, et al. Prognosis and longitudinal changes of physical activity in idiopathic pulmonary fibrosis. BMC Pulm Med. 2017;17(1):104.
7. Gimeno-Santos E, Frei A, Steurer-Stey C, de Batlle J, Rabinovich R a, Raste Y, et al. Determinants and outcomes of physical activity in patients with COPD: a systematic review. Thorax. 2014;69(8).
8. Demeyer H, Burtin C, Van Remoortel H, Hornikx M, Langer D, Decramer M, et al. Standardizing the analysis of physical activity in patients with COPD following a pulmonary rehabilitation program. Chest. 2014;146(2):318–27.
9. Pitta F, Troosters T, Probst VS, Spruit MA, Decramer M, Gosselink R. Quantifying physical activity in daily life with questionnaires and motion sensors in COPD. Eur Respir J. 2006;27(5):1040–55.
10. Pitta F, Troosters T, Spruit MA, Probst VS, Decramer M, Gosselink R. Characteristics of Physical Activities in Daily Life in Chronic Obstructive Pulmonary Disease. 2005;171:972–7.
11. Dale MT, McKeough ZJ, Munoz PA, Corte P, Bye PT, Alison JA. Physical activity in people with asbestos related pleural disease and dust-related

interstitial lung disease: an observational study. BMC Pulm Med. 2013;13:1–12.

12. Atkins C, Baxter M, Jones A, Wilson A. Measuring sedentary behaviors in patients with idiopathic pulmonary fibrosis using wrist-worn accelerometers. Clin Respir J. 2016;12:746–53.

13. Wallaert B, Monge E, Le Rouzic O, Wémeau-Stervinou L, Salleron J, Grosbois JM. Physical activity in daily life of patients with fibrotic idiopathic interstitial pneumonia. Chest. 2013;144(5):1652–8.

14. Dowman LM, Mcdonald CF, Hill CJ, Lee AL, Barker K, Boote C, et al. The evidence of benefits of exercise training in interstitial lung disease : a randomised controlled trial. Thorax. 2017;0:1–10.

15. Wallaert B, Monge E, Le Rouzic O, Wémeau-Stervinou L, Salleron J, Grosbois JM. Physical activity in daily life of patients with fibrotic idiopathic interstitial pneumonia. Chest. 2013;144(5):1652–8.

16. Silva H, Aguiar WF, Gonçalves AFL, Silva TG, Loyola WAS, Pereira PS, et al. Is physical activity equally reduced in patients with respiratory disease? – Preliminary results. Eur Respir J. 2018 Sep 15;52(suppl 62):PA5427.

17. Antoniou KM, Margaritopoulos GA, Tomassetti S, Bonella F, Costabel U, Poletti V. Interstitial lung disease. Eur Respir Rev. 2014;23:40–54.

18. Wells AU, Hirani N. Interstitial lung disease guideline: the British Thoracic Society in collaboration with the Thoracic Society of Australia and New Zealand and the Irish Thoracic Society. Thorax. 2008;63(Supplement 5):v1–58.

19. Chetta A, Marangio E, Olivieri D. Pulmonary function testing in interstitial lung diseases. Respiration. 2004;71(3):209–13.

20. Martinez FJ, Flaherty K. Pulmonary function testing in idiopathic interstitial pneumonias. Proc Am Thorac Soc. 2006;3(4):315–21.

21. Vogiatzis I, Zakynthinos S. Factors Limiting Exercise Tolerance in Chronic Lung Diseases. Compr Physiol. 2012;2(July):1779–817.

22. O'Donnell DEO, Elbehairy AF, Berton DC, Domnik NJ. Advances in the Evaluation of Respiratory Pathophysiology during Exercise in Chronic Lung Diseases. Front Physiol. 2017;8(February):1–24.

23. Hansen JE, Wasserman K. Pathophysiology of activity limitation in patients with interstitial lung disease. Chest. 1996;109(6):1566–76.

24. Panagiotou M, Church AC, Johnson MK, Peacock AJ. Pulmonary vascular and cardiac impairment in interstitial lung disease. Eur Respir Rev. 2017;26:1–9.

25. Agusti AGN, Roca J, Gea J, Wagner PD, Xaubet A, Rodriguez-roisin R. Mechanisms of Gas-exchange Impairment in Idiopathic Pulmonary Fibrosis 1 - 4. Am Rev Respir Dis. 1991;143:219–25.

26. Ferrazza AM, Martolini D, Palange P. Cardiopulmonary Exercise Testing in the Functional and Prognostic Evaluation of Patients with Pulmonary Diseases. Respiration. 2009;77:3–17.

27. Osamu N, Hiroyuki T, Yasuhiro K, Tomoki K, Pt OT, Pt WF, et al. Quadriceps Weakness Is Related to Exercise Capacity in Idiopathic Pulmonary Fibrosis *. Chest. 127(6):2028–33.

28. Watanabe F, Taniguchi H, Sakamoto K. Quadriceps weakness contributes to exercise capacity in nonspecific interstitial pneumonia. Respir Med. 2013;107(4):622–8.

29. Panagiotou M, Polychronopoulos V, Strange C. Respiratory and lower limb muscle function in interstitial lung disease. Chron Respir Dis. 2016;13(2):162–72.

30. Mendoza LA, Gogali AT, Shrikrishna DI, Cavada GA, Kemp SA V, Natanek SAA, et al. Quadriceps strength and endurance in fibrotic idiopathic interstitial pneumonia. Respirology. 2014;138–43.

31. Holland AE. Exercise limitation in interstitial lung disease - mechanisms, significance and therapeutic options. Chron Respir Dis. 2010;7(2):101–11.

32. Verges S, Bachasson D, Wuyam B. Effect of acute hypoxia on respiratory

muscle fatigue in healthy humans. Respir Res. 2010;11(109):1–9.

33. Katayama K, Amann M, Pegelow DF, Jacques AJ, Dempsey JA. Effect of arterial oxygenation on quadriceps fatigability during isolated muscle exercise. Am J Physiol Regul Integr Comp Physiol. 2007;292:1279–86.

34. Ferguson B. ACSM's Guidelines for Exercise Testing and Prescription 9th Ed. 2014. Vol. 58, The Journal of the Canadian Chiropractic Association. 2014. p. 328.

35. Vainshelboim B, Kramer MR, Izhakian S, Lima RM, Oliveira J. Physical Activity and Exertional Desaturation Are Associated with Mortality in Idiopathic Pulmonary Fibrosis. J Clin Med. 2016;5(8):1–11.

36. Bahmer T, Kirsten A-M, Waschki B, Rabe KF, Magnussen H, Kirsten D, et al. Clinical Correlates of Reduced Physical Activity in Idiopathic Pulmonary Fibrosis. Respiration. 2016;91(6):497–502.

37. Mermigkis C, Bouloukaki I, Schiza SE. Sleep as a new target for improving outcomes in Idiopathic Pulmonary Fibrosis. Chest. 2017;152(6):1327–38.

38. Mavroudi M, Papakosta D, Kontakiotis T, Domvri K, Kalamaras G, Zarogoulidou V, et al. Sleep disorders and health-related quality of life in patients with interstitial lung disease. Sleep Breath. 2017;

39. Fulton BG, Ryerson CJ. Managing comorbidities in idiopathic pulmonary fibrosis. Vol. 8, International Journal of General Medicine. 2015.

40. Lewthwaite H, Effing TW, Olds T, Williams MT. Physical activity, sedentary behaviour and sleep in COPD guidelines: A systematic review. Chron Respir Dis. 2017;14(3):231–44.

41. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ, III CFR, et al. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193–213.

42. Bertolazi AN, Fagondes SC, Hoff LS, Dartora EG, Miozzo IC da S, Barba MEF de, et al. Validation of the Brazilian Portuguese version of the Pittsburgh Sleep

Quality Index. Sleep Med. 2011;12(1):70–5.

43. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Vol. 14, Sleep. 1991. p. 540–5.

44. Bertolazi AN, Fagondes SC, Hoff LS, Pedro VD, Barreto SSM, Johns MW. Validação da escala de sonolência de Epworth em português para uso no Brasil. J Bras Pneumol. 2009;35(9):877–83.

45. Sargent C, Lastella M, Halson SL, Roach GD. The validity of activity monitors for measuring sleep in elite athletes. J Sci Med Sport. 2016;19(10):848–53.

46. Slater JA, Botsis T, Walsh J, King S, Straker LM, Eastwood PR. Assessing sleep using hip and wrist actigraphy. Sleep Biol Rhythms. 2015;13(2):172–80.

47. Spina G, Spruit MA, Alison J, Benzo RP, Calverley PMA, Clarenbach CF, et al. Analysis of nocturnal actigraphic sleep measures in patients with COPD and their association with daytime physical activity. Thorax. 2017;72(8):694–701.

# APÊNDICES

## APÊNDICE A

### TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Conforme a Resolução 466 de 12 de Dezembro de 2012, do Conselho Nacional de Saúde/Ministério da Saúde.

Prezado(a) Senhor(a):

O(A) Sr(a) está sendo convidado para participar de um projeto de pesquisa chamado "**Associação entre progressão da doença e desfechos clínicos em pacientes com doenças intersticiais pulmonares**", realizado no Laboratório de Pesquisa em Fisioterapia Pulmonar da Universidade Estadual de Londrina (Londrina, Brasil). O objetivo do estudo é avaliar por um período de até 2 anos o impacto de possíveis mudanças na função pulmonar em diferentes aspectos clínicos (incluindo os níveis de atividade física na vida diária) em indivíduos com doenças intersticiais pulmonares e em indivíduos sem a doença. A sua participação é muito importante e ela se daria da seguinte forma: Os participantes realizarão algumas avaliações em cinco momentos: no início do protocolo, após 6 meses, 1 ano, 18 meses e 2 anos. Em cada momento serão realizadas as seguintes avaliações:

- Avaliação da função pulmonar por meio de pletismografia/espirometria e capacidade de difusão de monóxido de carbono (DLCO);
- Atividade física na vida diária que será realizada durante 6 dias consecutivos pelo aparelho Actigraph® (aparelho pequeno e leve, utilizado na cintura, de manuseio extremamente simples que monitora todas as atividades físicas realizadas pelo participante, permitindo saber o quanto ativo ele é). Nos 6 dias de avaliação, o participante permanecerá durante 24 horas com o aparelho, havendo a necessidade de retirá-lo apenas durante o banho e atividades realizadas em piscina (por exemplo: natação, hidroginástica).
- Força muscular por meio de dinamometria de membros superiores e inferiores e teste de 1 repetição máxima; força muscular respiratória por meio de manovacuometria; fadiga muscular periférica por meio eletromiografia de superfície;
- Capacidade funcional de exercício por meio do teste da caminhada de 6 minutos e; capacidade máxima de exercício por meio do teste cardiopulmonar de esforço;
- Capacidade funcionais por meio dos testes: Teste de caminhada de 4 metros, teste de Sentar e levantar por 30 segundos e Teste do degrau de 6 minutos
- Composição corporal por meio do teste de bioimpedância elétrica;
- Ansiedade e depressão por meio da *Hospital Anxiety and Depression Scale (HADS);* Qualidade de vida relacionado à saúde por meio dos questionários: *Short Form Health Survey (SF-36)* e *Saint George Respiratory Questionnaire* específico para pacientes com doença intersticial pulmonar (SGRQ-I); Função congnitiva por meio do Mini Exame do Estado Mental (MEEM); sono e sonolência por meio do Índice de Qualidade de Sono de Pittsburgh (PSQI) e escala de sonolência de Epworth (ESE); Falta de ar no dia-a-dia por meio da escala do *Medical Research Council (MRC) e pelo Short of breath questionnaire do centro médico UCSD (UCSD-SOBQ).* HADS, SF-36, MRC, MEEM, PSQI, ESE e UCSD-SOBQ serão administrados a todos os pacrticipantes. SGRQ-I será administrado apenas para pacientes com doenças intersticiais pulmonares;
- Exames de sangue (marcadores inflamatórios e estresse oxidativo).

**Benefícios esperados do estudo:** Os resultados deste estudo ajudarão a compreender o efeito que uma possível progressão da doença (ou seja, mudanças na função pulmonar) tem sobre diferentes aspectos clínicos da doença. Isso poderá contribuir para que, no futuro, novos tratamentos surjam e ajudem pacientes com doença pulmonar intersticial. **Benefícios diretos ao participante:** Após cada avaliação, se for de seu interesse, você receberá um relatório com os resultados de todos os testes. Esses resultados podem ser entregues ao seu médico para uma avaliação mais completa do seu estado de saúde. Além disso, os participantes sem acompanhamento médico no momento da inclusão do estudo serão cadastrados no Ambulatório de Especialidades do Hospital Universitário da UEL. **Riscos:** Nenhum dos procedimentos utilizados constitui risco direto para a integridade física ou moral dos participantes. Em alguns casos, após a coleta de sangue é

possível que se forme um pequeno hematoma na região onde a coleta ocorreu. Além disso, caso algum teste gere mal estar (físico ou emocional) ele será interrompido sem que haja risco real para a saúde do participante. **Custos:** Informamos que o(a) senhor(a) não pagará nem será remunerado por sua participação. Garantimos, no entanto, que todas as despesas de transporte, por meio público, serão ressarcidas, se necessário, quando devidas e decorrentes especificamente de sua participação na pesquisa. No entanto, em caso de eventuais danos ocorridos exclusivamente por causa deste estudo, o(a) Sr(a) terá direito a tratamento médico completo oferecido pela instituição do estudo. **Participação no estudo:** Uma vez que o(a) Sr(a) aceitar participar do estudo, os pesquisadores iniciarão o agendamento das visitas e realizarão as avaliações após garantir que o(a) Sr(a) tenha compreendido o que será avaliado em cada momento. É importante que o(a) Sr(a) saiba que tem a opção de não fornecer o seu consentimento e não participar desta pesquisa. Sua decisão não interferirá no seu atendimento no Hospital Universitário Regional do Norte do Paraná da Universidade Estadual de Londrina. Além disso, os participantes poderão abandonar o estudo a qualquer momento que se achar conveniente, sem qualquer prejuízo em nenhum sentido. **Sigilo:** Embora os resultados da pesquisa possam ser divulgados em publicações e eventos científicos, a identidade dos participantes será sempre preservada de maneira sigilosa, ou seja, em segredo, conforme previsto pela lei. Quando os resultados forem analisados, não aparecerá o nome de nenhum participante e sim um código. Desse modo, a identidade não será revelada. **Acompanhamento da pesquisa:** Você poderá solicitar informações ou esclarecimentos sobre o andamento da pesquisa em qualquer momento da pesquisa. Para tanto, você poderá telefonar para (43) 3371-2490 / 3371-2477 e falar com o Professor Carlos Augusto Marçal Camilo. Se você tiver reclamações sobre a condução ética deste estudo, assim como preocupações, dúvidas ou reclamações sobre seus direitos como participante da pesquisa, você poderá entrar em contato com o Comitê de Ética em Pesquisa (CEP) do Hospital Universitário Regional do Norte do Paraná da Universidade Estadual de Londrina no endereço: LABESC - Laboratório Escola de Pós-Graduação - sala 14 - Campus Universitário - Rodovia Celso Garcia Cid, Km 380 ou pelo telefone (43) 3371-5455, de segunda a sexta, das 08:00 às 11:30hrs. O CEP trata-se de um grupo de indivíduos com conhecimentos científicos e não científicos que realizam a revisão ética inicial e continuada de propostas de pesquisas para mantê-lo seguro e proteger seus direitos. Você também tem a opção de entrar em contato diretamente com a Comissão Nacional de Ética em Pesquisa (CONEP) através do Fone de denúncia: (61) 3315-3927 ou (61) 3315-2472.

Caso o(a) Sr(a) aceite esse convite e concorde voluntariamente em participar do estudo assinando este termo de consentimento, consideramos que o(a) Sr(a) acredita que foi suficientemente informado(a) por um dos pesquisadores responsáveis sobre a pesquisa, os procedimentos envolvidos nela, assim como os possíveis riscos e benefícios decorrentes dessa participação. Ressaltamos novamente que o(a) Sr(a) pode retirar seu consentimento a qualquer momento, sem que isto leve a qualquer prejuízo em nenhum sentido.

Colocamo-nos à disposição para qualquer esclarecimento que se fizer necessário nos telefones (43) 3371-2490 / 3371-2477 ou pessoalmente no Ambulatório de Fisioterapia Respiratória do Hospital Universitário Regional Norte do Paraná: Av. Robert Koch, 60 – Vila Operária – Londrina – PR (perguntar pelo Professor Carlos Augusto Marçal Camilo).

Atenciosamente,
*Prof. Dr. Carlos Augusto Marçal Camilo*
*Prof. Dr. Fábio de Oliveira Pitta*
*Prof. Dr. Marcos Ribeiro*

Eu, abaixo assinado

.....,
(Nome do participante em maiúsculas)

Declaro ter sido informado verbalmente além de ser provido com as informações do estudo por escrito. Eu também tive a oportunidade de fazer perguntas e discutir o estudo com os Professores Carlos Augusto Marçal Camillo e/ou Fábio de Oliveira Pitta e/ou Marcos Ribeiro ou ainda por algum pesquisador do estudo.
Declaro que recebi respostas para todas as minhas perguntas (caso tenham ocorrido). Estou ciente de que a minha participação é completamente voluntária e que a qualquer momento posso retirar meu consentimento, sem que isto leve a qualquer prejuízo em nenhum sentido. Eu também sei que a participação no estudo não me trará vantagem ou prejuízo em nenhuma atenção médica atual ou futura oferecida pelo Sistema Único de Saúde – SUS.

Paciente ou Responsável:

___ / ___ / ___ (DD/MM/AA) _____
Assinatura (ou impressão papiloscópica)

Pesquisador:

___ / ___ / ___ (DD/MM/AA) _____
Assinatura

# ANEXOS

## ANEXO A

Parecer do comitê de ética em pesquisa

UNIVERSIDADE ESTADUAL DE LONDRINA - UEL

**PARECER CONSUBSTANCIADO DO CEP**

**DADOS DA EMENDA**

**Título da Pesquisa:** Associação entre progressão da doença e desfechos clínicos em pacientes com doenças intersticiais pulmonares

**Pesquisador:** CARLOS AUGUSTO MARCAL CAMILLO

**Área Temática:**

**Versão:** 3

**CAAE:** 69698317.5.0000.5231

**Instituição Proponente:** CCS - Progr. de Pós-Grad. em Ciências da Reabilitação

**Patrocinador Principal:** Financiamento Próprio

**DADOS DO PARECER**

**Número do Parecer:** 2.484.871

**Apresentação do Projeto:**

Trata-se de solicitação de emenda ao projeto.

**Objetivo da Pesquisa:**

Objetivo Primário:

Avaliar o impacto do declínio da função pulmonar nas mudanças nos níveis de atividade física de pacientes com doenças intersticiais pulmonares

Objetivo Secundário:

Avaliar o impacto do declínio da função pulmonar em outros desfechos clínicos: função muscular (força, resistência e fadigabilidade); capacidade de exercício (máxima e funcional), qualidade de vida relacionada à saúde e sintomas. Além disso, investigar associações entre o nível de atividade física (e suas mudanças ao longo do tempo) e hospitalizações e mortalidade em pacientes com DIP durante o período do estudo. Por último, também serão verificadas possíveis associações entre função pulmonar (e suas mudanças ao longo do tempo) com os demais desfechos investigados.

**Avaliação dos Riscos e Benefícios:**

Segundo o pesquisador, "nenhum dos procedimentos utilizados constitui risco direto para a integridade física ou moral dos participantes. Em alguns casos, após a coleta de sangue é possível

que se forme um pequeno hematoma na região onde a coleta ocorreu. Além disso, caso algum teste gere mal estar (físico ou emocional) ele será interrompido sem que haja risco real para a saúde do participante.
Benefícios:
Benefícios esperados do estudo: Os resultados deste estudo ajudarão a compreender o efeito que uma possível progressão da doença (ou seja, mudanças na função pulmonar) tem sobre diferentes aspectos clínicos da doença. Isso poderá contribuir para que, no futuro, novos tratamentos surjam e ajudem pacientes com doença pulmonar intersticial.

**Comentários e Considerações sobre a Pesquisa:**
O pesquisador solita a inclusão de realização de três testes funcionais. Estes testes apresentam relação com força de membros inferiores além de risco de quedas, sarcopenia e consequentemente hospitalizações. A realização dos testes ocorrerá nas mesmas visitas já programadas pela pesquisa e implicará em aumento de 10 - 15 minutos em cada visita.
Tendo vista que a hospitalização é um desfecho do estudo, a solicitação é pertinente.

**Considerações sobre os Termos de apresentação obrigatória:**
Não se aplica.

**Recomendações:**
Incluir a explicação dos 3 testes agregados ao estudo no TCLE.

**Conclusões ou Pendências e Lista de Inadequações:**
Não há.

**Considerações Finais a critério do CEP:**
Prezado (a) Pesquisador (a),
Este é seu parecer final de aprovação da emenda solicitada, vinculado ao Comitê de Ética em Pesquisas Envolvendo Seres Humanos da Universidade Estadual de Londrina. É sua responsabilidade imprimi-lo para apresentação aos órgãos e/ou instituições pertinentes.
Coordenação CEP/UEL.

**Este parecer foi elaborado baseado nos documentos abaixo relacionados:**

| Tipo Documento | Arquivo | Postagem | Autor | Situação |
|---|---|---|---|---|
| Informações | PB_INFORMAÇÕES_BÁSICAS_102844 | 29/01/2018 | | Aceito |

| | | | | |
|---|---|---|---|---|
| Básicas do Projeto | _E1.pdf | 10:36:22 | | Aceito |
| TCLE / Termos de Assentimento / Justificativa de Ausência | TCLE_Adendo290118.pdf | 29/01/2018 10:25:44 | Humberto Silva | Aceito |
| Recurso Anexado pelo Pesquisador | Adendo_de_projeto.pdf | 29/01/2018 10:17:05 | Humberto Silva | Aceito |
| Folha de Rosto | Folha_de_rosto_Camillo.pdf | 29/01/2018 10:14:17 | Humberto Silva | Aceito |
| Cronograma | Cronogramas_Camillo_Versao01.pdf | 09/06/2017 15:38:20 | CARLOS AUGUSTO MARCAL CAMILLO | Aceito |
| Orçamento | Orcamento_Camillo_Versao01.pdf | 09/06/2017 15:35:25 | CARLOS AUGUSTO MARCAL CAMILLO | Aceito |
| Declaração de Instituição e Infraestrutura | Declaracao_Infraestrutura_Camillo_Versao01.pdf | 09/06/2017 15:32:25 | CARLOS AUGUSTO MARCAL CAMILLO | Aceito |
| Projeto Detalhado / Brochura Investigador | Protocolo_Camillo_Versao01.pdf | 09/06/2017 15:30:39 | CARLOS AUGUSTO MARCAL CAMILLO | Aceito |

**Situação do Parecer:**
Aprovado

**Necessita Apreciação da CONEP:**
Não

LONDRINA, 05 de Fevereiro de 2018

**Assinado por:**
**Alexandrina Aparecida Maciel Cardelli**
**(Coordenador)**

## ANEXO B

## Normas de submissão para revista Respiratory Medicine

Submission

Our online submission system guides you stepwise through the process of entering your article details and uploading your files. The system converts your article files to a single PDF file used in the peer-review process. Editable files (e.g., Word, LaTeX) are required to typeset your article for final publication. All correspondence, including notification of the Editor's decision and requests for revision, is sent by e-mail.

Submit your article

Please submit your article via http://ees.elsevier.com/yrmed.

Submissions are allocated to a handling editor, typically an Associate Editor. Should the paper be considered suitable for peer review, appropriate reviewers will be recruited. Authors are required to provide the name and full contact details of 2 potential reviewers, though choice of reviewers is at the discretion of the handling editor.

The final decision-making responsibility lies with the handling editor, who reserves the right to reject the paper despite favourable reviews depending on the priorities of the journal.

Reviews

The journal welcomes submission of state-of-the-art reviews on important topics with a clinical relevance. Potential review authors are encouraged to contact the Deputy Editor Dr N. Hanania hanania@bcm.tmc.edu in advance with their review proposals.

Case Reports

Case reports will no longer be considered for publication in Respiratory Medicine, but instead should be directed to the sister publication Respiratory Medicine Case Reports. Please note that this is a separate publication. Case reports

should be submitted for consideration by Respiratory Medicine Case Reports via http://ees.elsevier.com/rmcr/. Respiratory Medicine Case Reports is an open access journal and all authors will be required to pay a £250 processing fee to cover the costs of publishing the article, which authors will be required to pay once an article has passed peer review.

Brief Communications

These should be submitted as detailed above but should not exceed 1000 words, and may normally contain only one illustration or table. Brief communications containing new information may be selected for rapid peer review and publication at the discretion of the editor and editorial board.

NEW SUBMISSIONS

Submission to this journal proceeds totally online and you will be guided stepwise through the creation and uploading of your files. The system automatically converts your files to a single PDF file, which is used in the peer-review process.

As part of the Your Paper Your Way service, you may choose to submit your manuscript as a single file to be used in the refereeing process. This can be a PDF file or a Word document, in any format or lay-out that can be used by referees to evaluate your manuscript. It should contain high enough quality figures for refereeing. If you prefer to do so, you may still provide all or some of the source files at the initial submission. Please note that individual figure files larger than 10 MB must be uploaded separately.

References

There are no strict requirements on reference formatting at submission. References can be in any style or format as long as the style is consistent. Where applicable, author(s) name(s), journal title/book title, chapter title/article title, year of publication, volume number/book chapter and the article number or pagination must be present. Use of DOI is highly encouraged. The reference style used by the journal will be applied to the accepted article by Elsevier at the proof stage. Note that missing data will be highlighted at proof stage for the author to correct.

Formatting requirements

There are no strict formatting requirements but all manuscripts must contain

the essential elements needed to convey your manuscript, for example Abstract, Keywords, Introduction, Materials and Methods, Results, Conclusions, Artwork and Tables with Captions.

If your article includes any Videos and/or other Supplementary material, this should be included in your initial submission for peer review purposes.

Divide the article into clearly defined sections.

Figures and tables embedded in text

Please ensure the figures and the tables included in the single file are placed next to the relevant text in the manuscript, rather than at the bottom or the top of the file. The corresponding caption should be placed directly below the figure or table.

Peer review

This journal operates a single blind review process. All contributions are typically sent to a minimum of two independent expert reviewers to assess the scientific quality of the paper. The Editor is responsible for the final decision regarding acceptance or rejection of articles. The Editor's decision is final.

REVISED SUBMISSIONS

Use of word processing software

Regardless of the file format of the original submission, at revision you must provide us with an editable file of the entire article. Keep the layout of the text as simple as possible. Most formatting codes will be removed and replaced on processing the article. The electronic text should be prepared in a way very similar to that of conventional manuscripts (see also the Guide to Publishing with Elsevier). See also the section on Electronic artwork.

To avoid unnecessary errors you are strongly advised to use the 'spell-check' and 'grammar-check' functions of your word processor.

Article structure

Subdivision - unnumbered sections

Divide your article into clearly defined sections. Each subsection is given a

brief heading. Each heading should appear on its own separate line. Subsections should be used as much as possible when cross-referencing text: refer to the subsection by heading as opposed to simply 'the text'.

## Introduction

State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

## Material and methods

Provide sufficient details to allow the work to be reproduced by an independent researcher. Methods that are already published should be summarized, and indicated by a reference. If quoting directly from a previously published method, use quotation marks and also cite the source. Any modifications to existing methods should also be described.

## Results

Results should be clear and concise.

## Discussion

This should explore the significance of the results of the work, not repeat them. A combined Results and Discussion section is often appropriate. Avoid extensive citations and discussion of published literature.

## Conclusions

The main conclusions of the study may be presented in a short Conclusions section, which may stand alone or form a subsection of a Discussion or Results and Discussion section.

## Appendices

If there is more than one appendix, they should be identified as A, B, etc. Formulae and equations in appendices should be given separate numbering: Eq. (A.1), Eq. (A.2), etc.; in a subsequent appendix, Eq. (B.1) and so on. Similarly for tables and figures: Table A.1; Fig. A.1, etc.

Essential title page information

• Title. Concise and informative. Titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible.

• Author names and affiliations. Please clearly indicate the given name(s) and family name(s) of each author and check that all names are accurately spelled. You can add your name between parentheses in your own script behind the English transliteration. Present the authors' affiliation addresses (where the actual work was done) below the names. Indicate all affiliations with a lower-case superscript letter immediately after the author's name and in front of the appropriate address. Provide the full postal address of each affiliation, including the country name and, if available, the e-mail address of each author.

• Corresponding author. Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. This responsibility includes answering any future queries about Methodology and Materials. Ensure that the e-mail address is given and that contact details are kept up to date by the corresponding author.

• Present/permanent address. If an author has moved since the work described in the article was done, or was visiting at the time, a 'Present address' (or 'Permanent address') may be indicated as a footnote to that author's name. The address at which the author actually did the work must be retained as the main, affiliation address. Superscript Arabic numerals are used for such footnotes.

A structured abstract, by means of appropriate headings, should provide the context or background for the research and should state its purpose, basic procedures (selection of study subjects or laboratory animals, observational and analytical methods), main findings (giving specific effect sizes and their statistical significance, if possible), and principal conclusions. It should emphasize new and important aspects of the study or observations. The abstract must not exceed 250 words.

A list of three to six keywords should be supplied: full instructions are provided when submitting the article online.

Abbreviations

Define abbreviations that are not standard in this field in a footnote to be placed on the first page of the article. Such abbreviations that are unavoidable in the

abstract must be defined at their first mention there, as well as in the footnote. Ensure consistency of abbreviations throughout the article.

## Acknowledgements

Collate acknowledgements in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided help during the research (e.g., providing language help, writing assistance or proof reading the article, etc.).

## Formatting of funding sources

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

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

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

If no funding has been provided for the research, please include the following sentence:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Units

Follow internationally accepted rules and conventions: use the international system of units (SI). If other units are mentioned, please give their equivalent in SI.

## Math formulae

Please submit math equations as editable text and not as images. Present simple formulae in line with normal text where possible and use the solidus (/) instead of a horizontal line for small fractional terms, e.g., X/Y. In principle, variables are to

be presented in italics. Powers of e are often more conveniently denoted by exp. Number consecutively any equations that have to be displayed separately from the text (if referred to explicitly in the text).

Footnotes

Footnotes should be used sparingly. Number them consecutively throughout the article. Many word processors build footnotes into the text, and this feature may be used. Should this not be the case, indicate the position of footnotes in the text and present the footnotes themselves separately at the end of the article.

Artwork

Electronic artwork

General points

• Make sure you use uniform lettering and sizing of your original artwork.

• Preferred fonts: Arial (or Helvetica), Times New Roman (or Times), Symbol, Courier.

• Number the illustrations according to their sequence in the text.

• Use a logical naming convention for your artwork files.

• Indicate per figure if it is a single, 1.5 or 2-column fitting image.

• For Word submissions only, you may still provide figures and their captions, and tables within a single file at the revision stage.

• Please note that individual figure files larger than 10 MB must be provided in separate source files.

A detailed guide on electronic artwork is available.

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

Formats

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

EPS (or PDF): Vector drawings. Embed the font or save the text as 'graphics'.

TIFF (or JPG): Color or grayscale photographs (halftones): always use a minimum of 300 dpi.

TIFF (or JPG): Bitmapped line drawings: use a minimum of 1000 dpi.

TIFF (or JPG): Combinations bitmapped line/half-tone (color or grayscale): a minimum of 500 dpi is required.

Please do not:

• Supply files that are optimized for screen use (e.g., GIF, BMP, PICT, WPG); the resolution is too low.

• Supply files that are too low in resolution.

• Submit graphics that are disproportionately large for the content.

Color artwork

Please make sure that artwork files are in an acceptable format (TIFF (or JPEG), EPS (or PDF), or MS Office files) and with the correct resolution. If, together with your accepted article, you submit usable color figures then Elsevier will ensure, at no additional charge, that these figures will appear in color online (e.g., ScienceDirect and other sites) regardless of whether or not these illustrations are reproduced in color in the printed version. For color reproduction in print, you will receive information regarding the costs from Elsevier after receipt of your accepted article. Please indicate your preference for color: in print or online only. Further information on the preparation of electronic artwork.

Illustration services

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

Figure captions

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

used.

Tables

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

References

Citation in text

Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with either 'Unpublished results' or 'Personal communication'. Citation of a reference as 'in press' implies that the item has been accepted for publication.

Reference links

Increased discoverability of research and high quality peer review are ensured by online links to the sources cited. In order to allow us to create links to abstracting and indexing services, such as Scopus, CrossRef and PubMed, please ensure that data provided in the references are correct. Please note that incorrect surnames, journal/book titles, publication year and pagination may prevent link creation. When copying references, please be careful as they may already contain errors. Use of the DOI is highly encouraged.

A DOI is guaranteed never to change, so you can use it as a permanent link to any electronic article. An example of a citation using DOI for an article not yet in an issue is: VanDecar J.C., Russo R.M., James D.E., Ambeh W.B., Franke M. (2003). Aseismic continuation of the Lesser Antilles slab beneath northeastern Venezuela.

Journal of Geophysical Research, https://doi.org/10.1029/2001JB000884. Please note the format of such citations should be in the same style as all other references in the paper.

Web references

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

Data references

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

Reference management software

Most Elsevier journals have their reference template available in many of the most popular reference management software products. These include all products that support Citation Style Language styles, such as Mendeley. Using citation plug-ins from these products, authors only need to select the appropriate journal template when preparing their article, after which citations and bibliographies will be automatically formatted in the journal's style. If no template is yet available for this journal, please follow the format of the sample references and citations as shown in this Guide. If you use reference management software, please ensure that you remove all field codes before submitting the electronic manuscript. More information on how to remove field codes from different reference management software.

Users of Mendeley Desktop can easily install the reference style for this journal by clicking the following link: http://open.mendeley.com/use-citation-style/respiratory-medicine.

When preparing your manuscript, you will then be able to select this style using the Mendeley plug-ins for Microsoft Word or LibreOffice.

Reference formatting

There are no strict requirements on reference formatting at submission. References can be in any style or format as long as the style is consistent. Where applicable, author(s) name(s), journal title/book title, chapter title/article title, year of publication, volume number/book chapter and the article number or pagination must be present. Use of DOI is highly encouraged. The reference style used by the journal will be applied to the accepted article by Elsevier at the proof stage. Note that missing data will be highlighted at proof stage for the author to correct. If you do wish to format the references yourself they should be arranged according to the following examples:

Reference style

Text: Indicate references by number(s) in square brackets in line with the text. The actual authors can be referred to, but the reference number(s) must always be given.

Example: '..... as demonstrated [3,6]. Barnaby and Jones [8] obtained a different result ....'

List: Number the references (numbers in square brackets) in the list in the order in which they appear in the text.

Examples:

Reference to a journal publication:

[1] J. van der Geer, J.A.J. Hanraads, R.A. Lupton, The art of writing a scientific article, J. Sci. Commun. 163 (2010) 51–59. https://doi.org/10.1016/j.Sc.2010.00372.

Reference to a journal publication with an article number:

[2] Van der Geer, J., Hanraads, J.A.J., Lupton, R.A., 2018. The art of writing a scientific article. Heliyon. 19, e00205. https://doi.org/10.1016/j.heliyon.2018.e00205.

Reference to a book:

[3] W. Strunk Jr., E.B. White, The Elements of Style, fourth ed., Longman, New York, 2000.

Reference to a chapter in an edited book:

[4] G.R. Mettam, L.B. Adams, How to prepare an electronic version of your

article, in: B.S. Jones, R.Z. Smith (Eds.), Introduction to the Electronic Age, E-Publishing Inc., New York, 2009, pp. 281–304.

Reference to a website:

[5] Cancer Research UK, Cancer statistics reports for the UK. http://www.cancerresearchuk.org/aboutcancer/statistics/cancerstatsreport/, 2003 (accessed 13 March 2003).

Reference to a dataset:

[dataset] [6] M. Oguro, S. Imahiro, S. Saito, T. Nakashizuka, Mortality data for Japanese oak wilt disease and surrounding forest compositions, Mendeley Data, v1, 2015. https://doi.org/10.17632/xwj98nb39r.1.

Journal abbreviations source

Journal names should be abbreviated according to the List of Title Word Abbreviations.

Video

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

Data visualization

Include interactive data visualizations in your publication and let your readers interact and engage more closely with your research. Follow the instructions here to find out about available data visualization options and how to include them with your article.

Supplementary material

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

Research data

This journal encourages and enables you to share data that supports your research publication where appropriate, and enables you to interlink the data with your published articles. Research data refers to the results of observations or experimentation that validate research findings. To facilitate reproducibility and data reuse, this journal also encourages you to share your software, code, models, algorithms, protocols, methods and other useful materials related to the project.

Below are a number of ways in which you can associate data with your article or make a statement about the availability of your data when submitting your manuscript. If you are sharing data in one of these ways, you are encouraged to cite the data in your manuscript and reference list. Please refer to the "References" section for more information about data citation. For more information on depositing, sharing and using research data and other relevant research materials, visit the research data page.

Data linking

If you have made your research data available in a data repository, you can

link your article directly to the dataset. Elsevier collaborates with a number of repositories to link articles on ScienceDirect with relevant repositories, giving readers access to underlying data that gives them a better understanding of the research described.

There are different ways to link your datasets to your article. When available, you can directly link your dataset to your article by providing the relevant information in the submission system. For more information, visit the database linking page.

For supported data repositories a repository banner will automatically appear next to your published article on ScienceDirect.

In addition, you can link to relevant data or entities through identifiers within the text of your manuscript, using the following format: Database: xxxx (e.g., TAIR: AT1G01020; CCDC: 734053; PDB: 1XFN).

Mendeley Data

This journal supports Mendeley Data, enabling you to deposit any research data (including raw and processed data, video, code, software, algorithms, protocols, and methods) associated with your manuscript in a free-to-use, open access repository. During the submission process, after uploading your manuscript, you will have the opportunity to upload your relevant datasets directly to Mendeley Data. The datasets will be listed and directly accessible to readers next to your published article online.

For more information, visit the Mendeley Data for journals page.

Data statement

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

Online proof correction

Corresponding authors will receive an e-mail with a link to our online proofing system, allowing annotation and correction of proofs online. The environment is

similar to MS Word: in addition to editing text, you can also comment on figures/tables and answer questions from the Copy Editor. Web-based proofing provides a faster and less error-prone process by allowing you to directly type your corrections, eliminating the potential introduction of errors.

If preferred, you can still choose to annotate and upload your edits on the PDF version. All instructions for proofing will be given in the e-mail we send to authors, including alternative methods to the online version and PDF.

We will do everything possible to get your article published quickly and accurately. Please use this proof only for checking the typesetting, editing, completeness and correctness of the text, tables and figures. Significant changes to the article as accepted for publication will only be considered at this stage with permission from the Editor. It is important to ensure that all corrections are sent back to us in one communication. Please check carefully before replying, as inclusion of any subsequent corrections cannot be guaranteed. Proofreading is solely your responsibility.

Offprints

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