Universidade Estadual de Londrina

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CRIAÇÃO DO *LONDRINA ACTIVITIES OF DAILY LIVING PROTOCOL* (LAP) E A RELAÇÃO ENTRE A DESSATURAÇÃO DE OXIGÊNIO DURANTE O PROTOCOLO E NA VIDA DIÁRIA EM PACIENTES COM DPOC

Londrina
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Tese apresentada ao Programa de Pós-Graduação em Ciências da Saúde, como requisito parcial à obtenção do título de Doutora em Ciências da Saúde.

Orientador: Prof. Dr. Fabio de Oliveira Pitta.

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Dedico este trabalho ao meu marido, por ter sido minha principal fonte de perseverança e de paz nos períodos de turbulência. Também dedico aos meus pais e avós, pela torcida e pelo amor de sempre.

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“Só se vê bem com o coração. O essencial é invisível aos olhos”.
(Antoine de Saint-Exupéry – O Pequeno Príncipe)

SANT'ANNA, Thaís Jordão Perez. **Criação do Londrina *Activities of Daily Living Protocol (LAP)* e a relação entre a dessaturação de oxigênio durante o protocolo e na vida diária em pacientes com DPOC**. 2015. 101 f. Tese (Doutorado em Ciências da Saúde) – Universidade Estadual de Londrina, Londrina, 2015.

RESUMO

Contextualização: Pacientes com doença pulmonar obstrutiva crônica (DPOC) apresentam manifestações fisiopatológicas pulmonares e extra-pulmonares que podem levar à ocorrência de hipoxemia. A hipoxemia pode influenciar negativamente em desfechos naturais no curso da doença e pode ser representada por dessaturação de oxigênio avaliada por meio de oximetria de pulso. Adicionalmente, as manifestações da DPOC levam a sintomas como dispneia e fadiga que podem limitar a realização de atividades da vida diária (AVDs) nesses pacientes. Porém, os métodos utilizados atualmente para a avaliação das AVDs em pacientes com DPOC apresentam limitações. Além disso, não se sabe se possíveis episódios de dessaturação de oxigênio durante um protocolo de AVDs em laboratório estariam associados à dessaturação de oxigênio na vida diária dessa população. **Objetivos:** Desenvolver um novo protocolo para a avaliação do desempenho durante AVDs em pacientes com DPOC (*Londrina Activities of Daily Living [ADL] Protocol – LAP*) e avaliar a validade critério e a reprodutibilidade deste protocolo na mesma população. Adicionalmente, investigar se há relação entre a dessaturação de oxigênio durante a realização deste protocolo e na vida diária dos pacientes. **Métodos:** No primeiro estudo, foi realizada pesquisa bibliográfica e reuniões entre os autores do presente estudo para a seleção das atividades a serem incluídas no novo protocolo (LAP). Após a definição do protocolo, 20 pacientes com DPOC foram submetidos à realização de quatro repetições do LAP, além da avaliação da qualidade de vida e do estado funcional por meio de questionários, avaliação da capacidade funcional de exercício por meio do Teste de Caminhada de 6 minutos (TC6min) e avaliação da atividade física na vida diária (AFVD) por meio de sensores de movimento. No segundo estudo, 20 pacientes foram submetidos à oximetria de pulso durante a realização do LAP e durante 48 horas na vida diária, com monitorização concomitante da AFVD. **Resultados:** No primeiro estudo foi definida a composição do LAP incluindo cinco atividades baseadas em AVDs, envolvendo atividades de membros superiores, membros inferiores e flexão/inclinação de tronco. O LAP foi reprodutível (ICC>0,90, P<0,001). O desempenho no LAP se correlacionou com as variáveis de estado funcional e qualidade de vida ($0,32 \leq r \leq 0,59$) e com a distância percorrida no TC6min ($r = -0,64$). A intensidade de movimento durante o LAP correlacionou-se com a intensidade de movimento na vida diária ($r=0,71$). No segundo estudo, os episódios de dessaturação de oxigênio durante o LAP correlacionaram-se com os episódios de dessaturação de oxigênio na vida diária ($0,45 \leq r \leq 0,59$). **Conclusões:** O LAP é um protocolo válido e reprodutível para avaliar o desempenho nas AVDs em pacientes com DPOC. Os episódios de dessaturação durante um protocolo de AVDs realizado em laboratório estão moderadamente relacionados aos episódios de dessaturação na vida diária desses pacientes.

Palavras-chave: Doença pulmonar obstrutiva crônica. Atividades cotidianas. Atividade motora. Oximetria.

SANT'ANNA, Thaís Jordão Perez. **Development of the Londrina Activities of Daily Living Protocol (LAP) and the relationship between oxygen desaturation during the protocol and in daily life in patients with COPD**. 2015. 101 p. Thesis (Doctoral degree in Health Sciences) – Universidade Estadual de Londrina, Londrina, 2015.

ABSTRACT

Background: Patients with chronic obstructive pulmonary disease (COPD) present pathophysiological pulmonary and extra-pulmonary features which could lead to the occurrence of hypoxemia. Hypoxemia can lead to negative influence on the outcomes of the disease's natural course, and can be represented by oxygen desaturation assessed by pulse oximetry. Additionally, COPD manifestations lead to symptoms such as dyspnea and fatigue which can impair activities of daily living (ADL) performance in these patients. However, methods for ADL assessment in patients with COPD present some limitations. Furthermore, it is not clear whether possible episodes of oxygen desaturation during an ADL laboratory-based protocol present association with episodes of oxygen desaturation in daily life in this population. **Objectives:** To develop a new protocol to evaluate ADL performance in patients with COPD (Londrina ADL Protocol [LAP]) and to assess the criterion validity and the reliability of the protocol in the same population. Additionally, to investigate the relationship between oxygen desaturation during the protocol and in patients' daily life. **Methods:** In the first study, a bibliographic research and meetings among the authors of the present study were done to establish the activities to be included in the new protocol (LAP). After defining the protocol, 20 patients with COPD were submitted to four repetitions of the LAP, besides the assessment of quality of life and functional status by questionnaires, functional exercise capacity by the Six-minute Walking Test (6MWT) and physical activity in daily life (PADL) by motion sensors. In the second study, 20 patients with COPD were submitted to pulse oximetry while performing the LAP and during 48 hours in daily life, with simultaneous PADL monitoring. **Results:** In the first study, the composition of the LAP was defined including five activities based on ADL, involving movements of upper limbs, lower limbs and trunk flexion/inclination. The LAP was reliable (ICC>0.90, P<0.001). Movement intensity during the LAP was highly correlated with movement intensity during daily life (r=0.71). Performance in the LAP was correlated with functional status and quality of life outcomes ($0.32 \leq r \leq 0.59$) and with the distance walked in the 6MWT ($r = -0,64$). In the second study, the episodes of oxygen desaturation during the LAP were correlated with episodes of oxygen desaturation in daily life ($0,45 \leq r \leq 0,59$). **Conclusions:** The LAP is a valid and reliable protocol to evaluate ADL performance in patients with COPD. Episodes of oxygen desaturation during an ADL laboratory-based protocol are moderately related to episodes of oxygen desaturation in daily life in this population.

Keywords: Chronic obstructive pulmonary disease. Activities of daily living. Motor activity. Pulse oximetry.

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LISTA DE ABREVIATURAS E SIGLAS

6MWT	6-*Minute Walking Test*
ADL	*Activities of daily living*
AVDs	Atividades de vida diária
CAT	*COPD Assessment Test*
CI	*Confidence interval*
COPD	*Chronic obstructive pulmonar disease*
CVF	Capacidade Vital Forçada
DMM	*DynaPort Move Monitor*
DPOC	Doença pulmonar obstrutiva crônica
ED <88%	Episódios de saturação de oxigênio < 88% / *Number of episodes of oxygen saturation under 88%*
ED ≥ 4%	Episódios de dessaturação de oxigênio ≥ 4% / *Number of episodes of oxygen desaturation of* ≥ 4%
FEV_1	*Forced expiratory volume in the first second*
GOLD	*Global Initiative for Chronic Obstructive Lung Disease*
HIF-1	Fator Induzido por Hipóxia
HR	*Heart rate*
ICC	*Intraclass correlation coeficient*
LAP	*Londrina ADL Protocol*
LCADL	*London Chest Activities of Daily Living Questionnaire*
LL	*Lower limit*
LTOT	*Long-term oxygen therapy*
MET	*Metabolic equivalents of task*
NF-kB	Fator Nuclear kappa B
PADL	*Physical activity in daily life*
PaO_2	Pressão parcial arterial de oxigênio/*Partial arterial pressure of oxygen*
PFSDQ-M	*Pulmonary Functional Status and Dyspnea Questionnaire* versão modificada/*modified version*
SaO2	*Arterial blood oxygen saturation*
SpO_2	Saturação de oxigênio no sangue por meio da oximetria de pulso/*Pulse oximetry oxygen blood saturation*
SWA	*SenseWear armband*

TC6min	Teste de Caminhada de 6 minutos
TNFα	Fator de Necrose Tumoral Alfa
UL	*Upper limit*
VEF_1	Volume Expiratório Foçado no 1º segundo
VEGF	Fator de Crescimento Endotelial Vascular
VO_2	Consumo de oxigênio

SUMÁRIO

1. INTRODUÇÃO

DOENÇA PULMONAR OBSTRUTIVA CRÔNICA (DPOC):

Atualmente, a DPOC é a quarta principal causa de morte no mundo e, provavelmente, ocupará a terceira posição dentro dos próximos anos[1]. Sua principal causa é o tabagismo, mas indivíduos não-fumantes também podem ser acometidos pela doença por diversas outras causas como asma ou infecções respiratórias na infância, poluição do ar, exposição ocupacional a poeiras e tabagismo passivo, entre outras[2, 3]. Ela é definida como uma doença prevenível e tratável caracterizada por limitação persistente ao fluxo aéreo que é usualmente progressiva e associada a uma resposta inflamatória crônica das vias aéreas e dos pulmões a partículas nocivas e gases[4]. A obstrução crônica é causada pela associação entre o dano das pequenas vias aéreas e a destruição do parênquima pulmonar, sendo que a contribuição de cada tipo de acometimento varia entre os indivíduos portadores da doença[4]. Adicionalmente, exacerbações e comorbidades contribuem para a gravidade da doença[4].

Dispneia, tosse e acúmulo de secreção nas vias aéreas são sintomas característicos da DPOC. A dispneia é o principal sintoma relacionado à doença, sendo tipicamente descrita pelos pacientes como “sensação de esforço para respirar”, “aperto no peito” “fome de ar” ou estar “ofegante”[5]. A tosse é com frequência o primeiro sintoma que os pacientes com DPOC desenvolvem, mas eles costumam associá-la a uma simples consequência do hábito tabágico. Inicialmente, a tosse é esporádica, intermitente, mas, com o passar do tempo, torna-se um sintoma diário, podendo inclusive contribuir com a piora da limitação ao fluxo aéreo[4]. De maneira geral, o pacientes com DPOC costumam deslocar pequena quantidade de secreção espessa das vias aéreas após episódios de tosse. Pacientes que produzem grande quantidade de secreção nas vias aéreas podem ter complicações associadas, como a bronquiectasia. Além disso, o aumento da quantidade e a alteração no aspecto da secreção podem indicar uma exacerbação da doença[6].

Em pacientes que apresentam dispneia, tosse crônica e produção de secreção nas vias aéreas o diagnóstico clínico de DPOC deve ser considerado. Porém, a espirometria é necessária para a confirmação do diagnóstico neste contexto, devendo os pacientes apresentarem uma relação entre o Volume Expiratório Forçado no Primeiro Segundo e a Capacidade Vital Forçada (VEF_1 / CVF) menor que 0,70 após o uso de medicação broncodilatadora, de acordo com diretrizes internacionais[4, 7, 8].

Apesar de sua definição estar associada ao acometimento das vias aéreas, a DPOC apresenta manifestações sistêmicas importantes que em conjunto com o comprometimento

respiratório prejudicam a capacidade de exercício dos pacientes. Além de apresentarem limitações na ventilação pulmonar[9] e nas trocas gasosas[10], os pacientes podem apresentar disfunção cardíaca, especialmente sobrecarga do ventrículo direito[11]. Outra manifestação extrapulmonar comum é a disfunção muscular periférica, que pode ser atribuída à inflamação sistêmica, uso de corticoesteróides, estresse oxidativo e redução da massa muscular[12]. Pacientes com DPOC também costumam desenvolver anormalidades na composição corporal, como perda de peso e redução da porcentagem de massa magra[13]. Essas características contribuem para a sensação de dispneia e fadiga, frequentemente relatada pelos pacientes, inclusive durante a realização de simples atividades da vida diária nos casos mais graves[14].

DPOC E HIPOXEMIA:

Hipoxemia pode ser definida como uma redução da pressão parcial arterial de oxigênio (PaO_2), abaixo dos valores normais[15]. As alterações no sistema respiratório decorrentes da DPOC podem resultar em hipoxemia, o que colabora com o surgimento e a evolução de comorbidades extrapulmonares que caracterizam a DPOC[16]. O fator que mais contribui com a hipoxemia nessa população é o desequilíbrio na relação ventilação/perfusão, resultado da limitação progressiva ao fluxo aéreo e da destruição enfisematosa do leito capilar pulmonar[17]. O controle ventilatório prejudicado é outro componente que contribui para a ocorrência e a persistência de hipoxemia em pacientes com DPOC, sendo que a chave deste problema parece ser a hiperinsuflação pulmonar consequente à disfunção muscular inspiratória e à obstrução das vias aéreas[16].

Dentre as comorbidades que podem ser desenvolvidas ou agravadas por conta da hipoxemia, encontra-se a hipertensão pulmonar. Um fator importante para o aumento da resistência vascular pulmonar é a vasoconstrição pulmonar hipóxica, causada pela hipóxia alveolar[18]. Em outras palavras, a hipoxemia leva à redução da oxigenação tecidual alveolar (hipóxia) e a vasculatura pulmonar “responde” com sua vasoconstrição, levando ao aumento da pressão nos vasos pulmonares. Outra consequência indesejada da hipoxemia é a policitemia, caracterizada pelo aumento do hematócrito acima dos valores normais. Ela ocorre devido à resposta desequilibrada do Fator Induzido por Hipóxia (HIF-1) à hipoxemia. Na presença de hipoxemia, o HIF-1 pode induzir adaptações no Fator de Crescimento Endotelial Vascular (VEGF) e na eritropoetina[19]. Essa resposta desequilibrada, com atuação exacerbada do HIF-1 pela hipoxemia, gera policitemia nos pacientes com DPOC[16]. A inflamação sistêmica, naturalmente presente em pacientes com DPOC[20], pode ser agravada pela presença de hipoxemia[16]. A hipoxemia induz respostas do Fator Nuclear Kappa B (NF-

kB), um fator de transcrição que regula a resposta inflamatória, controlando a expressão de citocinas, como o Fator de Necrose Tumoral Alfa (TNFα) e a interleucina-8[21]. Na presença de hipoxemia, o NF-kB atua de maneira exacerbada, estimulando a expressão de citocinas pró-inflamatórias[22]. A hipoxemia também contribui com o desenvolvimento de uma das mais importantes manifestações extrapulmonares da DPOC: a disfunção muscular esquelética[23]. A piora da inflamação sistêmica causada pela hipoxemia, como descrito anteriormente, contribui com a disfunção muscular esquelética. Isso ocorre porque o TNFα pode provocar apoptose celular e degradação de proteínas[24]. Além disso, os níveis de TNFα e outras citocinas inflamatórias, como a interleucina-8, mostraram estar correlacionados com o grau de disfunção muscular em pacientes com DPOC[25]. Mais um possível fator que contribui para a disfunção muscular esquelética é o estresse oxidativo, que ocorre quando há um desequilíbrio entre a geração de espécies reativas de oxigênio e a capacidade oxidativa[16]. Isso dificulta a contração muscular e é tipicamente encontrado em pacientes hipoxêmicos crônicos[26].Tanto a inflamação sistêmica quanto o estresse oxidativo, ambos associados à hipoxemia, são sugeridos como mecanismos que levam a lesão neuronal. Adicionalmente, a disfunção de enzimas dependentes de oxigênio pode levar à depleção de neurotransmissores. Tais acontecimentos podem causar disfunção neurocognitiva nos pacientes com DPOC, quadro relativamente comum nessa população[16, 27, 28].

O perfil de saturação de oxigênio na vida diária verificado por meio da oximetria de pulso pode oferecer informações relevantes em grupos de pacientes que apresentam valores similares entre si de PaO_2 e de valor basal de saturação de oxigênio no sangue por meio da oximetria de pulso (SpO_2)[29]. Sabendo que a hipoxemia contribui para o desenvolvimento de manifestações extrapulmonares da DPOC[16], métodos de avaliação que contribuam com a identificação do perfil de saturação/dessaturação de oxigênio na vida diária são úteis para o manejo da doença. Considerando que a verificação da oximetria de pulso no dia-a-dia do paciente pode ser incômoda ou até mesmo interferir em suas AVDs, seria de grande valia que tal avaliação pudesse ser realizada em laboratório e mesmo assim representar a oximetria na vida diária do paciente. Adicionalmente, a possibilidade de se realizar a avaliação do perfil de saturação/dessaturação de oxigênio em laboratório, sem a necessidade de longas avaliações durante a vida diária, otimizaria o tempo do profissional avaliador e também dos pacientes, que obteriam os resultados da investigação com mais rapidez.

DPOC E ATIVIDADES DE VIDA DIÁRIA (AVDS):

Além do acometimento pulmonar, a DPOC também leva à ocorrência de manifestações extrapulmonares como inflamação sistêmica, aumento do estresse oxidativo, alterações na composição corporal, fraqueza muscular[20] e até mesmo distúrbios psicológicos como ansiedade e depressão[30]. As características da doença, pulmonares e extrapulmonares, levam à sensação de fadiga e dispneia, sintomas comumente relatados pelos pacientes durante a realização de atividades físicas, inclusive AVDs[14]. Sendo assim, os indivíduos portadores da DPOC passam a evitar a realização de atividades físicas no intuito de reduzir os sintomas, tornando-se cada vez mais descondicionados e menos ativos fisicamente. Com a redução na realização de atividades físicas e a consequente piora do condicionamento físico, os pacientes desenvolvem cada vez mais sintomas, o que, por sua vez, dificulta progressivamente a realização de atividades físicas[31]. Por essa razão, pacientes portadores de DPOC são significativamente menos ativos quando comparados a idosos saudáveis[32, 33].

AVDs são atividades relacionadas à rotina do indivíduo, geralmente ligadas a atividades domésticas, cuidado pessoal, lazer e atividades relacionadas ao trabalho. As AVDs podem ser classificadas como “básicas” ou “instrumentais”. As AVDs consideradas básicas são aquelas essenciais para a vida diária, como higiene pessoal, mobilidade, vestir-se e comer. Já as AVDs instrumentais representam atividades como cozinhar, realizar serviços domésticos, dirigir um automóvel e lavar a louça. Diferentemente das AVDs básicas, as AVDs instrumentais podem ser opcionais ou variar de acordo com a condição social e financeira do indivíduo[34]. Com a piora dos sintomas, pacientes com DPOC podem reduzir a quantidade de AVDs realizadas, tanto básicas quanto instrumentais. Em consequência, ocorre redução da qualidade de vida, desfecho associado às limitações na realização de AVDs[34]. Considerando a importância da limitação na performance de AVDs em pacientes com DPOC, a correta avaliação deste desfecho nessa população é fundamental.

A maneira mais comum de avaliar-se as AVDs é utilizando questionários. Alguns questionários são mundialmente utilizados na prática clínica e em pesquisas científicas, especificamente para avaliação das AVDs em pacientes com DPOC. São eles o *Pulmonary Functional Status and Dyspnea Questionnaire*-versão modificada (PFSDQ-M)[35, 36]e o *London Chest Activity of Daily Living questionnaire* (LCADL)[37, 38]. Por meio desses questionários, o paciente relata o quanto seus sintomas interferem na realização de AVDs. Apesar de questionários serem úteis para demonstrar como o paciente se vê frente às suas limitações[39], uma medida objetiva é importante para complementar a análise dessas

limitações, considerando que pacientes com DPOC podem apresentar dificuldade em relatar corretamente e quantitativamente a sua performance no dia-a-dia[27, 40].

Um método objetivo criado para a avaliação do estado funcional de pacientes com DPOC, relacionado à performance de AVDs, é o *Glittre ADL-test*. Neste protocolo, o paciente deve caminhar por um corredor de 10 metros, realizando diferentes atividades baseadas em AVDs ao longo do caminho, indo e voltando cinco vezes consecutivas. O percurso todo deve ser realizado com a maior velocidade possível e o tempo gasto para se completar o teste é o principal desfecho utilizado[41]. Devido ao perfil do teste, que deve ser realizado com a maior velocidade possível, é questionável o fato de que é um protocolo que representa as AVDs de pacientes com DPOC. Uma informação que reforça essa hipótese é a alta correlação entre o *Glittre ADL-Test* e o Teste de Caminhada de 6 Minutos (TC6min), um teste que sabidamente faz com que pacientes com DPOC atinjam alta porcentagem do seu consumo máximo de oxigênio (VO_2máx)[42], pois também exige que o indivíduo caminhe o mais rápido que puder[43]. Além disso, o *Glittre ADL-Test* não inclui uma avaliação aprofundada e objetiva das AVDs que envolvem os membros superiores, que também estão comumente afetadas negativamente em pacientes com DPOC[44].

O estudo de desfechos relacionados à performance de AVDs (hiperinsuflação dinâmica, dessaturação de oxigênio ou gasto energético, por exemplo) tem recebido considerável atenção da literatura mundial. Como a investigação desses desfechos ao longo da rotina do paciente tende a ser intrusiva e pouco viável, protocolos de laboratório têm sido criados para que tais análises sejam possíveis[45-51]. Entretanto, na maioria das vezes, esses protocolos não têm suas propriedades psicométricas avaliadas, não sendo possível inferir se realmente representam a vida diária dos pacientes. Adicionalmente, cada estudo elabora seu próprio protocolo de AVDs, dificultando comparações entre estudos.

Considerando a falta de um protocolo de laboratório padrão para a avaliação mais completa do desempenho de pacientes com DPOC durante a realização de AVDs, assim como a importância da verificação simplificada do perfil de saturação/dessaturação de oxigênio durante a vida diária dessa população, a presente tese visa preencher essas lacunas na literatura. Para isso, foram realizados dois estudos, os quais estão descritos em forma de artigos científicos e formatados de acordo com as normas dos periódicos para os quais serão submetidos para publicação.

2. OBJETIVOS

Objetivos gerais:

1) Criar e validar um protocolo para a avaliação do desempenho de pacientes com DPOC durante a realização de AVDs.
2) Analisar a relação entre os episódios de dessaturação de oxigênio durante o protocolo de AVDs realizado em laboratório e na rotina de vida diária em pacientes com DPOC.

Objetivos específicos:

1) Investigar a validade critério e a reprodutibilidade desse novo protocolo de AVDs.
2) Verificar se é possível determinar a ocorrência de episódios de dessaturação de oxigênio na vida diária com base em um protocolo de laboratório em pacientes com DPOC.
3) Verificar se os episódios de dessaturação de oxigênio estão associados ao nível de atividade física na vida diária em pacientes com DPOC.

3. MÉTODOS

Para a criação de um novo protocolo para a avaliação do desempenho de pacientes com DPOC durante a realização de AVDs, foi realizada, inicialmente, uma busca bibliográfica a estudos que aplicaram diferentes protocolos de AVDs nessa população. Com base nesses estudos, foram registradas as AVDs incluídas nos protocolos existentes e verificadas as AVDs que mais se repetiam entre os diferentes protocolos. Posteriormente, foram realizadas reuniões entre os autores do presente estudo, onde discutia-se sobre as AVDs normalmente incluídas nos estudos já existentes na literatura científica. Essas discussões tiveram como objetivo eleger as atividades que deveriam ser incluídas no novo protocolo de AVDs. Os critérios utilizados para a seleção das atividades a serem incluídas no protocolo foram: atividades que fizessem do protocolo um teste simples e prático de ser realizado; atividades que envolvessem a utilização de membros superiores, membros inferiores e flexão/inclinação de tronco; atividades que reproduzissem o que comumente é realizado no dia-a-dia da maioria das pessoas; atividades que pudessem ser realizadas da maneira mais real possível, evitando simulações (por exemplo: solicitar ao paciente que finja estar tomando banho, que finja estar varrendo algo no chão, que finja estar fazendo a barba, etc.). Por fim, antes de se analisar as propriedades psicométricas do novo protocolo de AVDs, ele foi aplicado em alguns adultos jovens saudáveis e em pacientes com DPOC, para que limitações práticas do protocolo fossem identificadas e corrigidas. Este novo protocolo foi denominado *Londrina Activities of Daily Living (ADL) Protocol (LAP)*, pois seu processo de criação ocorreu no Laboratório de Pesquisa em Fisioterapia Pulmonar da Universidade Estadual de Londrina, Brasil.

Vinte e um pacientes com DPOC foram incluídos para a realização da presente tese. Como critérios de inclusão, eles deveriam apresentar o diagnóstico da doença de acordo com critérios internacionais[4], estabilidade clínica (pelo menos três meses sem exacerbações graves da doença), ausência de distúrbios neuromusculares ou esqueléticos que pudessem interferir na performance de AVDs e não apresentar valores basais de PaO_2 e SpO_2 compatíveis com indicação para oxigenoterapia domiciliar. A pesquisa foi aprovada pelo Comitê de Ética da Universidade Estadual de Londrina, Brasil (031/2013) e todos os participantes assinaram o Termo de Consentimento Livre e Esclarecido.

As avaliações foram realizadas em quatro momentos: na primeira visita ao laboratório, os pacientes foram submetidos à coleta de dados antropométricos, medida da SpO_2 basal na posição sentada, avaliação da função pulmonar por meio de espirometria[8, 52], impacto da doença no estado de saúde por meio do *COPD Assessment Test* (CAT)[53] e estado funcional por meio do LCADL[37, 38] e do PFSDQ-M[35, 36]. Na segunda visita, os

pacientes realizaram o LAP quatro vezes, com intervalos suficientes para recuperarem os valores basais de SpO_2, frequência cardíaca (FC) e esforço percebido (Escala de Borg Modificada)[54]. Duas dessas realizações do LAP ocorreram com os pacientes utilizando uma máscara conectada a um analisador de gases portátil que pesa em torno de 2 kg (Oxycon ™ Mobile Device, CareFusion, Estados Unidos da América)[55], registrando o consumo de oxigênio (VO_2). A ordem das realizações do LAP (com e sem máscara para análise de gases) foi determinada por meio de aleatorização. Durante todas as realizações do LAP, SpO_2 e FC foram monitoradas continuamente por meio de oxímetro de pulso (Nonin WristOx2 ™ 3150, Estados Unidos da América). Além disso, gasto energético (por meio do SenseWear® armband [SWA], Body Media, Estados Unidos da America)[56] e intensidade de movimento (por meio do DynaPort Move Monitor® [DMM], McRoberts, Holanda)[57] foram registrados. Antes e depois dos LAPs, as sensações de fadiga e dispneia também foram avaliadas por meio da Escala de Borg Modificada[54]. O principal desfecho proveniente do LAP é o tempo gasto pelos pacientes para realizar o protocolo, *i.e*., a "duração do LAP". Após a realização dos quatro LAPs, os pacientes relataram o grau de dificuldade em cada realização do LAP, de acordo com uma escala Likert. Essa escala apresenta valores de 0 a 10, onde 0 representa "nenhuma dificuldade" e 10 representa "difícil demais". Na terceira visita, os pacientes foram submetidos à avaliação da capacidade funcional de exercício por meio do Teste de Caminhada de Seis Minutos (TC6min)[43, 58] e receberam os dois monitores de atividade física e o oxímetro de pulso utilizados durante o LAP. Quarta e última visita: os pacientes trouxeram de volta os monitores de atividade física e o oxímetro de pulso. Nesta mesma visita os pacientes foram submetidos à coleta de sangue para realização de gasometria arterial[59].

Apesar da composição final do LAP ser um dos resultados do primeiro estudo desta tese, optamos por descrevê-lo nesta sessão de métodos, no intuito de esclarecer ao leitor como o protocolo foi realizado durante a investigação de sua validade e reprodutibilidade:

Londrina ADL Protocol (LAP): É composto por cinco atividades e organizado em "estações" dentro de uma sala. A posição das "estações de atividade" e a distância entre elas estão representadas ao longo da descrição dos artigos científicos descritos posteriormente nesta tese. A sequência das estações é:

1) ***Movendo objetos sobre a mesa:*** O paciente senta-se em uma cadeira de frente para uma mesa onde há uma linha demarcada separando a mesa em duas metades (esquerda e direita). A mesa contém 10 objetos sobre ela (4 objetos de 250g, 4 objetos de 500g e 2 objetos de 1kg), todos juntos na metade esquerda da mesa. O paciente pega os objetos, um de cada vez, com as duas mãos, e os

coloca na metade direita da mesa. Posteriormente, o paciente retorna todos os objetos da mesma maneira para a metade esquerda da mesa novamente. Não há uma sequência padronizada para a organização do objetos sobre a mesa, nem posição específica para cada objeto, devendo o paciente apenas reposicioná-los no lado direito e depois no lado esquerdo da mesa.

2) ***Caminhando com sacolas:*** O paciente caminha sobre uma faixa de 6 metros de comprimento desenhada no chão, três vezes consecutivas, carregando duas sacolas, uma em cada mão. Dentro das sacolas há uma carga representando 10% do peso corporal do paciente, 5% em cada sacola.

3) ***Posicionando objetos em prateleiras:*** O paciente posiciona-se em frente a quatro prateleiras, uma sobre a outra, com uma mesa ao lado. Sobre a mesa há 12 objetos (4 objetos de 250g, 4 objetos de 500g, 2 objetos de 1kg e 2 objetos de 2kg). O paciente pega os objetos, um de cada vez, com as duas mãos, e os coloca nas prateleiras. O paciente deve organizar os objetos nas prateleiras de forma que hajam três objetos em cada prateleira. Quando todos os objetos estão posicionados nas prateleiras, o paciente coloca-os novamente sobre a mesa da mesma maneira. Não há uma sequência padronizada para a colocação dos objetos nem prateleira e/ou posição específica para cada um.

4) ***Pendurando roupas no varal:*** O paciente psociona-se em frente ao varal, que deve estar posicionado na altura dos olhos do paciente. Há uma bacia/cesto no chão, ao lado do paciente, contendo 10 peças de roupas variadas. O paciente pega as peças de roupa, uma de cada vez, com as duas mãos e as pendura no varal. Após pendurar todas as roupas, o paciente as retorna para a bacia/cesto, uma de cada vez, com as duas mãos.

5) ***Caminhando:*** O paciente caminha novamente sobre a faixa de seis metros descrita na atividade 2, três vezes consecutivas, mas sem carregar as sacolas.

As atividades são realizadas consecutivamente, em velocidade usual. Entre as “estações de atividade”, o paciente também caminha em velocidade usual. Antes do paciente realizar o LAP, o avaliador demonstra as atividades na ordem de realização, explicando como elas devem ser realizadas. As instruções fornecidas ao paciente são: “Realize essas atividades como se você as estivesse realizando em casa, no seu dia-a-dia. Você pode parar para descansar se sentir que é necessário. Não se preocupe com a ordem das atividades, porque nós o lembraremos qual é a próxima atividade ao longo do protocolo”. Durante o protocolo, apenas a próxima

atividade é lembrada ao paciente, mas nenhum encorajamento é realizado. Caso o paciente opte por descansar durante o protocolo, o tempo continuará sendo registrado normalmente, sem pausa no cronômetro.

Avaliação da atividade física na vida diária (AFVD): Os monitores de atividade física (SWA e DMM) foram utilizados simultaneamente durante dois dias consecutivos da semana, 24 horas por dia[60, 61]. Os dias de avaliação foram considerados válidos se o paciente utilizasse os monitores durante pelo menos 80% do tempo requerido de medida. Eles foram instruídos a retirar os monitores para o banho e a manter sua rotina. Os dois monitores são leves, não oferecem nenhum risco aos pacientes e são amplamente utilizados em pesquisas. O SWA é utilizado no braço esquerdo, sobre a região do tríceps. Os dados são coletados com base nos registros de um acelerômetro triaxial e sensores fisiológicos. Os principais desfechos provenientes deste monitor são o gasto energético total, o gasto energético durante atividades físicas, a média de equivalentes metabólicos (MET), o tempo gasto em atividades físicas e o tempo gasto em atividades de diferentes intensidades[56]. O DMM é um acelerômetro triaxial utilizado sobre a região lombar, fixado por uma cinta. As principais variáveis fornecidas por ele são o tempo gasto em diferentes atividades e posturas como caminhar, ficar em pé, sentar e deitar e também a intensidade de movimento[57]. Os resultados provenientes do SWA e do DMM são baseados na média dos dois dias de medida.

Avaliação da SpO_2: Para todas as medidas de SpO_2 realizadas neste estudo, o mesmo oxímetro de pulso foi utilizado. O WristOx2 ^{TM} 3150 (Nonin Estados Unidos da América) é um oxímetro de pulso utilizado no punho, como um relógio. O sensor é posicionado em um dos dedos da mão e é confeccionado de material emborrachado. Ele foi utilizado pelos pacientes tanto durante o LAP como durante as 48 horas de avaliação da AFVD, sempre no membro superior não-dominante, com o sensor posicionado no dedo de preferência do paciente. Os pacientes foram instruídos a retirar o aparelho sempre que tivessem contato com água ou quando fossem ao banheiro. O oxímetro possui uma memória interna capaz de registrar dados por até 45 dias. O aparelho possui um recurso em seu software, não descrito em detalhes pelo fabricante, que identifica movimentações do tipo artefato e minimiza a probabilidade destes artefatos serem interpretados como pulso de boa qualidade. Os dados são transferidos para um computador para análise por meio do software que acompanha o oxímetro. As principais variáveis fornecidas pelo aparelho que foram utilizadas no presente estudo são o número de episódios de dessaturação de

oxigênio > 4% por dia (ED>4%) e o número de episódios de SpO_2 abaixo de 88% por dia (ED<88%), levando em consideração a média dos dois dias de medida.

Cálculo do tamanho amostral (estudo 1): A intensidade de movimento durante a vida diária, desfecho registrado objetivamente por meio de monitorização da atividade física, foi eleita a principal variável para se verificar a validade do LAP como um protocolo que representa a performance real dos pacientes durante AVDs. Uma amostra de catorze pacientes seria necessária para encontrar uma correlação de ao menos 0,70 entre a intensidade de movimento durante o LAP e a intensidade de movimento durante a vida diária, considerando $\alpha = 0,05$ e $\beta = 0,80$. Este cálculo foi realizado por meio do programa BioStat 3.0. Apesar da intensidade de movimento ter sido a principal variável para a avaliação da validade do LAP, outras variáveis, provenientes de outros instrumentos, também foram incluídas nas análises, com o objetivo de se obter uma análise mais ampla do protocolo.

Cálculo do tamanho amostral (estudo 2): Para ser possível encontrar uma correlação de 0,60 entre os episódios de dessaturação durante o LAP e durante a vida diária, seriam necessários 20 pacientes compondo a amostra do estudo. O cálculo foi realizado considerando-se $\alpha = 0,05$ e $\beta = 0,80$, por meio do programa BioStat 3.0.

Análise estatística (estudo 1): A distribuição dos dados foi analisada por meio do teste de Shapiro-Wilk. De acordo com a normalidade na distribuição dos dados, estes foram descritos como média e desvio-padrão ou mediana e intervalo interquartílico, as correlações entre as variáveis verificadas por meio dos coeficientes de Pearson ou Spearman e as comparações por meio do Teste T de *Student* pareado ou teste de Wilcoxon. A reprodutibilidade e a concordância do LAP foram verificadas por meio do Coeficiente de Correlação Intraclasse do tipo *two-way mixed*, *single measurement* (3,1), e da análise gráfica de Bland & Altman, respectivamente. A significância estatística foi estabelecida em $P<0,05$. As análises foram realizadas utilizando-se os programas SPSS 20.0 e GraphPad Prism 6.0.

Análise estatística (estudo 2): A distribuição dos dados foi verificada por meio do teste de Shapiro-Wilk. De acordo com a normalidade na distribuição dos dados, estes foram descritos como média e desvio-padrão ou como mediana e intervalo interquartílico e as correlações verificadas por meio dos coeficientes de Pearson ou Spearman. Para se investigar se os desfechos da oximetria durante o LAP podem influenciar os mesmos desfechos na vida real, foi realizada análise de

regressão linear univariada. A significância estatística foi estabelecida em $P<0,05$ e os programas estatísticos utilizados para a análise foram o SPSS 20.0 e o GraphPad Prism. 6.0.

4. ARTIGO 1

Development, validity and reliability of the Londrina Activities of Daily Living (ADL) Protocol (LAP) for patients with COPD: ADL in one LAP

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ABSTRACT

Introduction: As a consequence of increased symptoms, patients with chronic obstructive pulmonary disease (COPD) reduce the amount of activities of daily living (ADL). Hence, this leads to a reduction in quality of life, which is associated with limitations to perform ADL. Considering the impact of a limited ADL performance on the daily life of patients with COPD, it is relevant for clinical practice to be able to evaluate ADL performance in a standardized manner in this population. **Objectives:** To develop a new protocol to evaluate ADL performance in patients with COPD (Londrina ADL Protocol [LAP]) and to assess the criterion validity and the reliability of the protocol in this population. **Methods:** Twenty subjects with COPD (12 men, 70±7 years old, FEV1=54±15% predicted) performed the LAP four times, two of them wearing a portable gas analyzer. During the LAP performance they wore two motion sensors simultaneously. They were also submitted to assessments of lung function, functional exercise capacity, functional status, impact on health status and physical activity in daily life. **Results:** LAP duration presented high values of intraclass correlation coefficient, even using a mask for gas analisys (ICC>0.90, P<0.001). Intensity of movement during the LAP performance was highly correlated to intensity of movement in daily life (r=0.71). LAP duration was correlated with functional status and impact in health status variables from questionnaires ($0.32 \leq r \leq 0.59$). There was also a correlation between functional exercise capacity and LAP duration (r= -0.64). **Conclusion:** The LAP is a valid and reliable protocol to evaluate ADL performance in patients with COPD. It is a protocol which can be used in clinical practice and in future studies in order to investigate ADL outcomes, including those studies which require gas analysis and the need for wearing a mask.

Key Words: Chronic obstructive pulmonary disease, Activities of daily living, Functionality impaired elderly, Motor activity, Chronic limitation of activity, Symptoms.

INTRODUCTION

Dyspnea and fatigue are the most common symptoms reported by patients with chronic obstructive pulmonary disease (COPD)[1], a progressive disease, with pulmonary and extra-pulmonary manifestations[2]. Therefore, patients involve themselves in a negative spiral, reducing participation in physical activities intending to avoid symptoms[3]. However, the less they perform physical activities, the higher is the worsening in physical conditioning and symptoms[4]. This vicious cycle affects even simple features such as activities of daily living (ADL)[4]. ADL are activities related to subject's routine and are generally linked to domestic tasks, personal care, leisure and work-related activities. ADL are commonly classified as basic or instrumental. Basic ADL are those essentially required for daily life, such as personal hygiene, toileting, dressing, eating and physical mobility. On the other hand, many of the instrumental ADL are optional, depending on the social and financial condition. Examples of these activities are housework, driving a car, cooking, gardening and doing the laundry[5]. As a consequence of increased symptoms, patients reduce the amount of all ADL, both basic and instrumental. Hence, this leads to a reduction in quality of life, which is associated with limitations to perform ADL[5]. Considering the impact of a limited ADL performance on the daily life of patients with COPD, it is relevant for clinical practice to be able to evaluate ADL performance in a standardized manner in this population.

A term often used to describe the level of ADL impairment and performance is "functional status"[6]. The most common instruments available to evaluate ADL and functional status are questionnaires. Examples of widespread used questionnaires for these purposes, validated for use in patients with COPD, are the Pulmonary Functional Status and Dyspnea Questionnaire-Modified version (PFSDQ-M)[7, 8] and the London Chest Activity of Daily Living questionnaire (LCADL)[9, 10]. In these questionnaires, patients report to which degree symptoms interfere on their ADL performance. Although it is very important to know how patients perceive their own ADL performance and limitations, an objective assessment of this outcome can provide valuable complementary information. The Glittre ADL-test is a protocol

created to assess functional status in patients with COPD. For this, individuals perform four different activities (rising up from sitting position, walking, interposing a two-step staircase and organizing objects on shelves) through a 10-meter corridor, going back and forth five times along the corridor. The protocol has to be performed as fast as possible and the time spent to complete it is the test's main outcome[11]. However, the Glittre ADL-test does not comprise an in-depth and objective assessment of problematic activities involving the upper limbs, which are often limited in patients with COPD[12]. Furthermore, it was shown that the Glittre ADL-test induces a higher oxygen uptake than the 6-minute walking test (6MWT)[13], an exercise capacity test. Moreover, the Glittre ADL-test does not correlate well with a functional status questionnaire but rather correlates more strongly with 6MWT[11]. Since it is known that the 6MWT frequently makes patients with COPD achieve their near-maximal oxygen consumption during the test[14], it is then questionable to associate the Glittre-ADL test to a real life ADL representation but more likely to associate it with a test of functional exercise capacity.

Another gap in the literature is that when researchers want to investigate any outcome coming from or associated to ADL (e.g., dynamic hyperinflation, SpO_2 or energy expenditure), it is common to create ADL protocols specifically for their studies[15-21]. This leads to a lack of standardization in the objective assessment of ADL in patients with COPD. Furthermore, almost all of these protocols did not have their psychometric properties evaluated. Obviously, this is a practice which imposes a methodological bias in scientific investigations, hindering comparisons among different studies.

Summarizing the limitations in ADL performance assessment in patients with COPD identified in the literature, it is clear that subjective methods only partially investigate the subjects' performance during ADL, only looking at the subjects own perspective about their performance; the objective method available for the assessment of ADL performance has few upper limbs movements in its composition (movements that are predominant during ADL in real life) and presents characteristics that could define it as an exercise capacity

evaluation method, instead of a method representing ADL; and there are several studies in the literature investigating outcomes coming from ADL performance based on different protocols without assessment of psychometric properties, impairing comparisons among studies and imposing methodological bias to their results. Therefore, the development of a laboratory-based protocol that indeed reflects ADL, that is reliable and that objectively quantifies ADL performance would be useful to standardize the assessment of ADL performance and consequently contribute to the in-depth evaluation of patients with COPD. For these reasons, we propose a new protocol of objective ADL assessment in patients with COPD, the Londrina ADL protocol (LAP), which intends to counteract the disadvantages of the available tools. After creating the protocol, the present study investigated the validity and reliability of this new protocol in the same population.

METHODS

For the development of a new protocol to assess ADL performance in patients with COPD, a bibliographic research was undertaken in order to find studies which used different ADL protocols in this population. Based on these studies, the ADL included in those protocols were registered and the most prevalent ADL were verified. After that, meetings with the authors of the present study were undertaken to discuss the ADL normally included in the previous studies. These meetings had the objective of defining the activities that should be included in the new ADL protocol. The criteria used to select the activities to be included in the new protocol were: activities that could compose a simple and feasible protocol; activities that involved upper limbs, lower limbs and trunk flexion/inclination; activities that reproduced what is commonly performed on the day-by-day of most of people; activities that could be performed in the highest possible “real life” way, avoiding simulations (i.e., avoiding activities in which it might be necessary to “pretend”, such as having a shower, sweeping the floor, shaving, etc.). It is important to highlight that each activity included in the LAP does not represent the intention to evaluate the subject’s performance in that specific activity, but in activities with similar movements to that one. In other words, when an activity such as “hanging clothes in a clothes line” was included, the objective was not to evaluate subject’s performance only while hanging clothes in a clothes line, even because several subjects never do it in daily life. Actually, the objective was to evaluate the subject’s performance during an activity which includes upper limbs movement sustained above the head and associated with trunk movement on the standing position. Finally, before investigating psychometric properties of the new protocol, it was applied in a few young healthy adults and patients with COPD in order to identify practical limitations of the protocol and to correct them. The new protocol was named Londrina ADL Protocol (LAP), because it was created in the Laboratory of Research in Respiratory Physiotherapy, from the Londrina State University, Brazil.

For the analysis of LAP's criterion validity and reliability, twenty subjects with COPD were included. As inclusion criteria, they presented diagnosis of COPD according to the GOLD criteria [2], clinical stability (at least three months without severe exacerbation of the disease), absence of neuromuscular or skeletal disorders that could impair ADL performance, and not having resting PaO_2 and SpO_2 values consistent with indication of long-term oxygen therapy ($PaO_2 \leq 55$ mmHg or $SaO_2 < 88\%$). Subjects would be excluded if they were not able to execute the proposed evaluations. This research was approved by the Ethics Committee of the State University of Londrina, Brazil (031/2013) and all participants provided informed consent.

Assessments were done in three moments: At the first visit to the laboratory, subjects had their anthropometric data collected, were submitted to assessment of lung function by spirometry[22, 23], impact on health status by the COPD Assessment Test (CAT)[24] and functional status by the PFSDQ-M[7, 8] and the LCADL[9, 10]. At the second visit, subjects performed the LAP four times, with sufficient intervals to recover basal SpO_2, heart rate (HR) and perceived effort (Modified Borg Scale)[25]. Two of these LAP tests occurred with patients wearing a portable gas analyzer (Oxycon™ Mobile Device, CareFusion, United States of America)[26], registering the oxygen consumption (VO_2). The portable gas analyzer weighs around 2 Kg and requires wearing an oral-facial mask. The order of LAP tests (with and without the mask) was randomized. During all LAP tests, SpO_2, HR, energy expenditure (SenseWear® armband [SWA], Body Media, United States of America)[27] and intensity of movement (DynaPort Move Monitor® [DMM], McRoberts, The Netherlands)[28] were registered. Before and after the LAPs, dyspnea and fatigue were also assessed by the Modified Borg Scale[25]. The main outcome gathered from the LAP is the time spent by patients to perform the protocol, i.e., the LAP duration. After performing the four LAPs, subjects reported the degree of difficulty in performing each protocol by grading a Likert scale. This scale ranged from 0 to 10, where 0 represents "not difficult at all" and 10 represents "too much difficulty". At the third visit, patients were submitted to assessment of

functional exercise capacity by the 6MWT[29] and received the two activity monitors (SWA and DMM). Subjects wore the devices during two consecutive weekdays, 24 hours/day. The main outcomes from the activity monitors were the total energy expenditure by the SWA and the movement intensity from the DMM.

Sample size calculation: The intensity of movement during daily life, an outcome registered objectively by physical activity monitoring, was selected as the main variable in order to study the LAP's validity as a method which represents patients' actual ADL performance. A sample of fourteen subjects would be necessary to find a correlation of at least 0.70 between movement intensity during the LAP and movement intensity during daily life, considering $\alpha = 0.05$ and $\beta = 0.80$. The calculation was done using the BioStat 3.0 software. Although movement intensity was the main outcome to evaluate the LAP's validity, other variables, provided from other instruments, were also studied with the aim of having a more in-depth analysis of the new protocol's characteristics.

Statistical analysis: Data distribution was analyzed by the Shapiro-Wilk test. According to normality in data distribution, data were described as mean and standard deviation or median and interquartile range. Correlations between outcomes were verified using Pearson or Spearman coefficients and comparisons were done using paired Student T-Test or Wilcoxon test. Reproducibility of the LAP was verified using two-way mixed, single measure, Intraclass Correlation Coefficient (ICC [3,1]), whereas agreement was studied by Bland and Altman plots. Statistical significance was set at $P < 0.05$. The analysis was performed using SPSS 20.0 and GraphPad Prism 6.0.

RESULTS

Five activities based on ADL were included in the LAP. It was possible to include activities which involve upper limbs, lower limbs and trunk flexion/inclination. It was also possible to include activities that can be completely and realistically performed (i.e., without "pretending"). Additionally, all the activities included are simply organized.

During the LAP application in three healthy young adults and three patients with COPD to identify limitations in the protocol, some original characteristics were adapted. For example: it was realized that some subjects used only one hand to perform some upper limb activities to avoid other body movements (e.g., trunk movement). For this reason, the instruction of "moving objects with both hands" was included. The order of the activities during the protocol was also adapted due to the fact that, in the first version of the protocol, the proposed order of the activities was leading to upper limbs fatigue in the patients and to the need of frequent resting intervals.

The final version of the LAP is described below:

Londrina ADL Protocol (LAP): It is composed by five activities and organized in "stations" inside a room (Figure 1). The room requires space enough to accomodate the distances between the "stations". The position of the "activity stations" and the distance among them are shown in Figure 2. The sequence of the stations is:

1) *Moving objects on a table:* subject sits on a chair in front of a table with a drawn line separating it in two halfs (left and right). The table has 10 objects above it (4 objects of 250g, 4 objects of 500g and 2 objects of 1kg), all together on the left half of the table. Subject takes the objects, one by one, with both hands, and puts them all on the right half of the table. After that, subject returns all the objects in the same way to the left side of the table again. There is no standardized order for objects positioning.

2) *Walking with handbags:* Subject walks over a line of 6 meter of length, three consecutive times, carrying two handbags, each one in one hand. Inside the

handbags there are loads representing 10% of patient's body weight, 5% in each handbag.

3) *Placing objects in shelves:* Subject stays in front of four shelves, one above the other, with a table next to it. On the table, there are 12 objects (4 objects of 250g, 4 objects of 500g, 2 objects of 1kg and 2 objects of 2kg). Subject takes the objects, one by one, with both hands, and put them on the shelves. Subject organizes the objects on the shelves in a way that three objects are placed on each shelve. When all the objects are placed on the shelves, subject returns the objects again to the table in the same way. There is no standardized order for objects positioning.

4) *Hanging clothes in a clothes line:* Subject stays in front of a clothes line, positioned at the eye level. There is a bowl/basket on the ground, next to the patient, containing 10 items of clothes. Subject takes all the items, one by one, with both hands, and hangs them on the clothes line. After hanging all the items, subject returns them to inside the bowl/basket again, taking it one by one and with both hands.

5) *Walking:* Subject walks again on the same 6-meter line described in activity 2, three consecutive times, but without carrying the handbags.

The activities are performed consecutively, at a normal (i.e., "usual") pace. Between the "activity stations", the subject also walks at the usual pace. Before the subject starts to perform the LAP, the evaluator demonstrates the activities in the order they will be performed, explaining how they have to be performed. The instructions given to the subject are: "Perform these activities as if you were doing them at home, in your usual day-by-day. You are allowed to stop to rest if you feel it is necessary. Do not worry about the order of the activities, because we will remind you the next activity as long as the protocol goes". During the protocol, the next activity is reminded to the patient but no encouragement is given.

For the criterion validity and reliability analysis twenty subjects with COPD were included in the study. Characteristics of the participants are described in Table 1. All patients were in the registers of the research laboratory as currently involved, previously involved or interested in being involved in a pulmonary rehabilitation program.

Results described in Table 2 concern LAP's reliability when the subjects were not wearing the portable gas analyzer. Reliability of LAP duration is also shown in Figure 3 (Panel A). There was no difference in LAP duration between test 1 and test 2 (6 min18 sec [5:54 – 7:06] *vs* 6 min 12 sec [5:36 – 7:00]; *P*=0.10). Moreover, Figure 3 (Panel B) illustrates the reliability of the reported difficulty in the two LAPs performed.

Also when patients were using a mask, LAP duration was reproducible (ICC=0.97, CI95%[0.93 – 0.99]; *P*<0.001), presenting a small difference between test 1 and test 2 (7 min 00 sec ± 0:18 vs 6 min 36 sec ± 0:18; *P* = 0.06). From the LAPs performed using the portable gas analyzer, peak VO_2 during the protocol was obtained, and it was also shown to be reproducible (ICC=0.89, CI95%[0.53 – 0.98]; *P*=0.002). There was no difference in peak VO_2 between test 1 and test 2 (14 ± 0.63 vs 13 ± 0.64 $ml.kg^{-1}.min^{-1}$; *P*=0.70).

LAP duration was reproducible between protocols performed with and without a mask for gas analysis, presenting ICC=0.94, CI95%[0.85 – 0.98]; *P*<0.001 (Figure 3, Panel C). However, as expected, the energy expenditure and the difficulty reported by patients showed lower reproducibility between protocols performed with and without the mask (ICC=0.73, CI95%[0.29 – 0.90]; *P*=0.005 and ICC=0.70, CI95%[0.21 – 0.88]; *P*=0.008, respectively).

For correlation analysis, the first LAP without the mask was used. Patient's movement intensity during LAP performance was well correlated with patient's movement intensity during locomotion in daily life (r = 0.71, *P* = 0.001) (Figure 4). Correlations between LAP duration and other outcomes are described in Table 3 and some of them are illustrated in Figures 5 and 6. There was no correlation between LAP duration and lung function outcomes.

The domains of questionnaires which better correlated with the difficulty reported by patients regarding LAP performance was “fatigue” from PFSDQ-M (r = 0.53, *P* = 0.01), whereas the same LAP outcome was also correlated with “dyspnea” and “activities” from PFSDQ-M, “physical activity” and total score from LCADL (r = 0.38, 0.33, 0.38 and 0.33, respectively, *P*<0.05 for all). Reported difficulty, differently from LAP duration, was correlated with FEV_1 (r = 0.43 and 0.31 for absolute and percentage of predicted values, respectively; *P*<0.05) and was not correlated with 6MWT (r = 0.12; *P*=0.60).

Relative peak VO_2 achieved during LAP performance was correlated with movement intensity (r = 0.62; *P*=0.02) and, consequently, inversely correlated with LAP duration (r = -0.42; *P*=0.01). Peak VO_2 was very modestly correlated with 6MWT (r = 0.30; *P*=0.01). No other correlations were found with relative peak VO_2. Finally, there was no correlation between the energy expenditure in daily life and the energy expenditure during LAP performance (r=-0.19; *P*=0.40).

DISCUSSION

This study introduces a new protocol developed to evaluate ADL performance in patients with COPD, the LAP. It provides the possibility of applying a standardized method to assess several outcomes during the performance of ADL in this population. LAP is a reliable test, since it has shown high test-retest ICC values. The fact of being highly reproducible suggests that LAP can be performed only once, even if a mask for gas analysis is being used for obtaining further outcomes. This is a useful finding, as studies have shown that dynamic hyperinflation plays a role in ADL performance[19, 30], and for measuring dynamic hyperinflation, a mask may be necessary. Therefore, the LAP duration has shown not to be jeopardized by the use of a face mask. However, researchers should remember that, using a mask makes LAP a more energy consuming and difficult protocol for patients with COPD. Considering that mean LAP duration is around 6 to 7 minutes, the whole protocol can be applied in 10 to 15 minutes (including the initial explanation to the patients). The above mentioned characteristics associated to the simplicity of the protocol, using simple objects and logistics, indicate the LAP as a feasible option for ADL performance evaluation in patients with COPD.

LAP is a valid ADL protocol, since there was high correlation between movement intensity in daily life and movement intensity during the LAP. This indicates that LAP represents patient's real life and is registering the subject's performance during ADL as it happens in real daily life. This was possibly achieved because the instructions given to the patients were to perform the activities at the usual pace, as they do in their homes on their day-by-day. Intensity of movement provided by the DMM is based on acceleration. This is an interesting outcome, as walking speed is associated with survival in the elderly according to the study by Studenski and colleagues. That study showed that the lower is the walking speed, the lower is the survival in this population[31]. Even with the correlation between movement intensity at home and during LAP performance, there was no correlation between energy expenditure on these two situations. An hypothesis to explain these findings is that

LAP duration was too short to present a correlation with the total energy expenditure measured by the SWA during ADLs in real life.

Moreover, the LAP is correlated with widely used functional status questionnaires, and even with a questionnaire that investigates COPD heath status impact. Although correlations between LAP and questionnaires are moderate, these are relevant results. The main LAP outcome (LAP duration) is an objective outcome and questionnaires present subjective outcomes, since they are based on patient's memory and feeling about their experiences in daily life. Thus, expecting high correlations between these instruments would not be realistic. It could be expected, therefore, that the Likert scale of difficulty for LAP performance correlated better with the questionnaires. It was not the case, probably because of the differences in design and recall period between instruments.

Although LAP was correlated with the 6MWT, an important outcome to characterize functional capacity, this correlation was less intense in comparison to another ADL protocol available in the literature[11]. The Glittre ADL-test is highly correlated with the 6MWT, possibly because of the test design, which stimulates patients to walk as fast as possible (the same instruction given to patients for the 6MWT). Taking into account that 6MWT represents the functional exercise capacity[29] and LAP represents functional performance, a very high correlation between these tests was not expected, since these tests investigate different concepts[32]. It also suggests that LAP is better representative for ADL performance than the above mentioned tests. According to Kocks and colleagues, an indication of the limitations that patients experience in daily life (functional performance) can be more informative for clinical management than functional capacity alone, both composing the functional status concept[33]. The functional capacity is defined as "one's maximum potential to perform activities". On the other hand, functional performance is "the physical, psychological, social, occupational and spiritual activities people actually do in the normal course of their lives to meet basic needs"[32].

There are several studies in the literature which aimed at investigating outcomes derived from ADLs[15-21]. To accomplish this goal, authors commonly create ADL protocols specifically for their studies. However, almost all of these protocols did not have their psychometric properties evaluated. Then, from the scientific point of view, it is not possible to affirm that they represent patients' real ADL performance. Another problem is that, with each study having its own protocol, this hinders comparisons between studies. By developing and describing the LAP's psychometric properties we expect to provide a valid, standardized, simple and useful tool to be used in clinical studies, circumventing the limitations of the Glittre ADL-test (i.e., little involvement of the upper limbs, and ADLs performed at the maximum and not the usual speed).

A limitation of the present study is that a gold-standard method for the analysis of the LAP validity was not used. However, to the best of the authors' knowledge, a gold-standard measure for ADL performance does not exist. Therefore, the option was to use movement intensity in daily life (objectively measured in real life by motion sensors) and questionnaires which are widely known as providing an evaluation of functional status related to ADL performance. Furthermore, in the present investigation it was not possible to study the LAP's responsiveness to interventions, reference values and minimal important difference. Future studies on these matters are welcome.

In conclusion, the LAP is a simple, valid and reliable protocol to evaluate ADL performance in subjects with COPD. It is a protocol which can be used in clinical practice and in future studies in order to investigate ADL outcomes, including those studies which require gas analysis and the need for wearing a mask.

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Table 1. Subjects characteristics (N = 20)

Gender (male/female)	12/8
Age (years)	70 ± 7
BMI (kg/m^2)	26 ± 5
FEV_1 (% predicted)	54 ± 15
6MWT (meters)	504 ± 83
6MWT (% predicted)	95 [66 – 104]
LAP duration (minutes)	6.3 [5.9 – 7.1]
LAP duration with mask (minutes)	7 ± 0.3
Peak VO_2 (ml.kg^{-1}.min^{-1})	14 ± 2
LCADL (points)	
Health care	5 [4 – 7.5]
Domestic	6 [2.5 – 9.7]
Physical activity	5 [3 – 5.7]
Leisure	3.5 [3 – 4.7]
Total	18 [16 – 23.7]
PFSDQ-M (points)	
Dyspnea	7 [2.7 – 17]
Fatigue	5 [3.2 – 11.7]
Activities	8 [3.2 – 21.2]

Data described as frequency, mean ± standard deviation or median [interquartile range 25% - 75%]. BMI = Body Mass Index; FEV_1 = Forced Expiratory Volume on the first second; 6MWT = distance walked in the 6-minute walking test; LAP = Londrina ADL-Protocol; Peak VO_2 = Peak of oxygen consumption; LCADL = London Chest Activities of Daily Living scale; PFSDQ-M = Pulmonary Functional Status and Dyspnea Questionnaire – modified version.

Table 2. Reliability values of LAP outcomes

Variable	**ICC**	**CI 95%**	***P* value**
LAP duration	0.90	0.74 – 0.96	< 0.001
Difficulty	0.96	0.90 – 0.98	< 0.001
Energy expenditure	0.83	0.57 – 0.93	< 0.001
Baseline SpO_2	0.89	0.71 – 0.96	< 0.001
Baseline HR	0.90	0.74 – 0.96	< 0.001
Baseline Borg dyspnea	0.95	0.88 – 0.98	< 0.001
Baseline Borg fatigue lower limbs	0.95	0.87 – 0.98	< 0.001
Baseline Borg fatigue upper limbs	0.88	0.70 – 0.95	< 0.001
Final SpO_2	0.84	0.60 – 0.94	< 0.001
Final HR	0.86	0.65 – 0.95	< 0.001
Final Borg dyspnea	0.92	0.81 – 0.97	< 0.001
Final Borg fatigue lower limbs	0.83	0.56 – 0.93	< 0.001
Final Borg fatigue upper limbs	0.84	0.60 – 0.94	< 0.001

LAP = Londrina ADL Protocol; SpO_2 = Oxygen blood saturation registered by pulse oximetry; HR = Heart rate.

Table 3. Correlations of LAP duration with different outcomes .

LAP duration *versus*:	**r**	***P* value**
CAT	0.41	0.03
LCADL		
Health care	0.59	< 0.001
Physical activity	0.44	0.004
Total Score	0.48	0.03
PFSDQ-M		
Dyspnea	0.48	0.006
Fatigue	0.36	0.02
Activities	0.47	0.01
6MWD (% predicted)	-0.64	< 0.001

Correlations analyzed with the Spearman coefficient. LAP = Londrina ADL Protocol; CAT = COPD Assessment Test; ADL = Activities of Daily Living; LCADL = London Chest Activities of Daily Living Questionnaire; PFSDQ-M = Pulmonary Functional Status and Dyspnea Questionnaire – modified version; 6MWD = 6-minute walking distance on the 6-Minute Walking Test.

Figure 1. Activities composing the LAP.

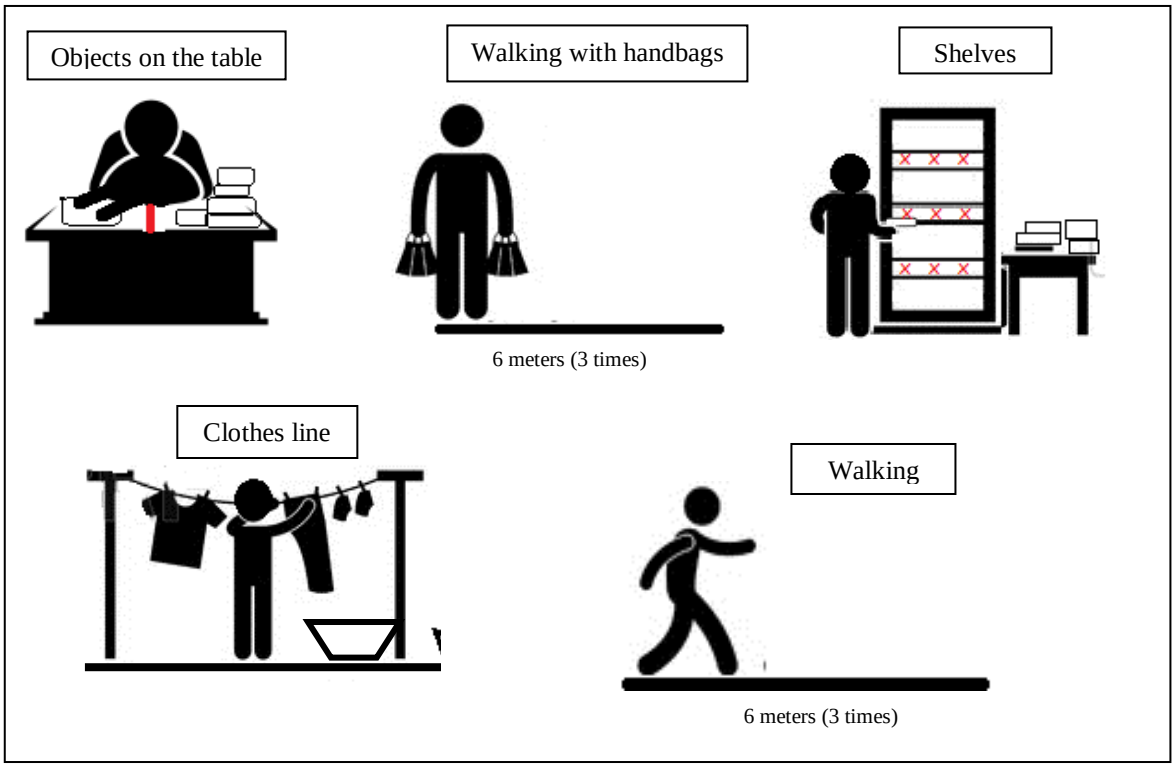


Figure 2. “Activity stations” positioning.

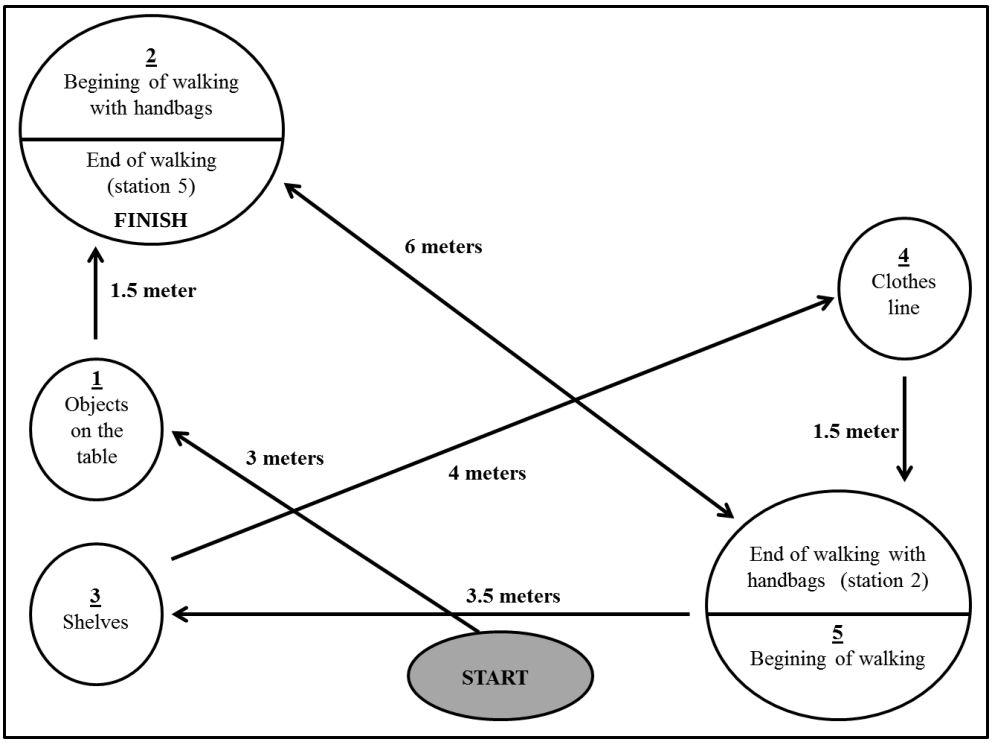
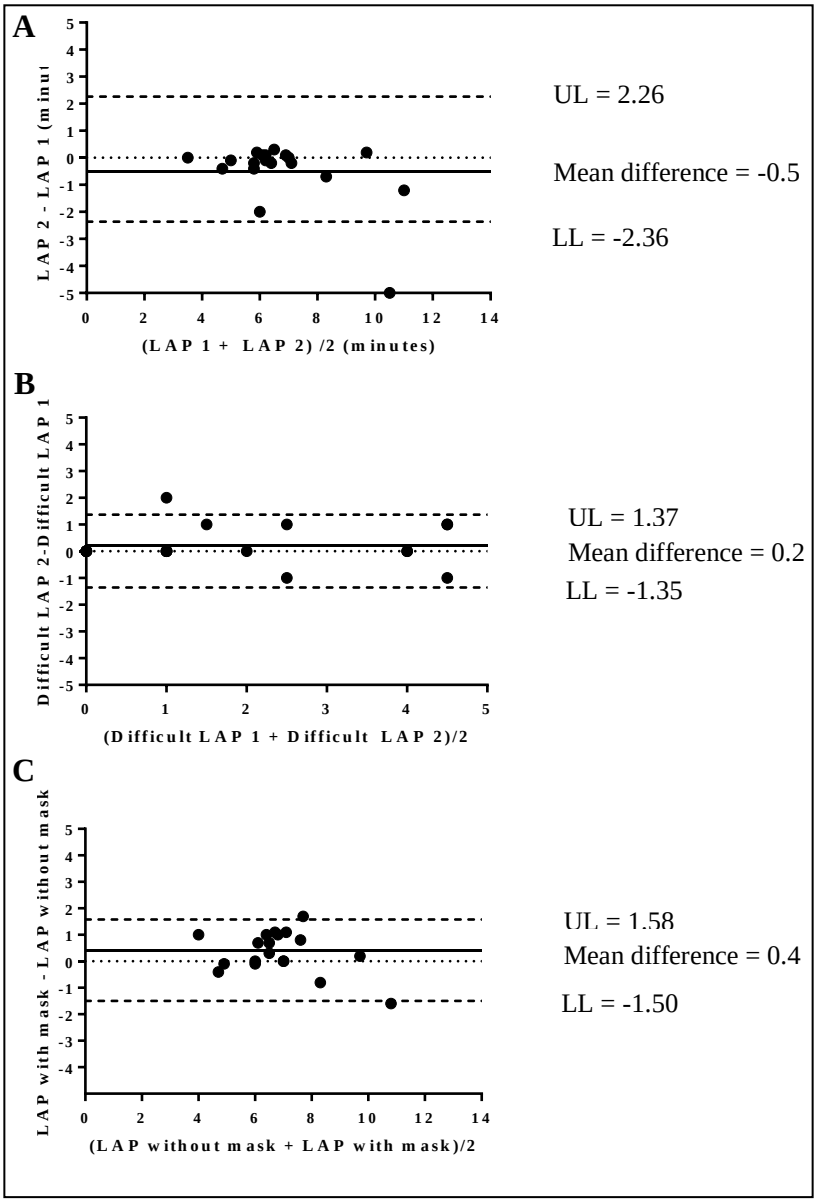
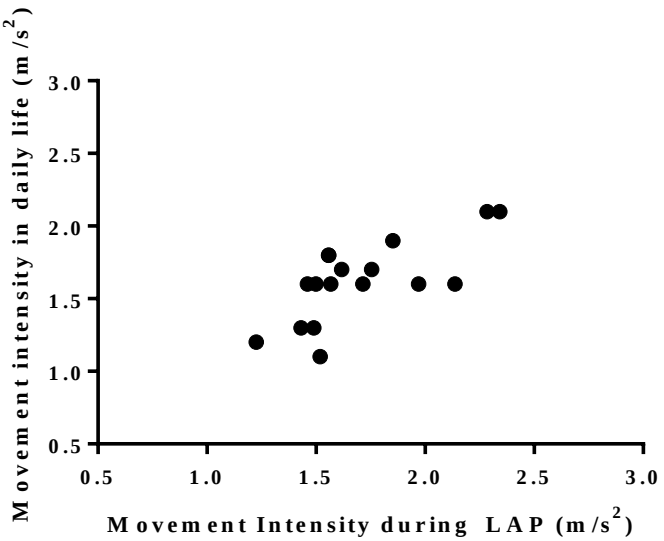


Figure 3. Bland and Altman plots showing agreement between the LAP outcomes in the first and second tests.



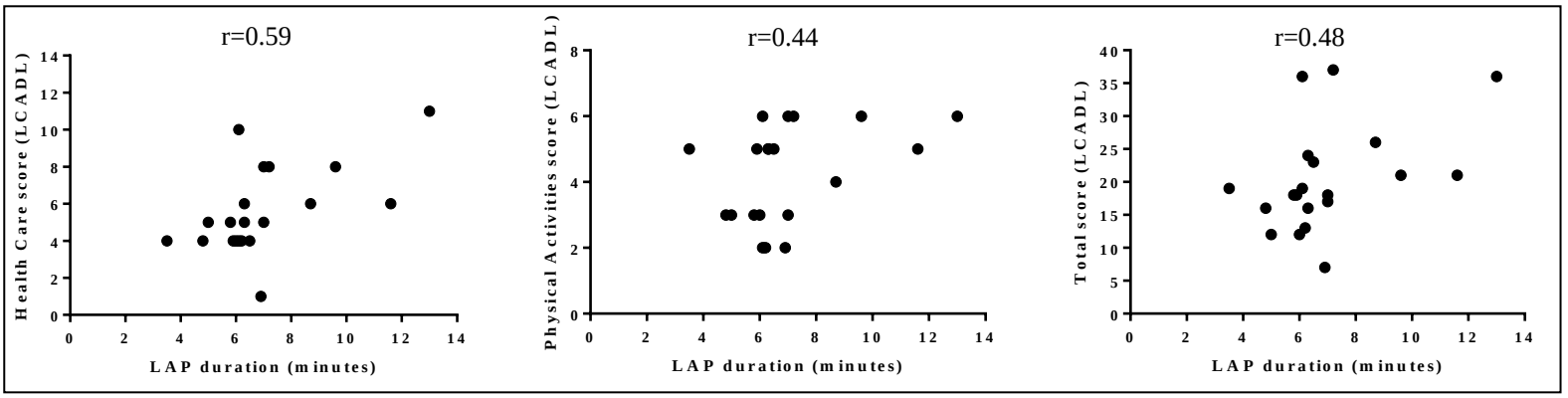
A: Bland and Altman plots showing agreement between the LAP duration in the first and second tests; **B:** Bland and Altman plot showing agreement between the reported difficulty in the first and second tests; **C:** Bland and Altman plot showing agreement between LAP duration with and without a mask for gas analysis. UL = Upper limit; LL = Lower limit.

Figure 4. Correlation between movement intensity during the LAP and movement intensity in daily life (r = 0.71; *P* = 0.001).



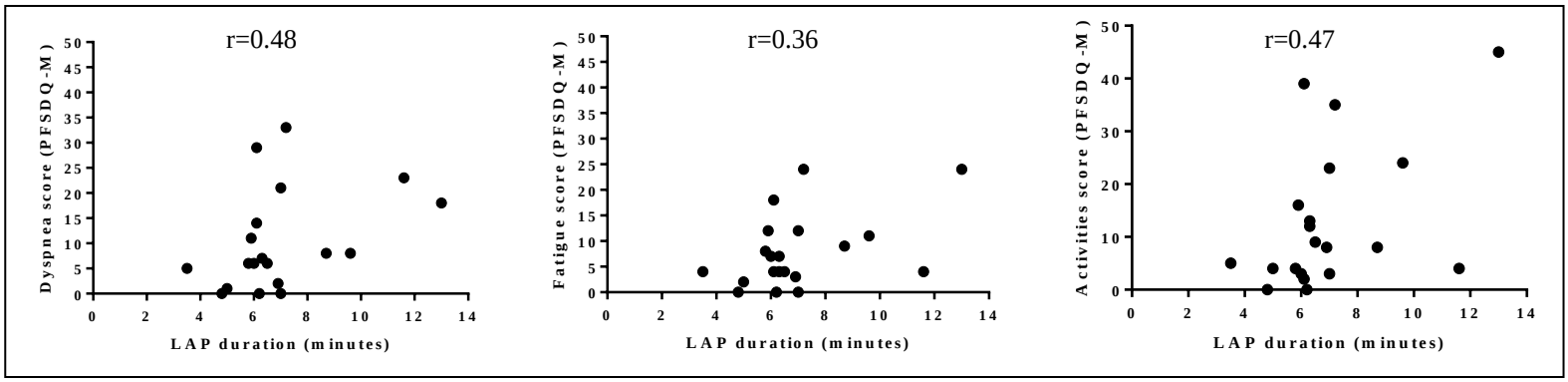
Correlations analyzed with the Pearson coefficient. LAP = Londrina ADL Protocol.

Figure 5. Correlation between LAP duration and LCADL items.



Correlations analyzed with the Spearman coefficient. LAP = Londrina ADL Protocol ; LCADL = London Chest Activities of Daily Living Questionnaire.

Figure 6. Correlation between LAP duration and PFSDQ-M items.



Correlations analyzed with the Spearman coefficient. LAP = Londrina ADL Protocol; PFSDQ-M = Pulmonary Functional Status and Dyspnea Questionnaire – modified version.

QUICK LOOK

Current Knowledge:

Dyspnea and fatigue are the most common symptoms reported by patients with chronic obstructive pulmonary disease (COPD). As a consequence of increased symptoms, patients reduce the amount of activities of daily living (ADL). Considering the impact of a limited ADL performance on the daily life of patients with COPD, it is relevant for clinical practice to be able to evaluate ADL performance in a standardized manner in this population.

What this paper contributes to our knowledge:

During the Londrina ADL Protocol (LAP) performance, patient's movement intensity was highly correlated to their movement intensity in daily life. Moreover, LAP duration was correlated to traditional functional status and quality of life questionnaire measurements. It was also a reliable test, also when patients were using a mask for gas analysis. It is a protocol which can be used in clinical practice and in future studies in order to investigate ADL outcomes, including those studies which require gas analysis and the need for wearing a mask. Therefore, the present study contributes to the current knowledge by creating the LAP and showing its validity and reliability, providing a useful standardized method for the assessment of ADL performance in patients with COPD.

5. ARTIGO 2

Oxygen desaturation in daily life and during a laboratory-based protocol of activities of daily living: is there relationship?

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ABSTRACT

Introduction: The progressive airflow limitation and emphysematous destruction of pulmonary capillary bed leads to ventilation/perfusion mismatch, contributing to hypoxemia in patients with chronic obstructive pulmonary disease (COPD). Alveolar hypoxia can contribute to several factors which lead to these patients' impairment in daily life. **Objective:** To analyze the relationship between oxygen desaturation episodes during a laboratory-based protocol of activities of daily living (ADL) and in real life routine in patients with stable COPD. **Methods:** Twenty patients with stable COPD (12 men, 70±7 years, FEV_1% 54±15 predicted) with no indication for long-term oxygen therapy (LTOT) were submitted to assessments including ADL performance by the Londrina ADL Protocol (LAP) and level of physical activity in daily life for two days, both while submitted to simultaneous activity and pulse oximeter monitoring. **Results:** Episodes of desaturation ≥4% (ED≥4%) during LAP was correlated with ED≥4% in daily life (r=0.45) and number of episodes of SpO_2 under 88% (ED<88%) in daily life (r=0.59) ED<88% during the LAP was also correlated with ED<88% in daily life (r=0.51), explaining 43% of its variance. **Conclusion**: In stable patients with COPD and no indication of LTOT, episodes of desaturation during a lab-based ADL protocol are moderately related to episodes of desaturation in daily (real) life, especially those episodes under 88%.

Key Words: Chronic Obstructive Pulmonary Disease, Activities of Daily Living, Pulse Oximetry, Motor Activity.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by pulmonary and extra-pulmonary manifestations[1]. The progressive airflow limitation and emphysematous destruction of the pulmonary capillary bed leads to ventilation/perfusion mismatch, contributing to hypoxemia in this population[2]. This occurs even in patients with mild COPD[3] and increases with disease progression[4].

Alveolar hypoxia can contribute to several factors which lead to the impairment of patients with COPD, such as polycythemia and pulmonary hypertension[5, 6]. Hypoxemia at rest also appears to be a factor contributing to neurocognitive dysfunction in patients with COPD[7]. Furthermore, one of the most important extra pulmonary consequences of COPD, skeletal muscle dysfunction, can also be aggravated by low levels of oxygen, since patients with COPD and chronic hypoxemia present accentuated muscle dysfunction which is partially reversed with supplemental oxygen therapy[8, 9]. Moreover, evidence shows that hypoxemia may also lead to an increase of symptoms, decrease in quality of life, higher predisposition to acute exacerbations and increase in risk of death[10].

The dynamic oxygen saturation profile assessed by pulse oximetry in daily life can offer important information in patients with similar pattern of resting arterial oxygen partial pressure (PaO_2) and basal oximetry-measured blood oxygen saturation (SpO_2)[11]. Considering the important influence of hypoxemia in the extra pulmonary manifestations of COPD, evaluation methods which contribute to identifying the profile of oxygen saturation/desaturation in daily life might be useful in the management of the disease. Furthermore, the relationship between oxygen desaturation and physical activity in daily life (PADL), another important prognostic factor of COPD[12], has not yet been investigated.

PADL = Physical activity in daily life; SWA = SenseWear armband; DMM = DynaPort Move Monitor; LAP = Londrina ADL Protocol; ED≥4% = Number of episodes of oxygen desaturation of at least 4%; ED<88% = Number of episodes of desaturation under 88%.

The main objective of the present study was to analyze the relationship between oxygen desaturation episodes during a laboratory-based protocol of activities of daily living (ADL) and in real life routine in patients with stable COPD. Additionally, the relationship between the profile of oxygen desaturation and the level of PADL in this population was also investigated.

MATERIAL AND METHODS

In this cross-sectional study, 21 patients with COPD were included. All patients were in the registers of the research laboratory as patients currently involved, previously involved or interested in being involved in a pulmonary rehabilitation program. As inclusion criteria, they presented diagnosis of COPD according to the GOLD criteria[1], clinical stability (at least three months without severe exacerbation), absence of neuromuscular or skeletal disorders that could impair PADL and PaO_2 and SaO_2 values not consistent to indication for long-term oxygen therapy (LTOT). Patients would be excluded if they were not able to execute the proposed evaluations. This research was approved by the Ethics Committee of the State University of Londrina, Brazil (031/2013) and all participants provided informed consent.

Assessments were done in four moments: at the first visit to the laboratory, patients had their anthropometric data collected, basal SpO_2 registered on the sitting position, and were submitted to assessment of lung function by spirometry[14, 15], impact on health status by COPD Assessment Test (CAT)[16] and functional status by two questionnaires: London Chest Activities of Daily Living Questionnaire (LCADL)[17, 18] and modified version of the Pulmonary Functional Status and Dyspnea Questionnaire (PFSDQ-M)[19, 20]. At the second visit, patients performed the LAP, and during its performance SpO_2 was continuously registered by a portable pulse oximeter (Nonin WristOx2™ 3150, United States of America). Moreover, patients wore two activity monitors during the LAP: SenseWear® armband (SWA, Body Media, United States of America)[21] and DynaPort Move Monitor® (DMM, McRoberts, The Netherlands)[22]. Before and after the LAP, dyspnea and fatigue were measured by the Modified Borg Scale [23]. At the third visit, patients were submitted to assessment of functional exercise capacity by the Six-minute Walking Test (6MWT)[24] and received (to be used at home) the same activity monitors and pulse oximeter used during the performance of the LAP. At the fourth and last visit, patients brought back the activity monitors and pulse oximeter. At this visit, they were submitted to collection of resting arterial blood for blood gas analysis[25].

Londrina ADL Protocol (LAP): The LAP is a new protocol of activities of daily living developed in the Laboratory of Research in Respiratory Physiotherapy, State University of Londrina, Brazil. It is composed by five activities (Figure 1) and organized in “stations” inside a room. The position of the “activity stations” and the distance between them are shown in Figure 2. The sequence of the stations is:

1) *Objects on the table*: patient sits on a chair in front of a table with a line separating it in two halfs (left and right). The table has 10 objects above it (4 objects of 250g, 4 objects of 500g and 2 objects of 1kg), all together on the left half of the table. Patient takes the objects, one by one, with both hands, and puts them all on the right half of the table. After that, patient returns all the objects in the same way to the left side of the table again.

2) *Walking with handbags*: Patient walks over a line of 6 meter of length, three consecutive times, carrying two handbags, each one in one hand. Inside the handbags there are loads representing 10% of patient’s body weight, 5% in each handbag.

3) *Shelves*: Patient stays in front of four shelves, one above the other, with a table next to it. On the table, there are 12 objects (4 objects of 250g, 4 objects of 500g, 2 objects of 1kg and 2 objects of 2kg). Patient takes the objects, one by one, with both hands, and put them on the shelves. Patient organizes the objects on the shelves in a way that three objects are placed on each shelve. When all the objects are placed on the shelves, patient returns the objects again in the same way to the table.

4) *Clothes line*: Patient stays in front of a clothes line, positioned at the eye level. There is a bowl/basket on the ground, next to the patient, containing 10 items of clothes. Patient takes all the items, one by one, with both hands, and hangs them

on the clothes line. After hanging all the items, patient returns them to inside the bowl/basket again, taking it one by one and with both hands.

5) *Walking*: Patient walks again on the same 6-meter line described in activity 2, three consecutive times, but without carrying the handbags.

The activities are performed consecutively, at a normal (i.e., “usual”) pace. Between the “activity stations”, the patient also walks at the usual pace. Before the patient starts to perform the LAP, the evaluator demonstrates the activities in the order they will be performed, explaining how they have to be performed. The instructions given to the patient are: “Perform these activities as if you were doing them at home, in your usual day-by-day. You are allowed to stop to rest if you feel it is necessary. Do not worry about the order of the activities, because we will remind you the next activity as long as the protocol goes”. During the protocol, only the next activity is reminded to the patient but no encouragement is given. The main outcome of the test is its duration (LAP duration).

Assessment of physical activity in daily life (PADL): The activity monitors (SWA and DMM) were used simultaneously during two consecutive week days, 24 hours per day[26, 27]. An assessment day was considered valid if patients accomplished at least 80% of the requested measurement time. Patients were instructed to take the monitors off only for bathing and to strictly maintain their routine. Both monitors are lightweight, do not offer any risk for patients and are widespread used in researches. SWA is worn on the left arm, on the triceps region. Data are registered based on a triaxial accelerometer and physiologic sensors. Main outcomes provided by this monitor are total energy expenditure, activity energy expenditure, average of metabolic equivalents (MET), total time spent in physical activity and time spent in different intensities of activities[21]. DMM is a triaxial accelerometer worn on the lower back region, to which it is fixed by a belt. Its main outcomes are the time spent in different activities and postures such as walking, standing, sitting and lying, besides the movement intensity[22]. Results of SWA and DMM were based on the average of the two assessment days.

Figure 1. Activities composing LAP.

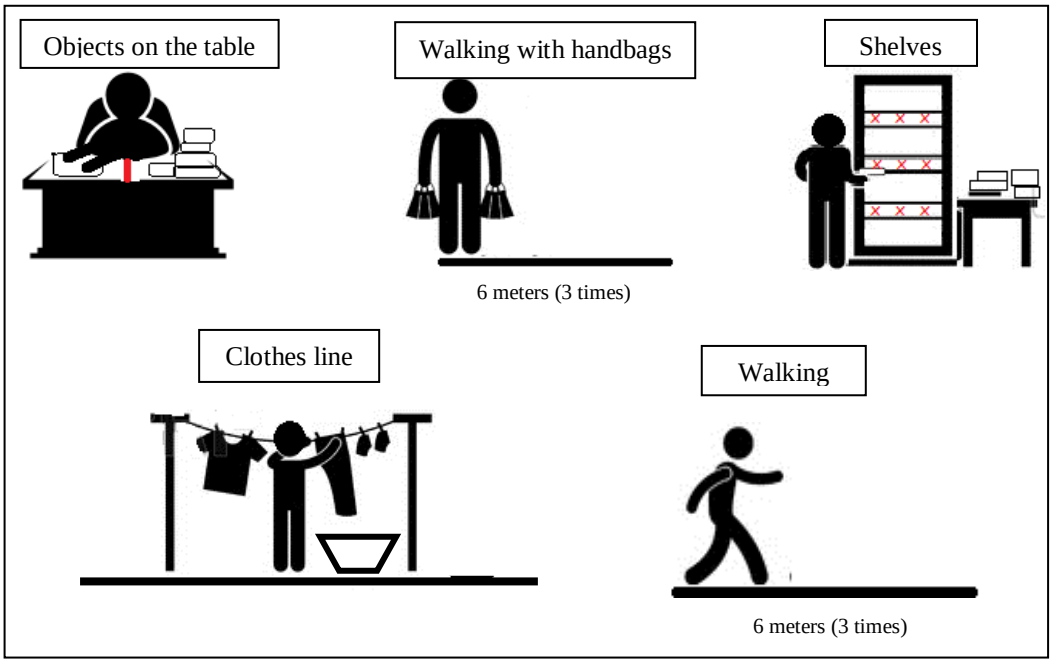
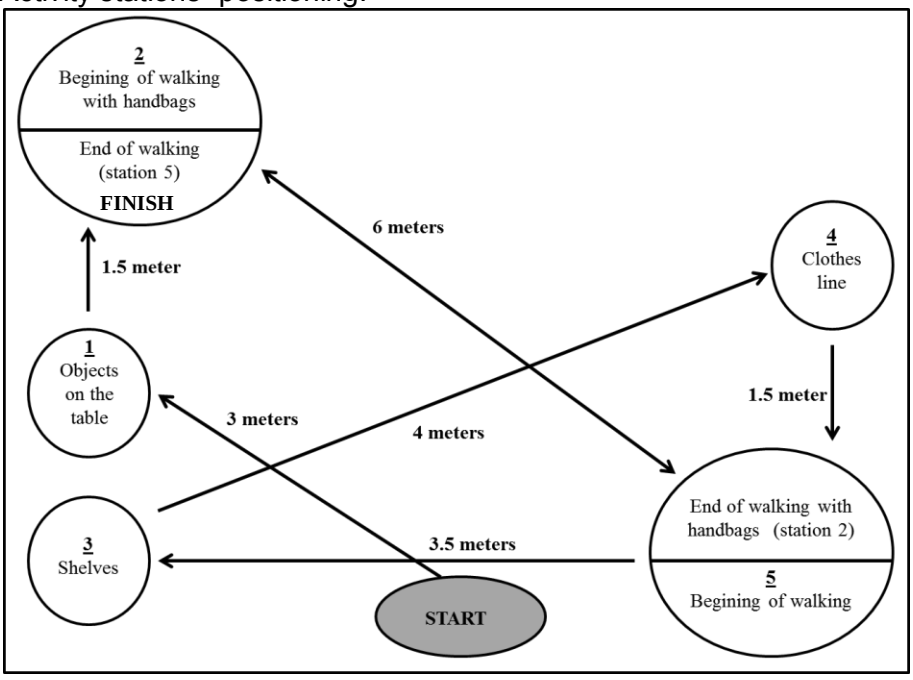


Figure 2. "Activity stations" positioning.



Assessment of SpO_2: For all SpO_2 registration done in this study, the same pulse oximeter was used. The WristOx2™ 3150 (Nonin, United States of America) is a pulse oximeter worn on the wrist, as a watch. The sensor is placed on a finger, involved by a rubber material. It was used by patients both during LAP performance and during the 2-day PADL assessment, always on the non-dominant hand, with the sensor positioned on the preferable finger chosen by patient. Patients were instructed to take the device off every time they had to lead with water and also when they had to use the toilet. The oximeter has an internal memory capable of recording data for up to 45 days. The device has motion tolerant software which minimizes the likelihood of motion artifact being misinterpreted as good pulse quality. Data is downloaded to a computer by the software accompanying the device. The main outcomes from the oxymeter applied in the present study were the number of episodes of oxygen desaturation ≥4% (ED ≥4%) and the number of episodes of SpO_2 under 88% (ED<88%), which are the desaturation thresholds provided by the device. For the 2-day assessment in daily life, the variables were calculated taking into account the average of the two assessment days.

Sample size calculation: To be able to find correlations of at least 0.60 between episodes of desaturation during the LAP and during daily life, twenty patients would be necessary to compose the sample of the present study. This calculation was performed considering $\alpha = 0.05$ e $\beta = 0.80$, by the BioStat 3.0 software.

Statistical analysis: Data distribution was analyzed by the Shapiro-Wilk test. According to normality in data distribution, data were described as mean and standard deviation or median and interquartile range, whereas correlations between outcomes were verified using Pearson or Spearman coefficients. To investigate if the oximetry outcomes during LAP explain the same outcomes in real life, linear regression analysis was performed. Statistical significance was set at $P < 0.05$, and analysis was performed using SPSS 20.0 and GraphPad Prism 6.0.

RESULTS

Out of the 21 patients included in the study, one did not conclude the assessments due to difficulties in transportation to return to the visits. Patients' characteristics are described in Table 1.

Table 1. Patients' characteristics (N = 20)

Gender (male/female)	12/8
Age (years)	70 ± 7
BMI (kg/m^2)	26 ± 5
FEV_1 (% of predicted)	54 ± 15
6MWD (meters)	504 ± 83
6MWD (% of predicted)	95 [66 – 104]
PaO_2 (mmHg)	76 [64 – 80]
SaO_2 (%)	95 [93 – 96]
Basal SpO_2 (%)	95 [92 – 96]
Pulse oximetry monitoring	
Total time of desaturation in daily life (minutes/per day)	75 [38 – 136]
ED ≥ 4% per day in daily life	93 [57 – 236]
ED<88% per day in daily life	13 [5 – 93]
LAP	
LAP duration (minutes)	6.3 [5.9 – 7.1]
ED ≥ 4% during the LAP	1 [0 – 2]
ED<88% during the LAP	0 [0 – 1]
PADL	
Time spent walking per day (hours)	1:28 ± 0:46
Time spent sitting per day (hours)	7:53 ± 1:59
Total energy expenditure per day (calories)	2034 ± 457
Average METs	1.4 ± 0.4
Time spent in moderate physical activites per day (hours)	1:27 ± 1:16
Sedentary time per day (hours)	21:27 [20:28 – 23:16]
LCADL	
Health care	5 [4 – 7.5]
Domestic	6 [2.5 – 9.7]
Physical activity	5 [3 – 5.7]
Leisure	3.5 [3 – 4.7]
Total	18 [16 – 23.7]
PFSDQ-M	
Dyspnea	7 [2.7 – 17]
Fatigue	5 [3.2 – 11.7]
Activities	8 [3.2 – 21.2]

Data described as frequency, mean ± standard deviation or median [interquartile range 25% - 75%]. BMI = Body Mass Index; FEV_1 = Forced Expiratory Volume on the first second; 6MWD = 6-minute walking distance; LAP = Londrina ADL-Protocol; PADL = Physical activity in daily life; Total ED = total episodes of desaturation; ED<88% = episodes of desaturation under 88%; LCADL = London Chest Activities of Daily Living scale; PFSDQ-M = Pulmonary Functional Status and Dyspnea Questionnaire – modified version.

All patients included in the study presented episodes of oxygen desaturation in daily life. Resting SpO_2 (from oximetry) was correlated with resting arterial oxygen saturation

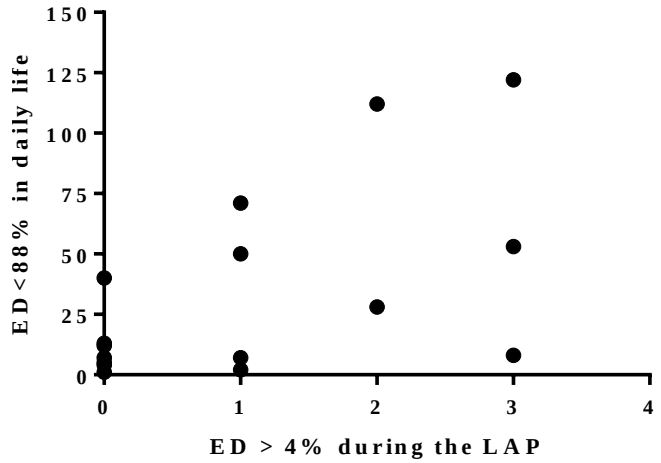
(SaO_2, from blood gas analysis) (r = 0.73, *P*=0.001) and with ED<88% in daily life (r = -0.52, P<0.001). ED ≥4% in daily life correlated with ED<88% in daily life (r = 0.84, *P*<0.001) and with ED ≥4% during the LAP (r = 0.45, *P*=0.04). ED ≥4% in daily life was correlated with the leisure domain of the LCADL (r = 0.48, *P*=0.04).

ED<88% in daily life was correlated to baseline PaO_2 and SaO_2 (r = -0.63 and 0.64, respectively, P<0.001) and to variables from the LAP: ED<88%, ED ≥4% and final Borg fatigue scale for the upper limbs (r = 0.51, 0.59 [figure 3] and 0.48, respectively; *P*<0.005 for all). ED<88% in daily life was also correlated to the 'physical activity' and 'leisure' domains of the LCADL (r = 0.50 and 0.51, respectively, *P*=0.003).

When ED ≥4% during the LAP was included in a linear regression analysis, it was not able to significantly predict ED ≥4% in real life (R^2 = 0.13, *P* = 0.09). On the other hand, ED<88% during the LAP presented an R^2 = 0.43 (*P*<0.002) when explaining ED<88% in daily life.

There was no significant correlation between oximetry measurements and any PADL variable, neither with the PFSDQ-M and the CAT (0.09 ≤ r ≤ 0.21, *P* > 0.10).

Figure 3. Correlation between ED >4% during the LAP and ED<88% in daily life (r=0.59).



Correlation analyzed with the Spearman coefficient. ED<88% in daily life = episodes of desaturation under 88% in daily life ; ED >4% during the LAP = total episodes of desaturation during the LAP .

DISCUSSION

The present study showed that although there is no correlation between oxygen desaturation and variables of PADL, oximetry outcomes during a laboratory-based ADL protocol are related to oximetry in daily life in patients with COPD. Moreover, oxygen desaturation during the ADL protocol was able to explain 43% of desaturation episodes in daily life. A study which investigated if the time to oxygen desaturation during the 6MWT is associated with 24-hour oxygen desaturation in daily life found a negative correlation of r = -0.42 between these outcomes, showing that many patients with COPD who present oxygen desaturation in the first minute of the 6MWT also present oxygen desaturation in daily life[28]. However, another study, investigating the lowest oxygen desaturation during 6MWT and its relationship with ambulatory oximetry, did not find a correlation between them[29]. Indeed, there are controversial results and variation in methodology regarding SpO_2 during 6MWT and daily life. The present study found an association between the episodes of low SpO_2 during an ADL protocol and in real life. The correlation between ED ≥4% during the LAP and ED<88% in daily life (r = 0.59) was higher than the correlations found in the above mentioned study. One possible explanation for that is that patients' movement intensity during the ADL protocol used in this study, the LAP, presented a good correlation with movement intensity in daily life, as shown in another research of our group (unpublished data). This means that the LAP could possibly represent better the performance in day-by-day activities than the 6MWT, a test aimed at assessing exercise capacity which demands very fast walking from patients[24]. Additionally, as the LAP is a test performed at the patient's usual pace, it could be better tolerated by patients with very severe disease in comparison to the 6MWT. It is important to highlight, however, that the present study does not aim at suggesting the replacement of the 6MWT by the LAP since these tests have different outcomes and aim at different purposes.

A simple measurement as resting SpO_2 presented a negative correlation with ED<88% in daily life. This is an useful finding, since ED ≥4% and ED<88% in real life were

highly correlated, suggesting that, in general, the majority of episodes of desaturation ≥4% reaches values under 88%.

Although no patient participating in this study presented low resting SpO_2 and also none of them used or had PaO_2 and SaO_2 values consistent with indication to LTOT, all of them presented episodes of oxygen desaturation in daily life. This finding is in agreement with the study by Casanova and colleagues, which has shown that stable patients with COPD without indication for LTOT present episodes of oxygen desaturation in daily life, suggesting that 24-hour oximetry could provide valuable information for a comprehensive evaluation of this population[11]. The same was shown in several studies investigating the utility of 24-hour oximetry in patients with COPD; these studies reported oxygen desaturation in most of the patients during ADL performance, even presenting good oxygenation at rest[29-32]. It is important to highlight that some of these studies also included hypoxemic patients using LTOT, differently from the present study. Another study investigated the oximetry profile of hypoxemic patients with COPD, all of them under LTOT. Besides concluding that SpO_2 monitoring in daily life is a feasible evaluation in hypoxemic patients with COPD, they surprisingly found that even while using the prescribed amount of oxygen, patients still presented several episodes of SpO2<90% during ADLs[33]. Therefore, according to the body of evidence, patients with COPD, either hypoxemic or not, are likely to present oxygen desaturation in daily life. Nevertheless, although all patients presented episodes of oxygen desaturation, the total time of desaturation for each 24 hours of assessment in the present study represented only 5% of the assessment time per day (as noted in Table 1: 75 [38-136] minutes/day), what does not characterize these patients as “desaturators” (considered as presenting 30% of the day with oxygen desaturation)[34]. This is in agreement with other study which evaluated the profile of oxygen desaturation in stable patients with COPD not receiving oxygen therapy. They also found that occurrence of oxygen desaturation in those patients was infrequent (3% of the patients presenting SpO_2 below 90% during the day)[35].

A previous study has shown that exercise-induced desaturation is correlated with the number of steps per day in daily life in patients with COPD (r = -0.31) [36]. Taking into account that step counting is not the most indicated physical activity outcome for this population[37, 38], the present study investigated the relationship between oximetry and other PADL variables in daily life. The lack of correlation between oximetry and PADL can be explained by a few hypothesis. It is possible that while some patients with COPD present oxygen desaturation episodes because they are very active, other patients can present a lower level of PADL because they present more episodes of oxygen desaturation and, possibly, more symptoms. This two-way possible oximetry/PADL characteristic could neutralize an expected correlation. Casanova and colleagues also did not find association between oxygen desaturation and clinical expressions of COPD. Although they did not investigate PADL, their hypothesis can be applied to the present results. They suggest that the body can adjust itself to some degree of transitory hypoxemia[11]. Moreover, patients with COPD participating in the present study presented a higher level of PADL than the expected for this population[39, 40], although it has been shown that Brazilian patients with COPD might present a higher PADL level in comparison to patients from Central Europe, for example[41]. Nevertheless, oxygen desaturation in daily life was correlated with 'physical activity' and 'leisure' domains from a functional status questionnaire. These results suggest that subjective assessment, showing how patients feel during ADLs, is more associated to episodes of oxygen desaturation than objective measurements of PADL. One hypothesis could be that the oxygen desaturation can initiate respiratory symptoms and it could be better reflected when patients report how they feel in daily life during their day-by-day activities.

We did not separate episodes of desaturation that happened during the day and during the night, and therefore we are not able to establish in which period of the day desaturation mostly occurs. However, the initial purpose of this study was to investigate a possible relationship between desaturation during an ADL protocol and total episodes of desaturation in real life. Future studies can be performed investigating if this relationship is

different when separating oximetry during the day and during the night. Additionally, further research could analyze if this relation is different in hypoxemic patients.

CONCLUSIONS

In conclusion, episodes of desaturation during a lab-based ADL protocol are moderately related to episodes of desaturation in daily life, especially those under 88%, in stable patients with COPD with PaO_2 and SaO_2 values not consistent to LTOT indication. All patients included in the study presented episodes of oxygen desaturation, even presenting resting SpO_2>90% and not having PaO_2 and SaO_2 consistent to LTOT indication. Nevertheless, considering the small period of the day they presented oxygen desaturation, they are not characterized as “desaturators”. There was no correlation between oxygen desaturation and the objectively measured level of physical activity in daily life.

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6. CONSIDERAÇÕES FINAIS

De acordo com os resultados dos estudos que compõem a presente tese, pode-se concluir que o LAP é um protocolo válido e reprodutível para avaliar o desempenho nas AVDs de pacientes com DPOC. É um protocolo que pode ser utilizado na prática clínica e em futuras pesquisas com o objetivo de investigar desfechos relacionados a AVDs, incluindo aqueles desfechos que requerem análise de gases e o uso de uma máscara. Adicionalmente, conclui-se que episódios de dessaturação de oxigênio durante a realização do LAP são moderadamente relacionados a episódios de dessaturação de oxigênio na vida diária, especialmente aqueles abaixo de 88%, em pacientes com DPOC estável e sem valores de PaO_2 e SaO_2 compatíveis com indicação de oxigenoterapia domiciliar. Entretanto, o curto período do dia em que os pacientes apresentaram dessaturação de oxigênio não os caracteriza como “dessaturadores”. Por fim, não houve correlação entre a dessaturação de oxigênio e o nível de atividade física na vida diária.

Durante a realização desta tese de doutorado, algumas dificuldades foram encontradas e enfrentadas. Não é missão fácil encontrar pacientes com DPOC que se disponham a colaborar com uma pesquisa científica que envolve vários dias de avaliações e testes que geram sensações desconfortáveis, como dispneia, fadiga e até mesmo a dor de uma coleta de sangue arterial. Por conta disso, temos imensa gratidão pelos pacientes que aceitaram participar do presente estudo. A fase da coleta de dados da tese também exigiu muita perseverança dos pesquisadores envolvidos no estudo, que, em meio a diversas outras atividades e trabalhos, sempre conseguiam disponibilizar parte especial do dia para a avaliação dos pacientes incluídos na pesquisa. Esses são apenas alguns exemplos das dificuldades enfrentadas durante o desenvolvimento deste trabalho. Porém, nenhum esforço foi em vão. Hoje, temos as primeiras evidências científicas a respeito do LAP, um protocolo padronizado de avaliação de AVDs para pacientes com DPOC, que pode favorecer grandiosamente a literatura científica e a prática clínica.

Pesquisas futuras ainda são necessárias para que seja possível verificar se o LAP também é válido e reprodutível na avaliação de pacientes com DPOC mais graves. Além disso, será necessário estabelecer o valor de referência para a “duração do LAP”, para que seja possível definir o que representa bom ou mau desempenho na realização do protocolo. Futuros estudos também poderão verificar se o LAP é responsivo a tratamentos medicamentosos e não medicamentosos (*i.e.*, Reabilitação Pulmonar).

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ANEXO 1 - Normas para submissão de artigo científico para publicação no periódico *Respiratory Care*

PREPARING THE MANUSCRIPT

Title Page

For each author include:

- First name, middle initial, last name
- Academic degrees (eg, MSc, PhD, EdD). The Journal does not publish bachelor degrees
- Credentials (eg, RRT, MD, RN)
- FAARC (Fellow of the American Association for Respiratory Care). The Journal does not publish any other honorary titles
- Institutional affiliation and location (division, department, hospital, university, city, state/province, country)

Indicate the specific contributions of each author to the paper:

- Literature search
- Data collection
- Study design
- Analysis of data
- Manuscript preparation
- Review of manuscript

Title Page must also include:

- Name and location of the institution where the study was performed
- Name, date, and location of any meeting or forum where research data were previously presented, and who presented
- Sources of financial support
- Conflict of interest statement. If no potential conflicts of interest exist, a statement to this effect must be included

Identify corresponding author and provide contact information

Abstract

Structured Abstract includes these sections: Introduction, Methods (how the study was performed, including the number of subjects or patients), Results (brief summary of the data), and Conclusions. Abstracts must not contain any facts or conclusions that do not also appear in the text.

Narrative Abstracts are written as a narrative paragraph and fewer than 300 words.

Include the Abstract in the main manuscript text file.

Key Words

List 6–10 key words or phrases that reflect the content of your manuscript. Key words may be selected from the Medical Subject Headings (MeSH terms) used by MEDLINE.

Text

Double-space all text (including Tables and References). Number the pages. Center and bold 1st level headings; flush-left and bold 2nd level headings; indent and bold 3rd level headings.

References

References must be listed and numbered in the sequence in which they are first cited in the text. Citations must conform to Journal style; see examples below. Authors are responsible for accuracy of their references.

EndNote contains the style for Respiratory
Care: http://endnote.com/downloads/style/respiratory-care

Journal Article

Article. List the first 6 authors, then "et al". Exception – in a paper with 7 total authors, list all 7:

Wallet F, Delannoy B, Haquin A, Debord S, Leray V, Bourdin G, et al. Evaluation of recruited lung volume at inspiratory plateau pressure with PEEP using bedside digital chest x-ray in patients with acute lung injury/ARDS. Respir Care 2013;58(3):416-423.

Corporate authors:

Chang SY, Dabbagh O, Gajic O, Patrawalla A, Elie MC, Talmor DS, et al; on behalf of the United States Critical Illness and Injury Trials Group: Lung Injury Prevention Study Investigators (USCIITG-LIPS). Contemporary ventilator management in patients with and at risk of ALI/ARDS. Respir Care 2013;58(4):578-588.

Article in a supplement:

del Giudice MM, Leonardi S, Ciprandi G, Galdo F, Gubitosi A, La Rosa M, et al. Probiotics in childhood: allergic illness and respiratory infections. J Clin Gastroenterol 2012;46(Suppl):S69-S72.

Corrected article:

Mireles-Cabodevila E, Hatipoğlu U, Chatburn RL. A rational framework for selecting modes of ventilation. Respir Care 2013;58(2):348-366. Erratum in: Respir Care 2013;58(4):e51.

Articles e-published online ahead of print:

Nozoe M, Mase K, Murakami S, Okada M, Ogino T, Matsushita K, et al. The relationship between spontaneous expiratory flow-volume curve configuration and airflow obstruction in elderly COPD patients. Respir Care 2013 [Epub ahead of print] doi: 10.4187/respcare.02296

Abstract. Citing abstracts is highly discouraged. Those more than 3 years old should not be used:

Blakeman TC, Rodriquez D, Branson RD. Evaluation of five chemical oxygen generators (abstract). Respir Care 2012;57(10):1751.

Editorial:

Rouby JJ, Arbelot C, Brisson H, Lu Q, Bouhemad B. Measurement of alveolar recruitment at the bedside: the beginning of a new era in respiratory monitoring? (editorial). Respir Care 2013;58(3):539-542.

Editorial, no author given:

Asthma: not just for kids (editorial). Johns Hopkins Med Lett Health After 50 2012;24(8):6.

Letter:

Haynes JM. Expiratory reserve volume maneuver may be the preferred method for some patients during spirometry testing (letter). Respir Care 2013;58(2):e14-e15. author response: e15.

Books

Book. Corresponding pages should be cited whenever reference is made to specific statements or content:

Wilkins RL, Stoller JK, Kacmarek RM. Egan's fundamentals of respiratory care, 9th edition. St Louis: Mosby|Elsevier; 2009:400-404, 917.

Corporate authors:

Panel on Understanding Cross-National Health Differences Among High-Income Countries; Committee on Population Division of Behavioral and Social Sciences and Education; Board on Population Health and Public Health Practice; National Research Council; Institute of Medicine of the National Academies. U.S. health in international perspective: shorter lives, poorer health. Washington, DC: National Academies Press; 2013.

Chapter:

Heffner JE. Chronic obstructive pulmonary disease. In: Hess DR, MacIntyre NR, Mishoe SC, Galvin WF, Adams AB. Respiratory care principles and practice, 2nd edition. Sudbury, MA: Jones & Bartlett; 2012:735-764.

Online Material

Static material must be listed in the References and include the digital object identifier (DOI). Use a DOI for content published online only. Because these items are static, there is no need to include an access date:

Ng S, King CS, Hang J, Clifford R, Lesho EP, Kuschner RA, et al. Severe cavitary pneumonia caused by a non-*equi Rhodococcus* species in an immunocompetent patient. Respir Care 2013;58(4):e47-e50. doi:10.4187/respcare.02017

Frequently changing material, such as an organization's homepage, should be cited in the text using the URL and access date. Do not include in References:

"….as recommended by the American Association for Respiratory Care (http://www.aarc.org, *Accessed January 27, 2015*) …"

News sources:

Productivity at work improved for sleep apnea patients using CPAP. Medical News Today: April 15, 2013. http://www.medicalnewstoday.com/releases/259016.php *Accessed January 27, 2015.*

Unpublished Work

Manuscript accepted but not yet published. A copy of cited unpublished manuscripts should be uploaded:

Strickland SL. Year in review: airway clearance. Respir Care 2015 (in press).

Research not yet accepted for publication should be cited in the text as personal communication. You must obtain written permission from the authors to cite unpublished data.

"Recently, Smith et al found this treatment effective in 45 of 83 patients (Smith R, personal communication, 2015)."

Your own unpublished work that has not been accepted for publication should be mentioned in the text: "We found this type of aerosol is no more effective than placebo (unpublished data)."

Quick Look

The Quick Look boxes in Respiratory Care provide readers with the concise take-home message of the study. Only Original Research articles have Quick Look boxes. Quick Look boxes have 2 headings, the first is *Current Knowledge*and the second is *What This Paper Contributes To Our Knowledge*.

Include your Quick Look text at the end of your main manuscript text file (after the References and any Figure Legends) under the heading Quick Look. Double-space all text.

Current Knowledge

Write 2–4 declarative sentences summarizing current understanding of the topic being studied. Think of it as defining the state of the art or establishing equipoise.

DO – State the current evidence on the subject

DO – Provide clear declarative statements

DO NOT – Ask a question

DO NOT – State what is not known or that a topic "requires further study" or "remains to be elucidated"

What This Paper Contributes To Our Knowledge

Write 2–4 declarative sentences summarizing the take-home message of the study. Use past tense. Provide only information supported by the data. Do not overstate the importance of your results and do not suggest further research; this section is about the paper at hand.
DO – Describe the main take-home points and findings
DO – Describe the environment (eg, if a lung model was used)
DO – Write statements that can be understood without re-stating the data
DO NOT – Allude to further work that needs to be accomplished
DO NOT – Overstate the importance of the findings or speculate. (eg, The use of APRV improved oxygenation [data from the study]. Due to improved oxygenation, APRV might reduce mortality in ARDS [speculation]).
DO NOT – Include statistics or numerical data
The Editors reserve the right to edit Quick Look boxes for accuracy, style, and length.

Example Quick Look

Current knowledge

The endotracheal tube cuff allows positive pressure ventilation and protects the airway from aspiration. Standard cuff pressures of 20–30 cm H_2O are typically used to prevent leakage of fluid around the cuff and to prevent mucosal injury. In recent years, laboratory evaluations of cuffs in glass models have demonstrated reduced fluid leakage, but clinical studies have not confirmed these findings in vitro.

What this paper contributes to our knowledge

In a realistic viscoelastic model of the trachea, endotracheal tube cuffs of different designs provided an adequate seal at a pressure of 12 cm H_2O. With increased PEEP, higher cuff pressures were required. Tubes with a subglottic suction channel performed best in the lateral position.

Figures

Use of Figures is encouraged. Include only Figures that clarify and augment the text. All Figures must be called-out in the text. Number consecutively as Figure 1, Figure 2, etc.
The first Figure in the report of a clinical trial must be a flow diagram showing phases of the trial (ie, enrollment, subject allocation, follow-up, and analysis). See CONSORT.
Each Figure must be uploaded to Manuscript Central as a separate image file, NOT embedded in the text.
Minimum 1200 dpi required for line art (graphs or drawings), 600 dpi required for images with labeling, and 300 required dpi for images (color or black and white) without labeling.
Radiographs must clearly identify the relevant details and contain no patient identifiers.
Any identifiable image must be accompanied with written consent (see Ethics of Investigation).

Identify stains and magnifications for all photomicrographs.

Arrows, numbers, letters, lines and other markers used to identify parts of a Figure must be defined in the Figure Legend.

Figures are redrawn for stylistic consistency. Contact the Editorial Office if you would like assistance in creating an original Figure.

Figure Legends

Every Figure must have a legend explaining every component of the Figure. The legend should be self-sufficient and allow the reader to understand the figure without referring to the text.

Legends are placed at the very end of the manuscript text file. Do not include legends in the Figure image files.

Tables

Each Table must be uploaded to Manuscript Central as a separate Microsoft Word file, NOT embedded in the text. Tables must have a title. The title should be self-sufficient and allow readers to understand the Table without referring to the text.

Tables should be numbered and cited consecutively in the text, Table 1, Table 2, etc. Any abbreviations and symbols must be explained in footnotes at the bottom of the Table. For footnotes use the following symbols, superscripted, in the following order: *, †, ‡, §, ||, ¶, **, ††.

Borrowed Figures and Tables

To include previously published Figures and Tables, you must obtain permission from the original copyright holder. Provide the reference citation in the Table footer so that appropriate credit can be acknowledged in accordance with copyright law.

Copyright is most often held by the publisher of the journal or book in which the Figure or Table originally appeared. It is the author's responsibility to secure permission. Payment of any fees required for borrowed material is the responsibility of the author.

Upload permissions documentation with your manuscript files.

Acknowledgements

Names of persons not eligible for authorship, and their contribution and institutional affiliation, should be listed in the Acknowledgments. You must obtain written permission from all individuals named in the Acknowledgments because inclusion can be taken as the individuals' approval of the paper's contents.

Equations

Write equations as normal text. Do not use the equation function in Microsoft Word or other mathematics software.

Statistical Analysis

For original research papers, the Editor recommends working with a biostatistician to assure appropriate analysis. The Editor may request a letter from your biostatistician assuring that the analysis is correct.

In the Methods section, identify the statistical tests used to analyze the data. Indicate the *P*-value that was taken to indicate significance. State whether tests were one-tailed or two-tailed; justify the use of one-tailed tests. Identify post-hoc analyses. Cite references to support your choice of tests and identify any statistical analysis software used. Indicate how the power analysis was conducted to determine appropriate sample size.

Report measurements with an appropriate degree of precision. Report both numerators and denominators for percentages.

For continuous data, description statistics should be expressed as mean and standard deviation (not standard error). For ordinal data, median and interquartile range should be reported.

For ratios (odds ratio, relative risk, etc.), provide 95% confidence interval.

Report actual *P* values rather than thresholds. Example: write "*P* = .18", not "*P* > .05" or "*P* = NS." Note that *P* cannot equal 0 or 1.

P values should be expressed to 2 digits for *P* ≥ .01. *P* < .001, rather than *P* < .0001 or *P* = .00001. If *P* > .99, *P* = .999 for example, it should be expressed as *P* > .99.

An exception is *P* values between .07 and .03, which the Journal expresses to 3 digits. This is to preserve potential meaning of values near .05.

Authors are encouraged to enlist the expertise of a local statistician. If questions arise during the peer review process regarding the statistical analysis, the Editor may ask for proof of input from a statistician when the revised manuscript is submitted.

Units of Measurement

Always report the units of measurement according to current scientific usage. Standard units of measurement and scientific terms may be abbreviated without explanation (eg, L/min, mm Hg, pH, O_2). The Journal uses most values in Systeme Internationale (SI) units. For blood gas values, we prefer mm Hg to kPa. For airway pressure, we prefer cm H_2O rather than millibars.

Pulmonary Terms and Symbols

Use the Preferred Pulmonary Terms and Symbols (Appendix 1). Use abbreviations sparingly. Do NOT invent new abbreviations for terms with long-held standard abbreviations. Use an abbreviation only if the term occurs 4 or more times in the manuscript.

The following commonly used abbreviations do not need to be defined: ARDS, CI, COPD, CPAP, DNA, FDA, FEV_1, F_{IO2}, FVC, ICU, P_{aO2}, P_{aCO2}, P_{O2}, P_{CO2}, PEEP, SD, S_{pO2}. We also do not define units (eg, mL, cm, µm, µL).

Drugs and Commercial Products

Precisely identify all drugs and chemicals, doses, and methods of administration.

Use generic names instead of trade (proprietary) names for both drugs and equipment.

At first mention, trade names may be given parenthetically after generic names, including the name and location of the manufacturer. For equipment, provide model numbers if available.

Subjects versus Patients

Individuals enrolled in research are referred to as subjects, not patients. This applies to both retrospective and prospective studies.

ANEXO 2 - Normas para submissão de artigo científico para publicação no periódico *Respiratory Medicine*

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.
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[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.
Reference to a book:
[2] W. Strunk Jr., E.B. White, The Elements of Style, fourth ed., Longman, New York, 2000.
Reference to a chapter in an edited book:
[3] 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.

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