THAYSE NEVES SANTOS SILVA

# INFLUÊNCIA DA OBSTRUÇÃO E HIPERINSUFLAÇÃO PULMONAR NA ATIVIDADE DOS MÚSCULOS RESPIRATÓRIOS E MOBILIZAÇÃO DE VOLUMES PULMONARES

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Dissertação apresentada ao colegiado do Curso de Mestrado em Ciências Biológicas, na área de concentração em Fisiologia, do Departamento de Fisiologia e Farmacologia do Centro de Ciências Biológicas da Universidade Federal de Pernambuco, como requisito para a obtenção do grau de Mestre em Fisiologia.

**Orientadores:**
Profa. Dra. Armèle Dornelas de Andrade
Prof. Dr. Milton Marcelino Filho

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Thayse Neves Santos Silva

**Influência da obstrução e Hiperinsuflação pulmonar na atividade dos músculos respiratórios e mobilização de volumes pulmonares durante testes de função muscular respiratória**

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**DEDICATÓRIA**

**Dedico este trabalho...**

**...Aos meus pais, João Batista S. Silva e Maria Cecília N.S. Silva.**
**...Aos meus irmãos Eduardo, Oswaldo e Rafaela.**
**...Ao meu noivo, Rogério de Aguiar.**
**...Aos meus sobrinhos, Lucas, Matheus e Natália.**
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**LISTA DE SIGLAS E ABREVIATURAS**

| | |
|---|---|
| DPOC | Doença Pulmonar Obstrutiva Crônica |
| EMG | Eletromiografia |
| RMS | Root-mean-square |
| fMD | Freqüência Média |
| Pimáx | Pressão Inspiratória Máxima |
| FR | Freqüência respiratória |
| Ti/Ttot | Ciclo de trabalho: Relação Tempo inspiratório/Tempo total |
| SpO2 | Saturação Periférica de Oxigênio |
| CRF | Capacidade Residual Funcional |
| CI | Capacidade Inspiratória |
| CPT | Capacidade Pulmonar Total |
| VR | Volume Residual |
| VC | Volume Corrente |
| PEEP | Pressão Positiva Expiratória Final |
| Pmus | Pressão dos músculos respiratórios |
| Psr | Pressão de recolhimento elástico do sistema respiratório |
| (l) | litros |
| ECMD | Esternocleidomastoideo |
| VEF1 | Volume Expiratório Forçado no 1º segundo |
| CVF | Capacidade Vital Forçada |
| VEF1/CVF | Relação entre o Volume Expiratório Forçado no 1º segundo e a Capacidade Vital Forçada |

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**RESUMO**

Os padrões ventilatórios adotados durante testes de resistência muscular têm sido alvo de vários estudos. No entanto, até o momento, os trabalhos comparando a contratilidade muscular e sua eficiência mecânica no sistema respiratório de pacientes com Doença Pulmonar Obstrutiva Crônica (DPOC) são escassos. O objetivo desse estudo foi avaliar a influência da obstrução e hiperinsuflação pulmonares na atividade dos músculos respiratórios e mobilização de volumes pulmonares. Foram avaliados 22 indivíduos de ambos os sexos sendo 14 pacientes portadores de DPOC ($VEF_1$ = 54,1 ± 15,9 % predito) e 8 voluntários (Controle, $VEF_1$ = 98,5 ± 17,6 % predito) e de idades 63,2 ± 11,3 (DPOC) e 56,5 ± 7,9 (Controle). Os voluntários foram submetidos ao teste de força (Pressão Inspiratória Máxima - Pimáx) e de resistência (Teste com Carga Incremental), sendo mensurada a atividade eletromiográfica do músculo escaleno, esternocleidomastoideo e diafragma, sendo também avaliada a estratégia ventilatória durante o teste incremental. Os dados foram analisados utilizando-se: teste t'Student ou Mann Whitney, 2-way ANOVA, ANOVA de medidas repetidas seguidos pelo teste de Tukey como *pos hoc*. Correlação de Spearman foi utilizada para identificar associações entre variáveis espirométricas, atividade eletromiográfica e volumes expirados durante teste com carga incremental. Apesar dos menores níveis Pimáx no grupo DPOC, a atividade eletromiográfica foi similar a do grupo controle. Além disso, a adição de cargas apenas alterou a atividade do músculo escaleno e, com cargas equivalentes a 60% da Pimáx observou-se predominância da atividade acessória na ventilação pulmonar. Os volumes inspiratórios e expiratórios durante o teste incremental foram menores no grupo DPOC quando comparados com o controle. Em conclusão, os déficits de força e resistência dos músculos inspiratórios estão mais relacionados às alterações mecânicas do sistema respiratório do que às modificações na contratilidade dos músculos inspiratórios.

**Palavras chaves:** músculos inspiratórios, eletromiografia, DPOC.

**ABSTRACT**

Ventilatory patterns adopted during muscular resistance tests have been reported in various studies however, there are few reports comparing muscular contractility and its mechanical efficiency on respiratory system in patients with COPD. The aim of this study was to assess Impact of pulmonary obstruction and hyperinflation on the respiratory muscles activity and pulmonary volumes mobilization. We evaluated 22 individuals from both sexes, 14 COPD patients ($FEV_1$ = 54.1 ± 15.9 % predicted) and 8 healthy volunteers (control, $FEV_1$ = 98.5 ± 17.6 % predicted), mean age (COPD 63.2 ± 11.3 and control 56.5 ± 7.9). All subjects were submitted to MIP and resistance tests (incremental loading test), and electromyography of scalene, sternocleidomastoid and diaphragm muscles and ventilatory strategy were measured through mobilized volumes during incremental loading test. Data were analyzed through Student t-test or Mann Whitney test, 2-way ANOVA, ANOVA with repeated measures followed by Tukey and Spearman correlation test also was run to identify associations between *variables spirometric,* EMG activies and *expired volume* values during test incremental loading. Although the level of MIP was lower in COPD group compared to control, electromyography was similar in both groups. Furthermore, the addition of load altered only scalene muscular activity, while loads equal to 60% MIP showed the predominance of accessory activity during ventilation. In conclusion, we suggested that force and resistance deficits of inspiratory muscles were more related to respiratory mechanics alterations than possible damages in the inspiratory muscles contractility.

**Key-words:** inspiratory muscle, electromyography, COPD.

## 1. INTRODUÇÃO

A ação mecânica de alguns músculos esqueléticos é essencialmente determinada pela anatomia destes músculos e pela carga que eles têm que deslocar quando se contraem. Os músculos respiratórios são músculos esqueléticos tanto morfologicamente quanto funcionalmente, e sua principal função é mover a parede torácica de forma rítmica, bombeado os gases para dentro e fora dos pulmões, com o intuito de manter os gases arteriais dentro de limites aceitáveis ( De Troyer e Estenne, 1988).

Em repouso ou durante atividades de baixa intensidade, o trabalho respiratório é relativamente pequeno e os músculos respiratórios não apresentam dificuldade para manter esta atividade contínua. Contudo, exercícios prolongados de alta intensidade promovem alterações na resistência dos músculos respiratórios, resultando em dispnéia e contribuindo para a intolerância à prática de esforços físicos (Orozco-Levi, 2003).

A doença pulmonar obstrutiva crônica (DPOC) acarreta prejuízos na mecânica pulmonar (Decramer,1997). A alteração da mecânica pulmonar é originada pela obstrução brônquica que acarreta um deslocamento do ponto de igual pressão para as vias aéreas que não possuem cartilagens, favorecendo o aprisionamento de ar. Cronicamente, este processo fisiopatológico tende a acarretar hiperinsuflação pulmonar, inicialmente reduzindo a capacidade física aos grandes esforços e, posteriormente, ao repouso (Celli e cols.,1995; Celli e MacNee, 2004). Esse estado patológico do pulmão induz ao remodelamento dos músculos inspiratórios, especialmente do diafragma, que tende a se retificar, diminuindo a zona de aposição, prejudicando a relação comprimento-tensão e reduzindo a força de contração deste músculo (Gorman e cols., 2002).

Alguns estudos vêm demonstrando outras linhas de interpretação para a resistência dos músculos respiratórios. Estas linhas sugerem que apesar do aumento de carga e do recrutamento muscular, a *endurance* dos músculos respiratórios está provavelmente aumentada na DPOC em decorrência de adaptações como o remodelamento muscular e o encurtamento da relação tempo inspiratório com o tempo total (Newell, McKenzie e Gandevia,1989)

## 2. REVISÃO DA LITERATURA

### Fibras musculares respiratórias

A capacidade de gerar força, a resposta contrátil e a resistência à fadiga variam entre os músculos de acordo com o tipo e proporção de fibras que os constituem. Estas fibras são divididas em grupos: lenta I, rápida 2A e rápida 2B. As primeiras são resistentes à fadiga devido ao seu metabolismo oxidativo, enquanto as rápidas possuem baixo conteúdo de hemoglobina, com metabolismo glicolítico predominante na 2A e exclusivo da 2B ( Polla e cols., 2004).

A biologia molecular tem mostrado que cada tipo de fibra resulta de um perfil específico de expressão gênica baseada em dois mecanismos principais: regulação da expressão quantitativa de muitos genes e a expressão seletiva de outros genes os quais existem em múltiplas cópias com pequenas diferenças (isogenes) e dão origem a isoformas, isto é, proteínas similares o bastante para substituir umas as outras, mas diversas a ponto de determinar características funcionais distintas (Schiaffino e Reggiani, 1996)

A habilidade de uma fibra muscular gerar tensão, encurtar-se e produzir potência mecânica é determinada principalmente pela composição proteica e, principalmente, pela composição das isoformas da miosina. A miosina é o motor da contração muscular, sua molécula é uma proteína hexamétrica composta de duas cadeias pesadas (MyHC) e quatro cadeias leves (MyLC), ambas existindo em várias isoformas. As isoformas da MyHC são utilizadas para a classificação do tipo de fibra muscular pois estão em maior proporção, determinam as propriedades contráteis e vários métodos disponíveis para determinação do tipo de fibra são baseados nas isoformas da MyHC. Quatro isoformas da MyHC são expressas na musculatura esquelética de mamíferos adultos : lentas, 2A, 2X e 2B. Contudo a isoforma MyHC-2B não é expressa em músculos humanos (Polla e cols., 2004).

As fibras lentas consomem pouco ATP e este é completamente ligado a oxidação aeróbica. Assim, a composição do citosol é pouco alterada durante a contração muscular. As fibras rápidas consomem bastante ATP e este, não está ligado apenas a produção mitocondrial, já que durante a contração há acúmulo de lactato e fosfato inorgânico (Polla e cols., 2004).

O diafragma como principal responsável pela respiração em repouso e em constante atividade é constituído por aproximadamente 55% de fibras lentas, 21% oxidativas rápidas e 24% rápidas glicolíticas (Reid e Dechman, 1995; Polla e cols., 2004).

No entanto, as características estruturais e funcionais das fibras dos músculos respiratórios não são fixas, podem ser modificadas em resposta a várias condições fisiológicas e patológicas tais como: treinamento com cargas, adaptação à hipóxia, mudanças relacionadas à idade e a doenças respiratórias (Orozco-Levi, 2003; Polla e cols. 2004).

**Avaliação dos músculos respiratórios**

Os músculos têm duas funções: desenvolver força e encurtar-se. No sistema respiratório, força é usualmente estimada como pressão e encurtamento como mudanças de volume ou deslocamento de estruturas da parede torácica. Assim, a caracterização quantitativa dos músculos respiratórios tem sido realizada através de medidas de volumes, deslocamento de estruturas, pressões e taxas de variações destas estruturas no tempo (ATS/ERS, 2002).

A relação entre pressão e força é complexa. Por exemplo, a geometria torácica apresenta a principal função na eficiência da conversão de força em pressão. A geração de pressão também depende das características mecânicas das costelas e da parede abdominal, com as quais os músculos interagem. Ou seja, um tórax rígido resiste melhor à distorção e, portanto, permite que mais pressão seja produzida pelo diafragma para um dado nível de força (Chihara e cols.,1996). Assim, isto significa que pressões devam ser melhor vistas como índices globais de rendimento dos músculos respiratórios do que como medida direta de suas propriedades contráteis (ATS/ERS, 2002).

Para testar as propriedades dos músculos, as pressões podem ser medidas durante manobras voluntárias ou involuntárias. A principal vantagem dos testes voluntários é dar uma estimativa da força dos músculos inspiratórios e expiratórios de forma simples e bem tolerados pelos pacientes. No entanto, pode ser difícil assegurar que o indivíduo esteja realmente realizando esforço máximo e, assim poder afirmar se há fraqueza muscular ou se é apenas ativação neural

reduzida. Apesar das limitações da técnica, na prática a presença de resultado normal pelo menos exclui fraqueza muscular (ATS/ERS, 2002).

***Avaliação da pressão inspiratória máxima (Pimáx)***

Convencionalmente, a força da musculatura inspiratória tem sido medida através da manobra de pressão inspiratória máxima (Pimáx), método simples e largamente utilizado capaz de avaliar a capacidade ventilatória e o desenvolvimento de insuficiência respiratória (Harik-Khan, Wise e Fozard 1998; Bellemare e cols., 2002; Windisch e cols., 2004). O método sugerido por Black e Hyatt até hoje serve como padrão para a realização da manobra (Black e Hyatt, 1969). No entanto, a Pimáx é pobremente reprodutível com variação média de 25% (Wijkstra e cols., 1995).

As medidas da pressão inspiratória estática máxima que o indivíduo pode gerar na boca é um caminho simples de se medir a força dos músculos inspiratórios. As pressões medidas durante essas manobras refletem a pressão desenvolvida pelos músculos respiratórios (Pmus) somada a pressão de recolhimento elástico do sistema respiratório (Psr). Ao nível da capacidade residual funcional (CRF), a Psr é zero, tal que a pressão ao nível da boca representa a Pmus. Contudo, a Pimáx é usualmente medida a partir do volume residual (VR) e, neste caso, a Psr pode chegar a -30cm$H_2O$ podendo contribuir em até 30% nos valores de Pimáx (ATS/ERS, 2002).

As medidas da contração muscular máxima na musculatura esquelética ocorrem sob condições isométricas, com o músculo em seu comprimento ideal. (ATS/ERS, 2002). No entanto, nos testes de força dos músculos respiratórios, modificações na relação força *versus* velocidade e força *versus* comprimento são comuns, podendo interferir nos resultados (Braun e cols., 1982; Road e cols. 1986).

Devido à relação força *versus* comprimento e à contribuição variada da Psr, as pressões respiratórias variam marcadamente com o volume pulmonar. Em pacientes com volumes pulmonares anormalmente altos, uma Pimáx baixa pode em parte refletir o encurtamento das fibras musculares inspiratórias associado ao

aumento do VR melhor que uma redução da força dos músculos (Wilson e De Troyer, 1992; ATS/ERS, 2002).

***Avaliação da resistência dos músculos respiratórios***

A resistência muscular é a capacidade de sustentar uma tarefa muscular específica no tempo. Medidas de resistência devem ser obtidas através de medidas específicas, pois, diferentes tarefas resultam em variados padrões de recrutamento de unidades motoras e de grupos musculares, cada qual variando em sua resistência à fadiga (ATS/ERS, 2002)

Uma grande variedade de técnicas tem sido desenvolvida para medir a resistência dos músculos respiratórios, as quais diferem em relação ao tipo de tarefa a ser executada. Para cada tarefa específica, uma curva de resistência pode ser gerada através da relação carga *versus* tempo, cargas de alta intensidade podem ser mobilizadas por apenas poucas repetições (ATS/ERS 2002). Por exemplo, uma pressão resistiva menor que 60% da Pimáx pode ser mantida indefinidamente, enquanto cargas maiores que 60% da Pimáx levam a insuficiência num curto período de tempo. Além do acréscimo de carga resistiva, a redução na força muscular inspiratória também predispõe a fadiga dos músculos inspiratórios (Mador, 1991).

Para estimar a resistência muscular utiliza-se teste onde se aumenta temporalmente e de forma padronizada a atividade muscular, até o pico de atividade ser identificado. Esse teste é conhecido como teste com carga incremental (Larson e cols., 1999; ATS/ERS, 2002; Nobre e cols., 2006).

O teste com carga incremental usando o dispositivo Threshold® é descrito desde a década de 80 (Martyn e cols., 1987; Morrison e cols. 1989). O Threshold® é um dispositivo comercialmente disponível, que corresponde a um cilindro plástico (peso 36.4 g; diâmetro 4.06 cm) dotado de uma válvula do tipo "spring-loaded" conectada a um bocal, a qual se abre a uma pressão mínima previamente ajustada fazendo com que a pressão do sistema permaneça praticamente constante (Gosselink e cols., 1996). Os limiares de pressão são independentes da taxa de fluxo e da freqüência respiratória, com alcance de 7 $cmH_2O$ a 41 $cmH_2O$.

Antes do teste com carga incremental, realizam-se medidas de Pimáx através de técnicas padronizadas (Black e Hyatt, 1969). Posteriormente, o teste é executado partindo de uma carga inicial de 30-40% da Pimáx com incrementos de carga equivalentes a 5 -10% da Pimáx, até a carga não ser mais tolerada por um tempo de 2 minutos. A maior carga sustentada por 2 minutos completos é considerada como a pressão de pico (Morrison e cols., 1989)

Esta técnica tem geralmente sido usada para medir a resistência dos músculos inspiratórios. O incremento de carga limiar, não sendo afetado por mudanças no padrão de fluxo ventilatório, foi proposto como melhor teste reprodutível para análise da resistência dos músculos inspiratórios (ATS/ERS 2002).

***Avaliação eletromiográfica dos músculos respiratórios***

A contração dos músculos depende de sua ativação elétrica, sendo os impulsos originados nos neurônios respiratórios do cérebro conduzidos através de nervos motores, transferidos através de junções neuromusculares e propagados através das membranas dos músculos. Falência em um destes locais pode resultar em fraqueza muscular reversível ou não. Diante do exposto, o objetivo do teste eletrofisiológico é avaliar a integridade do aparato neuromotor respiratório (ATS/ERS, 2002).

A Eletromiografia (EMG) é uma técnica que permite descrever as manifestações elétricas do processo de excitação decorrente da propagação dos potenciais de ação ao longo das membranas das fibras musculares. O sinal eletromiográfico é detectado através de eletrodos e então amplificado, filtrado e exibido em anteparo ou digitalizado para posterior análise (ATS/ERS, 2002). A velocidade de condução da fibra muscular tem se mostrado variar em função do diâmetro da fibra, da temperatura, dos gradientes eletrolíticos através da membrana celular, do pH e do grau de fadiga muscular (Metzger e Fitts, 1986; Juel, 1988).

A EMG dos músculos respiratórios pode ser usada para avaliar o nível e o padrão de ativação, detectar e diagnosticar patologias neuromusculares e, quando associada a testes de função mecânica, avaliar a eficácia da função

contrátil dos músculos respiratórios (ATS/ERS, 2002; Duiverman e cols., 2004); Dornelas de Andrade e cols., 2005).

### *Aplicação clínica*

O padrão de registro eletromiográfico não processado dos músculos respiratórios é útil para a determinação do tempo e nível de ativação durante atividades repiratórias. A EMG de superfície pode ajudar a determinar quais dos músculos respiratórios estão ativos nas fases respiratórias em diversas posturas do corpo, nos diferentes estados de consciência entre outras condições clínicas (ATS/ERS, 2002; Duiverman e cols., 2004; Dornelas de Andrade e cols., 2005).

A EMG pode também ajudar a quantificar a atividade dos músculos respiratórios em resposta a cargas inspiratórias, a estímulos ventilatórios através da inalação de $CO_2$, além de monitorar e controlar a ventilação mecânica. Quando associada à pressão ou força desenvolvida pelos músculos a EMG pode avaliar a eficiência mecânica destes músculos (ATS/ERS, 2002)

Estudos através da EMG de superfície também têm trazido subsídios para a avaliação do perfil das fibras musculares. Alguns autores relatam maiores valores de freqüência média e mediana em músculos com maior proporção de fibras tipo II (Gerdle e cols., 2000; Bilodeau e cols., 2003).

## DOENÇA PULMONAR OBSTRUTIVA CRÔNICA

A DPOC é uma enfermidade respiratória prevenível e tratável, que se caracteriza pela presença de obstrução crônica do fluxo aéreo, que não é totalmente reversível. A obstrução do fluxo aéreo é geralmente progressiva e está associada a uma resposta inflamatória anormal dos pulmões à inalação de partículas ou gases tóxicos, causada primariamente pelo tabagismo. A DPOC além de comprometer os pulmões, também produz conseqüências sistêmicas significativas. O processo inflamatório crônico pode produzir alterações dos brônquios (bronquite crônica), bronquíolos (bronquiolite obstrutiva) e parênquima pulmonar (enfisema pulmonar) (Celli e cols., 1995; Celli e MacNee, 2004).

A inalação de gases e partículas nocivas causa inflamação pulmonar, induzem destruição do parênquima pulmonar, prejudicam os mecanismos de defesa e interrompem os mecanismos de reparo que são capazes de restaurar a estrutura do tecido em resposta a algumas injúrias (Celli e cols., 1995; Celli e MacNee, 2004).

Em adição à inflamação, dois outros processos parecem estar relacionados à patogênese da DPOC: um desequilíbrio entre as proteases e as anti-proteases no pulmão e o estresse oxidativo. Estes processos podem ser conseqüências da infamação em si ou, surgir devido a fatores ambientais (ex. fumaça do cigarro) ou genéticos (ex. deficiência da alfa 1–anti-tripsina). A fumaça do cigarro ativa macrófagos e outras células epiteliais para produzirem fator de necrose tumoral (TNF)- alfa e outros mediadores como interleucina (IL)-8 e leucotrieno (LT)B4 (Barnes, 2000; Celli e MacNee, 2004).

Os resultados do dano ao tecido pulmonar são hipersecreção de muco, fibrose e estreitamento das vias aéreas, destruição do parênquima (enfisema) e alterações vasculares. Em resumo estas modificações patológicas levam a limitação do fluxo aéreo e outras anormalidades características da DPOC (Celli e cols., 1995; Celli e MacNee, 2004).

**Limitação ao fluxo expiratório e hiperinsuflação pulmonar**

A limitação ao fluxo expiratório é a principal alteração que caracteriza a DPOC. Esta limitação é primariamente irreversível, sendo decorrente do remodelamento (fibrose e estreitamento) das pequenas vias que produzem obstrução fixa e conseqüentemente aumento de sua resistência. A destruição do parênquima (enfisema) apresenta uma menor função no componente irreversível, mas contribui para o aumento da resistência das vias aéreas (ATS, 1995; Celli e MacNee, 2004).

A destruição das conexões inter-alveolares reduzem a habilidade das pequenas vias para manterem sua patência e assim contribui para a limitação ao fluxo expiratório. A destruição alveolar repercute na redução do recolhimento elástico dos pulmões, o qual diminui a pressão intra-alveolar que direciona a

exalação. A contração da musculatura lisa das vias aéreas, inflamação das vias aéreas, acúmulo intra-luminal de muco e exsudato plasmático podem ser responsáveis pela pequena parte da limitação ao fluxo aéreo reversível ao tratamento (Celli e cols., 1995; Celli e MacNee, 2004).

As mensurações diretas da resistência das vias aéreas periféricas mostram que as mudanças estruturais nas paredes das vias aéreas são as mais importantes causas de aumento da resistência das vias aéreas na DPOC. A limitação ao fluxo de ar é mensurada através da espirometria, a qual é a chave para o diagnóstico e tratamento da doença. As medidas espirométricas essenciais para o diagnóstico e o monitoramento dos pacientes DPOC são o volume expirado forçado no 1º segundo ($VEF_1$), a capacidade vital forçada (CVF) e a razão $VEF_1$/CVF. A redução da razão $VEF_1$/CVF é, freqüentemente, o primeiro sinal de desenvolvimento de limitação do fluxo expiratório (Vestbo e cols., 1996; Celli e cols., 1995; Fabbri e Hurd, 2003).

Embora as medidas de fluxo de ar sejam essenciais para o diagnóstico da DPOC e comumente usados para o estadiamento da doença, os efeitos da doença sobre os volumes pulmonares apresentam melhor correlação com o prejuízo na capacidade funcional dos pacientes. Em pulmões normais, o volume pulmonar expiratório final ou CRF representa o ponto no qual todos os músculos respiratórios estão em repouso e o equilíbrio é dado entre o vetor de força para fora da parede torácica e o vetor de força para dentro dos pulmões (recolhimento elástico) (Celli e cols., 1995; Celli e MacNee, 2004).

Na DPOC, a destruição do tecido elástico comumente associado às alterações enfisematosas altera o recolhimento elástico pulmonar, mudando a relação entre o volume pulmonar e a pressão de distensão (curva Pressão *versus* Volume). Logo, para um dado volume pulmonar há menor pressão de recolhimento no paciente DPOC do que no pulmão saudável. Esta mudança no recolhimento elástico altera o balanço entre as pressões do pulmão e da parede torácica. Assim, para haver compensação da pressão da parede torácica pelo recolhimento elástico pulmonar faz-se necessário maior volume pulmonar, ou seja, ocorre a hiperinsuflação pulmonar estática (Celli e cols., 1995; Celli e MacNee, 2004).

Além disso, a taxa de esvaziamento pulmonar lentificada em conseqüência da limitação ao fluxo expiratório faz com que, durante episódios de exacerbação da doença ou prática de atividade física, o esforço inspiratório seja iniciado antes que seja atingido o volume de relaxamento do sistema respiratório. Logo, haverá um aprisionamento adicional de ar acarretando a hiperinsuflação dinâmica (O'Donnell e Webb, 2003).

Dentre os demais volumes pulmonares, a capacidade inspiratória (CI) é de vital importância, ela representa a extensão onde ocorre o recrutamento do volume corrente (VC), podendo ser considerado como o volume disponível para a inspiração. A capacidade inspiratória é calculada pela diferença entre a capacidade pulmonar total (CPT) e CRF. Um aumento na CRF, comum à hiperinsuflação pulmonar, diminui a CI (Ferguson, 2006). Diversas formas de mensurar a CI vêm sendo empregadas para avaliar a hiperinsuflação pulmonar dinâmica induzida pelo exercício físico, através de seu decréscimo progressivo com o aumento da ventilação ao exercício (Diaz e cols., 2000; Marin e cols. 2001). Outros estudos também têm utilizado o valor da CI no repouso como parâmetro de hiperinsuflação, tanto o valor absoluto, quanto as frações relativas à CPT e à CI predita (Casanova e cols., 2005).

## DESORDENS DOS MÚSCULOS RESPIRATÓRIOS

O sintoma mais incapacitante da DPOC é a dispnéia, sendo que esta resulta primariamente de um decréscimo na capacidade dos músculos respiratórios associado a um aumento da carga mecânica do sistema respiratório (Grazzini e cols., 2005) .

Os mecanismos que contribuem para este desequilíbrio entre a carga do sistema respiratório e a capacidade muscular são: aumento da demanda energética da inspiração, hiperinsuflação pulmonar, déficit na geração de pressão respiratória, menor resistência dos músculos respiratórios, desnutrição e o uso crônico de corticóides (Laghi e Tobin, 2003).

**1) Aumento da demanda energética da inspiração**

Anormalidades referentes à troca gasosa (áreas de *shunt* e espaço morto) e à alta carga mecânica levam o paciente DPOC a gerar uma pressão intra-torácica mais negativa a fim de atingir uma ventilação alveolar mais adequada, sendo que a pressão gerada pelos músculos inspiratórios para manter a ventilação basal chega a três vezes o valor gerado em condições normais (Jubran e Tobin, 1997; Laghi e Tobin, 2003).

Várias alterações no parênquima pulmonar e vias aéreas contribuem para o aumento da demanda energética dos músculos: aumento da resistência ao fluxo inspiratório, cerca de quatro vezes maior; aumento na ventilação minuto (em torno de 50%); aumento das constantes de tempo; a limitação ao fluxo expiratório com retardo no esvaziamento pulmonar e início da inspiração antes que o sistema respiratório retorne ao volume de relaxamento (hiperinsuflação dinâmica) (Tobin e cols., 1983; Officer e cols., 1998; Sliwinski e cols., 1998; Eltayara e cols., 1996). Como conseqüência, há o aumento do consumo de oxigênio para manter os músculos respiratórios em atividade (Laghi e Tobin, 2003).

**2) Hiperinsuflação pulmonar**

A hiperinsuflação prejudica a capacidade dos músculos respiratórios em gerar pressão intra-torácica negativa através de vários mecanismos: piora da relação comprimento *versus* tensão, redução na zona de aposição, diminuição da curvatura do diafragma, mudanças no arranjo mecânico dos componentes crural e costal do diafragma e aumento no recolhimento elástico da parede torácica ( Laghi e Tobin, 2003).

Cassart e cols. observaram, através de um estudo com tomografia computadorizada, menor comprimento diafragmático ao nível da CRF nos pacientes DPOC comparados a idosos saudáveis: 45 contra 57 cm (Cassart e cols., 1997). Também foi observado que esta redução no comprimento diafragmático decorreu do decréscimo da zona de aposição, a qual corresponde à área contrátil do músculo, repercutindo assim na geração de pressão inspiratória (Laghi e cols., 1996). A zona de aposição representa, em condições normais,

cerca de 60% do comprimento total do músculo diafragma, sendo que nos pacientes DPOC é de aproximadamente 40% (Cassart e cols., 1997).

A hiperinsuflação tem sido tradicionalmente relacionada ao achatamento do diafragma aumentando seu raio de curvatura. De acordo com a lei de Laplace, um aumento no raio de curvatura causa elevação da tensão passiva do diafragma com redução de sua eficiência em gerar pressão transdiafragmática (Laghi e Tobin, 2003). No entanto outros estudos têm demonstrado pouca interferência do raio de curvatura ao longo da capacidade inspiratória tanto em pacientes com DPOC quanto em idosos saudáveis (McKenzie e cols., 2000).

Tem sido proposto que mais importante que alterações no raio de curvatura são as mudanças no comprimento das fibras musculares para determinar a capacidade contrátil do músculo diafragma, tanto ao nível da CRF quanto na CI (Laghi e Tobin, 2003).

Foi observado em estudo com cães que a adição de uma pressão positiva expiratória final (PEEP) modifica o arranjo mecânico das fibras do diafragma de em paralelo para em série, reduzindo sua habilidade como gerador de pressão inspiratória (Zocchi e cols., 1987). A mesma limitação pode ser aplicada a pacientes com DPOC que possuem os pulmões hiperinsuflados.

**3) Déficit na geração de pressão respiratória**

Pacientes com DPOC geram menor pressão inspiratória máxima que indivíduos saudáveis, os menores níveis pressóricos podem ser explicados pelo encurtamento muscular induzido pela hiperinsuflação pulmonar presente em alguns pacientes (Laghi e Tobin, 2003). No entanto, Similowski e colaboradores observaram que alguns pacientes portadores de DPOC têm maior pressão transdiafragmática (em resposta a estimulação do frênico) que indivíduos saudáveis com volumes equivalentes (Similowski e cols., 1991). Estes achados sugerem que os músculos inspiratórios se adaptam a hiperinsuflação, sendo que esta adaptação se dá através do encurtamento dos sarcômeros e redução em seu número, causando um desvio a esquerda na relação comprimento *versus* tensão.

Rochester e Braun sugeriram que a fraqueza muscular não é apenas inspiratória e sim de toda a musculatura esquelética. Esta suposição decorreu da forte correlação entre o déficit de força inspiratória e expiratória, sendo que estes

últimos não sofrem a ação de mudanças na mecânica do sistema respiratório (Rochester e Braun, 1985).

Vários mecanismos podem contribuir para a fraqueza muscular generalizada, entre eles: distúrbios eletrolíticos, anormalidades nos gases sanguíneos, descompensação cardíaca, perda de peso e miopatia por esteróides (Laghi e Tobin, 2003)

***Adaptações da musculatura respiratória na DPOC***

Estudos vêm demonstrando outras linhas de interpretação da resistência dos músculos respiratórios, sugerindo que apesar do aumento de carga e do recrutamento muscular, a *endurance* dos músculos respiratórios está provavelmente aumentada na DPOC. Propõem que adaptações como o remodelamento muscular e o encurtamento do ciclo de trabalho sejam os principais responsáveis (Newell e cols., 1989).

Evidências do remodelamento incluem aumento na concentração de mitocôndrias e mudanças na composição da fibra muscular (Laghi e Tobin, 2003). O diafragma de pacientes com DPOC, quando comparado ao de indivíduos normais, apresenta uma maior proporção de fibras tipo I resistentes a fadiga (61 versus 46%), uma menor proporção de fibras IIa resistentes a fadiga (31 versus 39%) e poucas fibras do tipo IIb sensíveis a fadiga (8 versus 15%) (Levine e cols. 1997).

As adaptações das fibras musculares acima citadas associadas ao aumento da capilaridade muscular, da densidade mitocondrial, da capacidade das enzimas mitocondriais oxidativas, além do aumento do fluxo sanguíneo para os músculos respiratórios durante os exercícios, justificam o aumento da resistência do músculo diafragma em pacientes com DPOC (Newell e cols., 1989).

Pacientes com DPOC têm uma freqüência de disparo do nervo frênico aproximadamente duas vezes maior e um recrutamento diafragmático cerca de cinco vezes maior que indivíduos saudáveis, durante a respiração em repouso, também demonstrando um mecanismo de adaptação a alteração da mecânica do sistema respiratório (De Troyer e cols., 1997).

***Eletromiografia em pacientes com DPOC***

Pouco material é disponibilizado utilizando a EMG para avaliar a função muscular respiratória. Duiverman e cols. concluíram que a técnica EMG apresenta-se reprodutível e sensível a mudanças na atividade dos músculos respiratórios, sugerido a EMG como uma ferramenta útil na avaliação dos músculos respiratórios ( Duiverman e cols., 2004).

Estudos anteriores também utilizaram a EMG para demonstrar mudanças no espectro eletromiográfico do diafragma durante exercícios físicos em pacientes com DPOC, e o atraso no relaxamento muscular inspiratório imediatamente pós-exercício foi consistente com um potencial padrão de contração de fadiga (Beck e cols., 1997).

O estudo do Duiverman e cols. também mostrou que pacientes com DPOC, quando respiram contra uma carga inspiratória crescente, aumentam a atividade de sua musculatura acessória, sendo que eles exibiram um menor aumento na atividade do seu diafragma do que os indivíduos sem essa doença ( Duiverman e cols., 2004).

Da mesma forma, Dornelas de Andrade e cols. evidenciaram que o diafragma nos pacientes DPOC não muda a intensidade de contração para superar a carga do Threshold® (Dornelas de Andrade e cols., 2005).

## 1.3. HIPÓTESE

Embora, medidas de eficiência mecânica do sistema respiratório tenha sido alvo de estudos através da análise dos padrões ventilatórios adotados durante testes de resistência muscular (Yan e Bates, 1999), na literatura são escassos os estudos (Dornelas de Andrade e cols., 2005) comparando a atividade muscular com a eficiência mecânica destes músculos no sistema respiratório de pacientes com DPOC.

As reduzidas pressões inspiratórias máximas e a limitação ventilatória durante testes com carga incremental não podem ser justificados apenas pelo déficit na atividade contrátil dos músculos inspiratórios (ATS/ERS, 2002). Assim, propomos que o prejuízo na mecânica pulmonar é que determina o menor desempenho dos músculos respiratórios em pacientes portadores de DPOC.

## 1.4. OBJETIVOS

### OBJETIVOS GERAIS:

Avaliar a influência da obstrução e hiperinsuflação pulmonar na atividade dos músculos respiratórios e mobilização de volumes pulmonares.

### OBJETIVOS ESPECÍFICOS:

1) Avaliar as repercussões da DPOC na geração de força muscular inspiratória através da medida da Pimáx;

2) Avaliar se os reduzidos valores de Pimáx e o menor rendimento ao teste com carga incremental, comuns a DPOC, são acompanhados de menor atividade dos músculos inspiratórios;

3) Avaliar através da EMG a participação dos músculos inspiratórios: escaleno, diafragma e esternocleidomastoideo (ECMD) na geração de pressão intra-torácica durante a manobra de Pimáx;

4) Avaliar a influência da obstrução e hiperinsuflação pulmonar nas estratégias ventilatórias em resposta ao teste com carga incremental;

5) Avaliar os volumes inspirados e expirados em resposta às cargas do teste incremental;

6) Avaliar as modificações induzidas pelas cargas nas proporções do ciclo respiratório medidas pela freqüência respiratória (FR) e ciclo de trabalho [relação entre o tempo inspiratório e o tempo total (Ti/Ttot)];

7) Avaliar as modificações induzidas pelo teste com carga incremental na saturação periférica de oxigênio ($SpO_2$);

8) Avaliar a resposta eletromiográfica, dos músculos: escaleno, ECMD e diafragma durante o teste com carga incremental.

# 5. ARTIGO SUBMETIDO AO PERIÓDICO:

# JOURNAL OF ELECTROMYOGRAPHY AND KINESIOLOGY

# IMPACT OF PULMONARY OBSTRUCTION AND HYPERINFLATION ON THE RESPIRATORY MUSCLES ACTIVITY AND PULMONARY VOLUMES MOBILIZATION IN COPD

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**ABSTRACT**

Ventilatory patterns adopted during muscular resistance tests have been reported in various studies however, there are few reports comparing muscular contractility and its mechanical efficiency on respiratory system in patients with COPD. The aim of this study was to assess Impact of pulmonary obstruction and hyperinflation on the respiratory muscles activity and pulmonary volumes mobilization. We evaluated 22 individuals from both sexes, 14 COPD patients ($FEV_1$ = 54.1 ± 15.9 % predicted) and 8 healthy volunteers (control, $FEV_1$ = 98.5 ± 17.6 % predicted), mean age (COPD 63.2 ± 11.3 and control 56.5 ± 7.9). All subjects were submitted to MIP and resistance tests (incremental loading test), and electromyography of scalene, sternocleidomastoid and diaphragm muscles and ventilatory strategy were measured through mobilized volumes during incremental loading test. Data were analyzed through Student t-test or Mann Whitney test, 2-way ANOVA, ANOVA with repeated measures followed by Tukey and Spearman correlation test also was run to identify associations between *variables spirometric,* EMG activies and *expired volume* values during test incremental loading. Although the level of MIP was lower in COPD group compared to control, electromyography was similar in both groups. Furthermore, the addition of load altered only scalene muscular activity, while loads equal to 60% MIP showed the predominance of accessory activity during ventilation. In conclusion, we suggested that force and resistance deficits of inspiratory muscles were more related to respiratory mechanics alterations than possible damages in the inspiratory muscles contractility.

**Key-words:** inspiratory muscle, electromyography, COPD.

**Abreviations:**

| | |
|---|---|
| COPD | Chronic Obstructive Pulmonary Disease |
| MIP | Maximum Static Inspiratory Pressure |
| EMG | Electromyography |
| HR | Heart Rate |
| BP | Blood Pressure |
| SpO2 | Peripheral Oxygen Saturation |
| V'E | Minute Ventilation |
| FVC | Forced Vital Capacity |
| MVV | Maximum Voluntary Ventilation |
| IC | Inspiratory Capacity |
| 6MWT | Six-minute walk test |
| MMRC | Modified Medical Research Council Scale |
| FRC | Functional Residual Capacity |
| TLC | Total Lung Capacity |
| RR | Respiratory Rate |
| Vins | Inspired Pulmonary Volume |
| Vexp | Expired Pulmonary Volume |
| Ti | Inspiratory Time |
| Ttot | Total Duration Of Respiratory Cycle |
| Ti/Ttot | Duty Cycle |
| SMM | Sternomastoid |
| RMS | Root Mean Square |
| fMD | Mean Frequency |
| WD | Walked Distance |
| BMI | Body Mass Index |

## INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a condition characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases. Impaired lung function is of central importance in the diagnosis of COPD (Cassart et al., 1997). In this line, lung mechanical changes are caused by the loss of lung elastic recoil and bronchial obstruction, which moved the equal pressure point to a part of the airway not supported by the cartilage, leading to flow limitation, air trapping and dynamic lung hyperinflation (Celli and MacNee, 2004). As a result of these ultra structural changes, there was an initial reduction in the exercise capacity during strenuous breathing efforts and later at rest (O'Donnell, 2006). In addition, lung hyperinflation yields muscle remodeling, especially the diaphragm, which assumes a more flattened position, with a reduced zone of apposition, modifying its resting length-tension position and decreasing its contraction force (Gorman et al., 2002).

In COPD patients, there is an increase in the work of breathing and a decrease in the muscle capacity to overcome the intrinsic high inspiratory load. The inspiratory muscles in COPD are characterized by an imbalance between load and capacity. If a skeletal muscle contracts above a certain proportion of its maximal force, the contraction cannot be maintained due to fatigue (ATS/ERS, 2002; Mador, 1991). Fatigue may be induced separately in the diaphragm or in rib cage muscles according to the breathing pattern (Mador, 1991). In short, both increased resistive load and reduced inspiratory muscle force yielded fatigue in COPD patients (ATS/ERS, 2002).

Inspiratory muscle pressure have been measured through maximum static inspiratory pressure (MIP) test, which is a widely used simple method (Bellemare et al., 2002; Windisch et al., 2004), able to evaluate the ventilatory capacity and to predict adverse respiratory outcomes (Harik-Khan, Wise, and Fozard, 1998).

Besides the MIP test, a great variety of techniques have been developed to measure respiratory muscle resistance. In this line, in the incremental loading test progressive and standardized increments in the loads are imposed on the

respiratory system in programmed intervals of time. Loading values and time interval vary according to specific protocol (ATS/ERS, 2002).

Respiratory muscles electromyography (EMG) should also be used to evaluate level and activation pattern and, when associated to mechanical function tests, assess respiratory muscle contractility(ATS/ERS, 2002).

There are many studies focusing on muscle mechanical efficiency of the respiratory system (Decramer, 1987, 1493-1498; Decramer, 1997), however there are few reports comparing muscle contractility with the mechanical efficiency of those respiratory muscles in COPD patients (Dornelas de Andrade, 2005). Therefore, this study aims: 1) to assess whether reduced MIP values and low response to incremental loading test in COPD patients is accompanied by a lower inspiratory muscle contractility; 2) to compare scalene and sternocleidomastoid muscle activity with the diaphragm intra-thoracic pressure generated during MIP test and to analyze their response to the load increments during incremental test; and 3) to evaluate the impact of pulmonary obstruction and hyperinflation on both electromyography response and ventilatory strategy.

## MATERIAL AND METHODS

### Subjects

Eight healthy subjects and fourteen COPD patients from both sexes were included in the study. Baseline characteristics are shown in Table 1. COPD was defined according to the American Thoracic Society criteria ($FEV_1$ < 80% from predict values, $FEV_1$/FVC relation < 0.7 and history of smoking > 20 packets-year) (ATS, 1995). Patients had to be in a stable condition, without signs or symptoms of an exacerbation in the last 3 months before the study. In addition, they did not interrupt bronchodilator therapy and had never been involved in pulmonary rehabilitation programs. Healthy subjects were defined as having a normal pulmonary function (Tiffeneau index >75%). Patients with other lung diseases than COPD were excluded.

The research protocol was approved by the Federal University of Pernambuco Ethics Committee and written informed consent was obtained in each case.

***Experimental Protocol***

The following parameters were measured: heart rate (HR), blood pressure (BP), peripheral oxygen saturation ($SpO_2$), weight, height, maximal inspiratory pressure (MIP), minute ventilation (V´E), pulmonary function test [forced vital capacity (FVC), maximum voluntary ventilation (MVV) and inspiratory capacity (IC) maneuvers], and a Six-minute walk test (6MWT). Functional dyspnea was assessed by using the modified Medical Research Council (MMRC) scale.

***Maximal inspiratory pressure***

The mouthpiece was held tightly against the face with the lips inside the tube. The maximum inspiratory effort (maximal inspiratory pressure-MIP) was obtained after requiring the patient to expire up to functional residual capacity (FRC) and then perform a maximum inspiratory maneuver with closed airway. To that end a differential pressure transducer (MV – 120, Marshall – Town Instrumentation Industries) was used. A 1 mm in diameter and 1 cm in length cardboard mouthpiece was used to reduce the effects of cheek muscles. An acceptable maneuver was defined as one that showed a 2-s plateau of inspiratory effort with no air leaks around the mouth and the three highest values had to be within 10% of each other. MIP was measured as the most negative pressure attained after the first second of effort (Harik-Khan, Wise, and Fozard, 1998).

***Pulmonary function test***

Spirometry was measured with the spirometer (Vitalograph Portable Spirometer 2120, Buckingham, UK). Tests were conducted according to American Thoracic Society criteria, with a minimum of three acceptable maneuvers (Wagner, 1998.). The predictive values for lung function parameters were derived from those published for the Brazilian population (Pereira, Barreto, and Simões, 1992)

***Inspiratory capacity***

All patients were instructed on the performance of the Inspiratory Capacity (IC) maneuver. The IC was determined using ventilometer (Wright Respirometer Mark 8, Ferraris Medical Limited, England) connected to the mouthpiece, using nose clips. After four to six consistent end-expiratory levels, the patient was instructed to inspire to Total Lung Capacity (TLC) and then to return to normal breathing. From at least three acceptable trials, the two largest IC measurements had to agree within 5% or 60 ml. The better of two reproducible maneuvers were recorded for analysis (Marin et al, 2001). Reference values of IC were calculated from the difference between predicted values of TLC and end-expiratory lung volume (Stocks and Quanjer, 1995).

***Six-minute walk test***

The six-minute walk test (6MWT) was conducted according to a standardized protocol (ATS, 2002). One well-trained researcher supervised the test. Patients were asked to walk at their own maximal pace along a 34-m long corridor. Subjects were asked to walk from end to end, covering as much ground as they could during the allotted time (6 min) without running. The patients were encouraged every 30 s using two phrases: "You are doing well" or "Keep up the good work," and were allowed to stop and rest during the test, but were instructed to resume walking as soon as they felt able to do so. Predicted values were obtained from equations proposed by Enright and Sherril. (Enright and Sherrill, 1998)

***Functional dyspnea index***

Functional dyspnea was measured using modified scale from Medical Research Council (MMRC). This includes five grades of physical activities that provoke dyspnea.

***Incremental Test***

Incremental loading test started from a load of 0% (Threshold® without the resistive membrane) and, from this original load increments were done using intervals of 2 minutes, with loads of 15, 30, 45 and 60% of maximal inspiratory

pressure. During the measurements, the subjects were sitting in a comfortable chair and were asked not to move or talk. During the measurement, the investigator stood at the left of the subjects and held the threshold device.

**Acquisition and analysis of ventilatory pattern during incremental test**

Inspired and expired pulmonary volumes (Vins and Vexp), respiratory rate (RR), inspiratory time (Ti), total duration of respiratory cycle (Ttot), and duty cycle (Ti/Ttot) were measured using a micro processed respiratory monitor (Trace-5, Intermed) (França, 2006). Flow sensor was located between mouthpiece and Threshold® device. $SpO_2$ was monitored through portable pulse oximetry (Morrya model 1003, SP).

Three measurements were performed using intervals of 30 seconds after the addition of each load. Thus, three values of each parameter were measured 30, 60 and 90 seconds after each test maneuver with incremental loading. An average of three measurements in each incremental test was used.

***Acquisition and analysis of muscle activity through Electromyography***

Electromyography (EMG) registration was obtained using a signal conditioner module of analogical digital signs (CAD 12/32 Module, EMG System, Brasil LTDA), converting plate A/D 12bits with frequency of 1000 Hz, input range of $\pm$ 5 mV, total internal gain of 1000 times, common rejection mode ratio > 120 dB and band pass filter with cut-off frequencies at 20 – 500 Hz. We used active bipolar superficial electrodes (EMG System, Brazil LTDA), consisting of two rectangular of stainless steel reference (30mm x 45mm x 1mm).

Electrodes placement were guided by bone prominences and the route of the muscle fibers as followed: 1. Sternomastoid on the right muscle womb at 5 cm in the mastoid process; 2. Scalene on the right muscle womb of scalene at 5 cm of sternoclavicular joint in direction to clavicle and at 2 cm above this point; diaphragm on the 7th right intercostal space from sternum, between hemiclavicle

and axilar line (Dornelas de Andrade et al., 2005; Duiverman et al., 2004). Electrodes were fastened in the positions previously described after skin tricotomy and cleanness with alcohol to decrease possible interferences during EMG signs acquisition.

Registrations from electromyography activity were made during MIP test maneuvers and incremental tests. To that end, the EMG signals related to the best MIP maneuver and basal activity (RMS value $_{\%}$ = RMS $_{MIP}$ / RMS $_{BASAL}$) were selected. To analyse the EMG signals during incremental test three stretches regarding inspiratory muscle activity were randomly selected. In addition, a stretch concerning to basal activity from the same duration (RMS value % $_{(LOAD)}$ = RMS $_{(LOAD)}$ / RMS $_{BASAL}$) was computed (Dornelas de Andrade et al., 2005). Mathematical treatment was via Matlab software with signal processing in domain of the time, through RMS values attainment and frequency domain (Mean frequency – fMD).

**Statistical analysis**

The normality of the data (Kolmogorov-Smirnov test with Lilliefors' correction) and the homogeneity of variances (Levene median test) were tested. If both conditions were satisfied, Student t-test was used to assess differences between COPD and control groups; in the negative case, Mann Whitney test was used. Mixed-design 2-way ANOVAs, followed by Tukey test, were used to determine the effect of group and muscle on EMG RMS values and fMD obtained during the maneuver of MIP. Spearman correlation test was run to identify associations between MIP and IC%, MIP and $FEV_1$/FVC (%) and MIP and RMS% of the SMM data. One-way ANOVA repeated measures followed by Tukey test was used to compare the changes in each variable with progressive inspiratory loading. Spearman correlation test also was performed to identify associations between spirometric variables (IC% e FEV1/FVC%) and expired volume values during test incremental loading test. SPSS 12.0 statistical software package (SPSS Inc., Chicago, IL, USA) was used. In all instances the significance level was set at 5% ($\alpha$ = 5%).

## RESULTS

Twenty two individuals**,** 8 in control group and 14 in COPD group were analyzed. Table 1 shows anthropometric and spirometric data, as well as parameters related to respiratory muscle performance (MIP, MVV). In the ventilatory analysis of incremental test, one subject from control group was excluded, due to technical difficulties. In a parallel study, electromyography analysis during incremental test was performed in 5 male volunteers ($FEV_1$= 93.23 ± 7.054% predicted, mean age 57.7 ± 1.5 years) and 9 COPD patients ($FEV_1$= 53.39 ± 5.81% predicted, mean age of 66.9 ± 1.13 years).

Table 1

### ***Analysis of ventilatory strategy used during incremental test***

#### Respiratory Rate (RR)

No significant effect of the *group* factor was found for RR values, indicating that similar values were observed for the two groups. No significant interaction between the *load* and *group* factors was found, reflecting the similar answer in COPD and control groups for all loads.

Significant effect of the *load* factor was found for RR values only in COPD group, RR reduced with loads of 15% (10.36 ± 0.17; p=0.008) and 30% (10.23 ± 0.14; p=0.007) of MIP values compared to basal RR values (14.64 ± 0.3).

#### Duty cycle (Ti/Ttot)

During incremental test, no significant effects of the group or load factors were found for *duty cycle* values. No significant interaction between the *load* and *group* factors was found.

**Expired volume (Vexp)**

Significant effect of the *group* (p=0.035) *or load* (p=0.003) factors were found for *expired volume* values. In addition interaction between *load* and *group* factors was observed (p=0.048).

In the control group, Vexp (l) augmented with the addition of all levels of loading compared to basal Vexp (0.68 ± 0.01 (0%) *versus* 1.5 ± 0.05 (15%); 1.5 ± 0.06 (30%); 1.6 ± 0.06 (40%) e 1.3 ± 0.07 (l) (60%); p<0.05). COPD group showed a significant increase in Vexp only in the presence of 30% of loading (1.22 ± 0.03 (l); p<0.05) compared to basal values (0.86 ± 0.02 (l)).

In the COPD group Vexp (l) was lower than the control group in the presence of 15% *(*1.5 versus 1.18 l; p=0.005) and 45% (1.6 versus 1.16 l; p=0.017) loads (figure 1)

Figure 1

**Inspired volume (Vins)**

Significant effect of the *group* (p=0.037) and *load* (p=0.001) factors were found for *expired volume* values. Additionally, interaction between the *load* and *group* factors (p=0.037) was observed.

In the control group we find a significant increased Vins in all levels of loading regarding to basal Vins (0.73 ± 0.03 (l) *versus* 1.53 ± 0.05 (15%); 1.4 ± 0.05 (30%); 1.57 ± 0.03 (45%) e 1.32 ± 0.06 (l) (60%); p<0.05). In the COPD group, there was significance only with loads of 30% (1.17 ± 0.02 (l); p=0.045) of basal loading values (0.85 ± 0.02 (l)).

Control group presented higher values with loads of 15% (1.53 *versus* 0.99 (l); p=0.001), 45% (1.57 *versus* 1.04 (l); p=0.001) and 60% (1.32 *versus* 0.84l; p=0.02) of MIP (figure 2).

Figure 2

**Peripheral oxygen saturation ($SpO_2$)**

No significant effect of the *group or load* factors was found for *expired SpO2* values. Interaction between the *load* and *group* factors (p=0.028) was observed. In the control group, $SpO_2$ increased from 96.34 to 98.43 % (p=0.009) with the last load of the incremental test.

**Correlation between Vexp (l), Obstruction level and Pulmonary Hyperinflation**

Expiratory volume with loads of 15, 30, 45 and 60% of MIP was significantly correlated with $FEV_1$ (%predicted), IC (l) and IC (%predicted) (table 2).

Tabela 2

***Electromyography activity analysis (RMS% and Hz) during MIP test***

**Root-mean-square ( RMS%)**

No significant effect of the *group* factor was found for RMS values, indicating that similar values were observed between the two groups. No significant interaction between the *muscle* and *group* factors was found, reflecting a similar recruitment in COPD and control groups for all muscles.

In COPD group, scalene (15.8 ± 0.8) and the SMM (23.5 ± 2.1) presented similar activities. SMM had higher activity than the diaphragm (23.5 ± 2.1 *versus* 5 ± 0.5; p=0.031). In the control group, scalene and SMM presented similar activities as well (34.43 ± 4.24 and 19.79 ± 1.47, respectively). SMM had higher activity than the diaphragm (p=0.01) (Figure 3).

Figure 3

There was a significant correlation between SMM muscle activity (RMS %) and MIP ($cmH_2O$) values (figure 4).

Figure 4

**Mean frequency ( fMD)**

No significant effect of the *group* factor was found for mean frequency values (fMD) indicating that similar values were observed for the two groups. In the same way, no significant interaction between the *muscle* and *group* factors was found.

In COPD group, fMD were higher in SMM (135.07 ± $1.74H_Z$; p=0.018) and diaphragm muscles (130.35 ± $2.33H_Z$; p=0.046) compared to scalene muscle (100.78 ± 2.62Hz). In the control group, no significant effect of the *muscle* factor was found for fMD values (figure 5).

Figure 5

**Pulmonary obstruction and hyperinflation *versus* MIP**

It was observed a pattern of positive correlation between MIP (cmH2O) and IC (%predicted) (r=0.482; p=0,023) and $VEF_1$/FCV (%predicted) (r=0.428; p=0.047) in the COPD group (figure 6).

Figure 6

***Muscle activity analysis in reply to incremental loading test***

**Electromyography activity ($EMG_{RMS\%}$)**

Significant effect of the *muscle* (p=0.014) and *load* (p=0.002) factors were found for *RMS%* values, as well as interaction between *load* and *muscle* factors (p=0.004). No significant effect of the *group* (p=0.782) factor was found.

EMG activity was similar in the control group independent of the load. In COPD group, electromyography activity of scalene increased with load of 30% ($RMS\%_{Scalene}$= 11.32 ± 0.63 p=0.001), 45% ($RMS\%_{Scalene}$ = 11.47 ± 0.53; p=0.001) and 60% ($RMS\%_{Scalene}$ = 13.3 ± 0.6; p<0.0001) of basal values. EMG activity of diaphragm and SMM with loads of 45% ($RMS\%_{SMM}$= 17.56 ± 1.19 *versus* $RMS\%_{Diaphragm}$ = 3.43 ± 0.18; p=0.001) and 60% ($RMS\%_{SMM}$ = 16.73 ± 1.42 *versus* $RMS\%_{Diaphragm}$ = 3.98 ± 0.3; p=0.056) was similar (figure 7).

Figure 7

**Electromyography activity ($EMG_{Hz}$)**

A significant effect of the *load* (p<0.000) factor was found for *RMS%* values, and no interaction was observed between *load* and *muscle* factors (p=0.636). No significant effect of the *group* (p=0.345) factor was found.

In both groups there wasn´t a proportional difference between muscle activity from all three muscles analyzed when activities were measured in Hz. Only, in COPD patients there was basal intermuscle activity, with SMM showing a higher fMD ($fMD_{SMM}$ = 198.8 ± 0.31Hz *versus* $fMD_{Scalene}$ = 144.8 ± 0.44Hz; p=0.004 and $fMD_{Diaphragm}$ = 167.53 ± 0.5Hz, p=0.01). We find reduction of fMD in all stages of incremental test regarding to basal level for both SMM and diaphragm in COPD and control groups. Thus, fMD recruitment from scalene muscle didn´t modified related to the applied loads (figures 8 and 9).

Figures 8 and 9

## DISCUSSION

Our study assessed COPD impact on the electromyographic activity of inspiratory muscles during maximum force test (MIP) and acute electromyographic and ventilatory responses to incremental load resistance test. It has been noted that in spite of lower MIP levels determined for the COPD group, electromyographic activity was equivalent to the control group, with both groups presenting low activity of the diaphragmatic muscle.

The scalene muscle was the principal factor for the COPD group respiratory system response to load addition during the incremental test, and at a 60% MIP the predominance of accessory activity for pulmonary ventilation became evident.

Nevertheless, the main differences determined in these patients were lower inspiratory and expiratory volumes during the incremental test. In addition, the lower inspired and expired volumes showed a correlation with disease severity measured by the degree of obstruction ($FEV_1$/FCV%) and hyperinflation (IC% predicted). These results suggest that inspiratory muscles' force and resistance deficit is much more related to the damage of the respiratory system mechanics than possible inspiratory muscles' contractility.

### Force deficit versus muscle contractility

Reduced MIP value in the COPD group was expected and also referred in other studies (Wijkstra et al., 1995; Laghi and Tobin, 2003; Harik-Khan, Wise, and Fozard, 1998) but the fact that the muscle activities of these patients is equivalent to the control group demonstrates inspiratory muscle activity preservation, indicating other causes for the low MIP values.

According to Windisch low MIP values do not necessarily indicate inspiratory muscles weakness. The relationship between pressure and force is complex (Windisch et al., 2004). This conversion is dependant upon the mechanical features of the ribs and abdominal walls interacting with the muscles. A rigid ribcage resists better to structural changes therefore allowing more pressure of the back ribs to a given force level. Therefore, the low MIP values

obtained can reflect the shortening of respiratory muscles resulting from hyperinflation instead of inspiratory muscle weakness (ATS/ERS, 2002).

**Contribution of respiratory muscles during the MIP maneuver and incremental load test**

When assessing intramuscle activity to generate intratoracic pressure, higher scalene and SMM muscles activity was determined, not only for COPD patients but for the control group as well. The diaphragm of both groups was not recruited enough to transform muscle tension in inspiratory pressure. This fact could be attributed by the excessive recruitment of accessory muscles reducing diaphragm activation.

COPD typical hyperinflation reduces the inspiratory muscles capacity to generate tension because it causes them to shorten more than in relaxation, but each one of these muscles is differently affected (Decramer, 1997).

Yan and Kayser induced hyperinflation in healthy subjects using a Starling resistor to assess diaphragm and other muscles contribution of the rib cage to insufflate the respiratory system, and determined that with hyperinflation increase there is more recruitment of the rib cage muscles than of the diaphragm (Yan and Kayser, 1997). Martinez also noted that with the increase of airway obstruction and pulmonary hyperinflation there's a greater involvement of the thoracic cage muscles to mobilize the current volume (Martinez, Couser, and Celli, 1990).

According to Raper the scalene and sternocleidomastoid muscles suffer a contraction force increase with the increment of pulmonary volume towards the TCP (Raper et al., 1966). Nevertheless, there are few data related to the hyperinflation effect in the scalene and SMM muscles. De Troyer et al demonstrated that activity in the SMM is rare even in patients with severe obstruction and hyperinflation considering that the scalene muscles are essential for inspiration in normal and in COPD patients (De Troyer et al., 1994).

Legrand studied these two muscles as well; using the reciprocity theorem of Maxwell describing that airway pressure is the product of three factors: muscle mass, maximum muscle tension per crosscut section area and variation in the muscle length per increased volume unit (Legrand et al., 2003). Based on this

theorem their findings demonstrated that in the presence of hyperinflation there's more shortening of the SMM than of the scalene muscles, but as the SMM possesses a larger mass, the inspiratory pressure generating capacity of both are similar.

Changes in the length of the scalene due to hyperinflation are relatively small. Therefore we are able to conclude that the mechanic advantage of these muscles is less harmed than the diaphragm. While the diaphragm is shortened up to 40% the scalene muscles shorten only 6% (Farkas and Rochester, 1986). Nevertheless, curve length form versus tension is not well known in humans (Decramer, 1997).

Studies in anesthetized and vagotomized dogs (Decramer, Jiang, and Demedts, 1987) demonstrated that muscles interaction alterations did not result from the neural debit modifications of the muscles but of mechanical effectiveness alterations of the respiratory muscles. We also noted the same muscle activity pattern during incremental test, where COPD patients recruited the scalene and SMM muscles in lieu of the diaphragm muscle. Notwithstanding the mechanical disadvantage of respiratory muscles in the COPD, the two groups did not demonstrate significant differences among themselves in RMS values or in fMD values.

Through prior electromyographic investigations utilizing incremental testing, we were able to determine diaphragm response in young adults to the external loads of 10, 20 and 30 $cmH_2O$ (Nobre et al., 2006). However, when evaluating diaphragm and SMM response to overcome a 30% MIP load (loads ranging between 20 and 30cmH20); patients with COPD as well as elderly people did not require additional recruiting from the diaphragm, which was confirmed by this study as well (Dornelas de Andrade et al., 2005).

Likewise, Duiverman et al. using incremental tests with loads of 7cmH2O, 14$cmH_20$ and 21$cmH_20$, determined the important role of the scalene muscles to overcome external loads in the COPD group (Duiverman et al., 2004). However, although COPD patients had a tendency for a more global activity of inspiratory muscles than healthy individuals, the activities of both groups were not different. This fact is corroborated by our findings as well, further suggesting the optimization of muscle adaptation mechanisms in COPD patients.

In the control group we would possibly have noticed the increase of muscle activity to higher loads if we had continued with test progression, but that was prevented by the Threshold® device imposing the maximum load of 41cm$H_20$, therefore, this group presented higher MIP levels and was only able to achieve 45% of MIP in the test.

A similar behavior of the studied groups can be justified by the fact that some physiological age related changes are similar to COPD induced changes. The most common are: decrease of elastic recoil pressure, intrinsic PEEP increase, diaphragm flattening and reduction of the spirometric $FEV_1$/FVC reaching up to 55% in apparently normal individuals (Zaugg and Lucchinetti, 2000).

***Changes in the mean frequency of the electromyographic signal during tests***

Myoelectric signal consists of a series of action potentials firing at certain frequencies. A common use power spectrum analysis has been the evaluation of local muscle fatigue. With a sustained muscle contraction, the high frequency components of the signal decrease, but the low frequency components gradually increase. This change results in a shift in the power spectrum towards lower frequencies (De Luca, 1984). fMD reduction occurs due to the speed reduction of the myoelectric signal transmission caused by the accumulation of metabolic residues (ATS/ERS, 2002).

In our study fMD reduction of SMM and diaphragm muscles was determined as a response to loads when compared with basal fMD. Nonetheless, there was no difference between load increment frequencies, that is, there was no difference related frequencies with load increment, therefore, we did not determine fMD reduction in the last test stages, and that is suggestive of fatigue.

Currently studies on variation of fatigue induced frequencies are accomplished through sustained isometric contractions (Hagg, 1992); this protocol is not viable for respiratory muscles considering their essential role in respiration. Therefore, we suggest that studies utilize electromyography as a methodological tool for a more objective assessment of fatigue signs in respiratory muscles. We could have possibly noted fMD alterations in the muscles if we had continued with

test progression using higher loads, but that was restricted, as mentioned before, by the device used for external loads addition.

The influence of muscle fibers size and composition in EMG obtained frequencies has been studied as well. Generally, higher values of fMD have been observed in muscles with a great percentile of type II fibers or large areas from type II fibers (Bilodeau et al., 2003; Gerdle et al., 1991; Gerdle et al., 2000; Gerdle, Wretling, and Henriksson-Larsen, 1988). In our study the assessment of respiratory muscles frequency during MIP maneuver determined higher results for SMM, consistent with the larger quantity of type II fibers. The diaphragm depicted high fMD values that might have occurred due to other muscles signal contamination.

The scalene muscles showed practically no fMD alteration during the test. This could be explained by the scalene muscle fiber composition with a higher proportion of type II fibers, as suggested by some of the histological studies (Campbell, 1955; Raper et al., 1966)

**Pulmonary Obstruction and Hyperinflation versus force and resistance deficit.**

In our study, MIP values presented a positive correlation with the degree of pulmonary hyperinflation and obstruction. Other studies also refer that MIP has a positive correlation with respiratory indexes as Peak flow, $FEV_1$ and FVC (Casanova et al., 2005), demonstrating COPD degree of influence over inspiratory pressure.

Elastic recoil loss and the development of expiratory flow constraint, characteristic of COPD justify progressive air capture with the increase of residual volume (RV) and FRC leading to flows and volumes reduction during pulmonary function test, and reduction of inspiratory capacity (Casanova et al., 2005).

Some of the studies have utilized the IC relaxation value as a hyperinflation parameter, including not only the absolute value but the TLC related fraction and pre-established IC as well (Casanova et al., 2005). Our data demonstrate that higher IC corresponds to higher pressure generation, suggesting that higher pulmonary hyperinflation corresponds to lower produced MIP.

Hayot et al through regression analysis, also found approximately 20% of hyperinflation interference in the MIP results, further suggesting that the FRC / TLC ratio is the main determinant of the inspiratory muscles force(Hayot et al., 1998).

Based on a prior electromyographic study in COPD patients we determined a possible pulmonary obstruction degree influence in the SMM muscle electromyographic activity in response to the loads applied (Dornelas de Andrade et al., 2005). These results motivated the current study capable of better demonstrating the influence of disease severety at the level of inspiratory muscle recruitment in response to muscle function tests.

**Ventilation strategy alterations in response to incremental test loads**

We determined, as a ventilatory strategy that in loads responses, COPD patients initially reduce the RR and do not change inspiratory time proportions in relation to total time. They also show lower inspiratory and expiratory volumes when compared to the control group. The $FEV_1$ (% predicted) and IC (%predicted) depicted a direct correlation with inspired and expired volumes. COPD patients depicted a RR reduction as an initial ventilatory strategy in response to 15 and 30% loads; this RR variation was not noted in the control group. These findings are consistent with the Yan and Bates study, who did not observe a significant RR variation in healthy humans when studying the ventilatory response to 2.5 to 20 $cmH_20$ loads (Yan and Bates, 1999).

As for RR modification induced by external loads in COPD patients, Larson et al (Larson et al., 1999) noted respiratory difficulties with respiratory frequency increase and pulmonary volumes decrease to complete the final test stage. We would have possibly noted a RR increase if we had continued load progression, which was limited by the test device, the Threshold®, with maximum load at $41cmH_20$.

As for the Ti/Ttot ratio, no alteration was found in COPD patients and the control group. In a study accomplished by Hayot et al (Hayot et al., 1998), comparing Ti and Ti/Ttot ratio of COPD and healthy patients, a significant

reduction in Ti of patients with COPD was determined, but equally without significant variation of the Ti/Ttot ratio.

Ventilatory response in the scope of expiratory (Vexp) and inspiratory volumes (Vins), determined by our study, demonstrated, in the control group, a significant increase in all load stages, consistent with the Yan and Bates study accomplishing a significant increase in the current volume as well as in the minute volume (Yan and Bates, 1999). Likewise, Eastwood et al studying healthy individuals also determined an increase of pulmonary volumes concurrently to load increment (Eastwood, Hillman, and Finucane, 2001).

In the case of COPD patients, alteration was restricted to 30% MIP load level, demonstrating patients' respiratory system limitation to respond to load increase. Larson et al applying the incremental test with 30 to 100% MIP loads in COPD patients obtained a reduction of the current volume and increase of the RR in the last load stages (Larson et al., 1999).

In the COPD group there was no $Sp0_2$ variation resulting from the incremental test, in the control group a $Sp0_2$ drop was determined during the last stage of the incremental test.

In a prior study performed in our laboratory a significant increase of $Sp0_2$ with a 30% MIP load not only in the control but in the COPD group was determined as well, but in this case patients presented a basal pulse oxymetry equivalent to 93%, that is, inferior to this groups (95.5%) (Dornelas de Andrade et al., 2005). Nevertheless, other studies indicated opposite results, Eastwood et al noted a significant reduction of $Sp0_2$ with the addition of excessive loads (Eastwood, Hillman, and Finucane, 2001).

Jeffrey et al confirmed this decrease in the COPD group in relation to the control, when verifying loads considered high (60%) attributing this to the increase of metabolic activity and to the excessive oxygen consumption of the respiratory muscles, compounded with the additional recruitment of accessory inspiration muscles (Mador, 1991).

## CONCLUSION

Our results showed, firstly, that inspiratory muscle force performed through voluntary maneuver of MIP seems undervalue inspiratory muscle global action, since the maneuver is performed mainly by neck muscles, and diaphragm presenting few activity in reply to the test, exactly in the control group. Moreover, interpretation from lower results found seems to reflect muscle weakness, therefore electromyography activity was similar for both groups.

In the same way, inspiratory muscle resistance assessment with incremental test seems to confirm similar behavior between both groups. However, we suggest that investigation of muscle weakness by specter frequency variation either carried through devices with higher levels of loading that allows inducing electromyography alterations common to fatigue.

Lower values displaced during incremental test by COPD group, despite electromyography activity similar to the control group, it suggest that functional deficit in COPD is a result from mechanical respiratory damage in function of the obstruction and pulmonary hyperinflation.

**LEGENDS TO TABLES:**

**Table 1**: Anthropometric and functional characteristics of patients with COPD and control subjects.

**Table 2**: Spearman correlation between spirometric variables and expired volumes during incremental loading test.

**LEGENDS TO FIGURES:**

**Figure 1:** Muscle activity level in root-mean-square normalized (RMS%) from both groups during maximal inspiratory pressure (MIP) test.

**Figure 2:** Correlation between sternocleidomastoid (SMM) muscle activity (RMS%) and maximal inspiratory pressure (MIP) values ($cmH_2O$) in COPD patients.

**Figure 3:** Muscle activity in mean frequency (Hz) from both groups during maximal inspiratory pressure (MIP) ($cmH_2O$) maneuver.

**Figure 4:** Correlation to maximal inspiratory pressure (MIP) ($cmH_2O$) and forced expiratory volume in 1 sec ($FEV_1$/FCV %) (A), and inspiratory capacity (IC %predicted) (B).

**Figure 5:** Basal values of Vexp (l) to loadings of 15, 30, 45 and 60% from maximal inspiratory pressure (MIP) ($cmH_2O$) test, during incremental loading test for both groups.

**Figure 6:** Basal Inspiratory Volume [Vins (l)] to loadings of 15, 30, 45 and 60% of their maximal inspiratory pressure (MIP) ($cmH_2O$) during incremental loading test for both groups.

**Figure 7:** Electromyography activity ($EMG_{RMS\%}$) of the respiratory muscles during 15, 30, 45 and 60% of their maximal inspiratory pressure (MIP) ($cmH_2O$) during incremental loading test in COPD group.

**Figure 8:** Mean frequency electromyography activity ($EMG_{Hz}$) of the respiratory muscles during 15, 30, 45 and 60% of their maximal inspiratory pressure (MIP) ($cmH_2O$) during incremental loading test in COPD group. (mean frequency - fMD = Hertz - Hz).

**Figure 9:** Mean frequency electromyography activity ($EMG_{Hz}$) of the respiratory muscles during 15, 30, and 45 % of their maximal inspiratory pressure (MIP) ($cmH_2O$) during incremental loading test in control group. (mean frequency - fMD = Hertz - Hz)

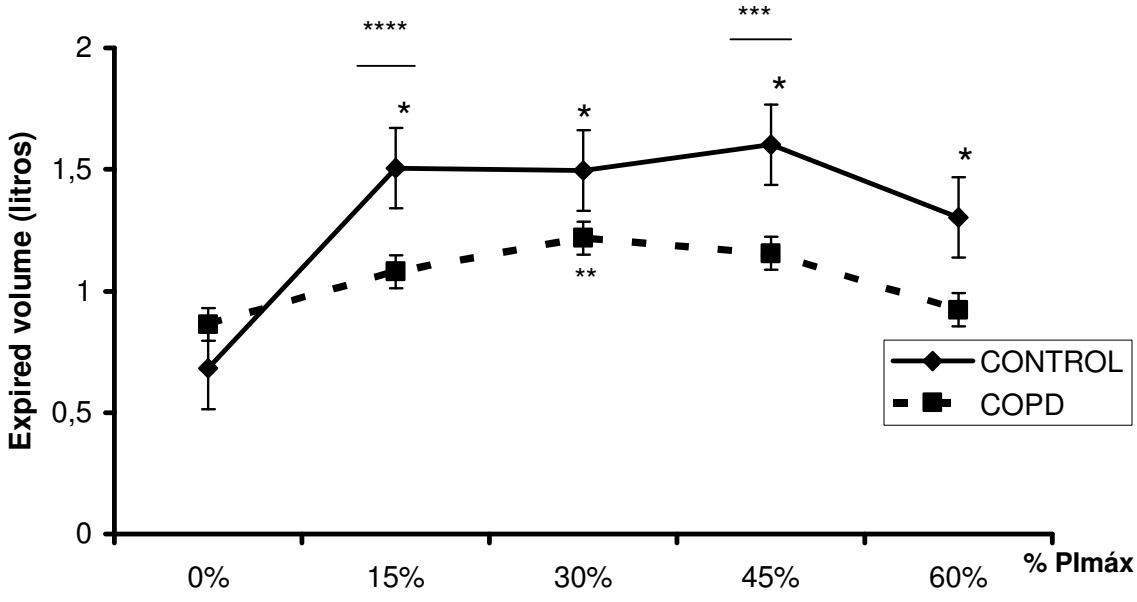
**Table 1:**

| Variables | COPD (N=14) | Control (N=8) | Significance (p value) |
|---|---|---|---|
| MIP($cmH_2O$) | 62.1 ± 24.2 | 93.7 ± 25.5 | 0.015 |
| MIP(%predicted) | 76.4 ± 27.3 | 94.9±17.3 | 0.020 |
| $FEV_1$ (%predicted) | 54.1 ± 15.9 | 98.5 ± 17.6 | <0.001 |
| $FEV_1$/FVC (%) | 58.51 ± 12.1 | 82.34 ± 8.9 | <0.001 |
| IC (L) | 1.9 ± 0.5 | 3.0 ± 0.7 | <0.001 |
| IC(%predicted) | 80.2 (55-96.7) | 105.45(82.3-57.5) | 0.002 |
| FVC (%predicted) | 7.01 ± 15.3 | 98.6 ± 14.4 | <0.001 |
| MVV (L/min) | 54.7 ± 27.1 | 125.2 ± 35.1 | <0.001 |
| MMRC | 1.64 ± 0.84 | 0.0± 0.0 | <0.001 |
| WD (meters) | 469.21± 11.52 | 536.6± 117.5 | NS |
| WD(%predicted) | 90.3 ± 20.9 | 100.1 ± 10.7 | NS |
| Age (years) | 63.2 ± 11.3 | 56.5 ± 7.9 | NS |
| BMI($Kg/cm^2$) | 26.45 ± 4.44 | 28.11 ± 5.51 | NS |

**Table 2:**

| | Vexp(15%) | Vexp(30%) | Vexp(45%) | Vexp(60%) |
|---|---|---|---|---|
| IC(%predicted) | 0.514* | 0.596** | 0.558* | 0.524* |
| IC (l) | 0.573** | 0.674** | 0.74** | 0.484* |
| $FEV_1$ (%predicted) | 0.562* | 0.557* | 0.521* | 0.564* |

**Figure 1:**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Expired volume (litros)
0%
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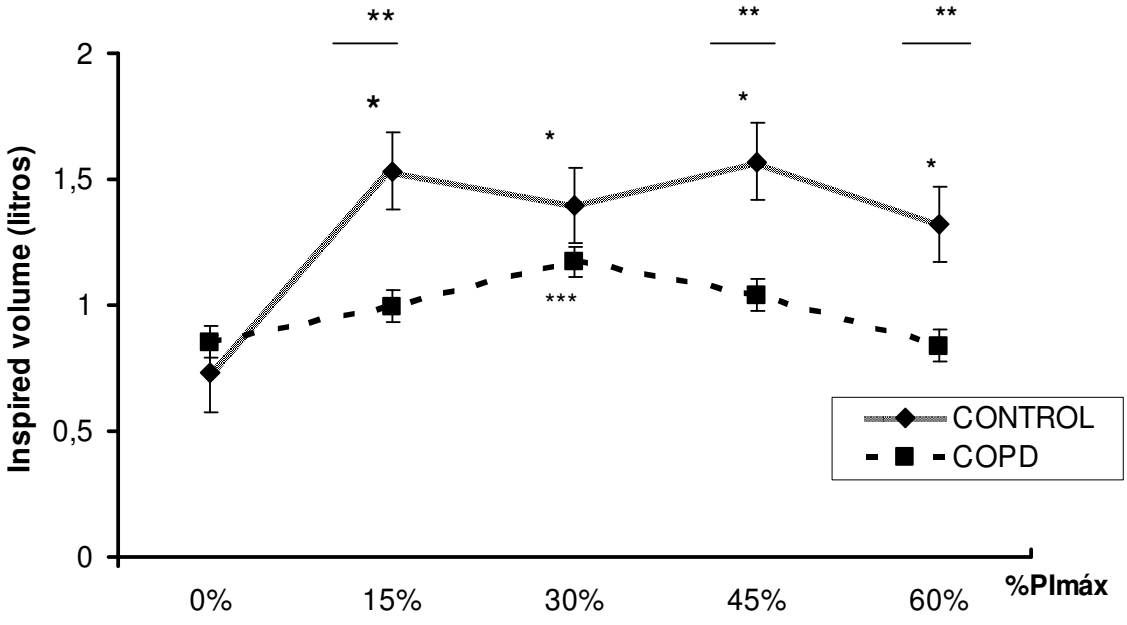
**Figure 2:**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Inspired volume (litros)
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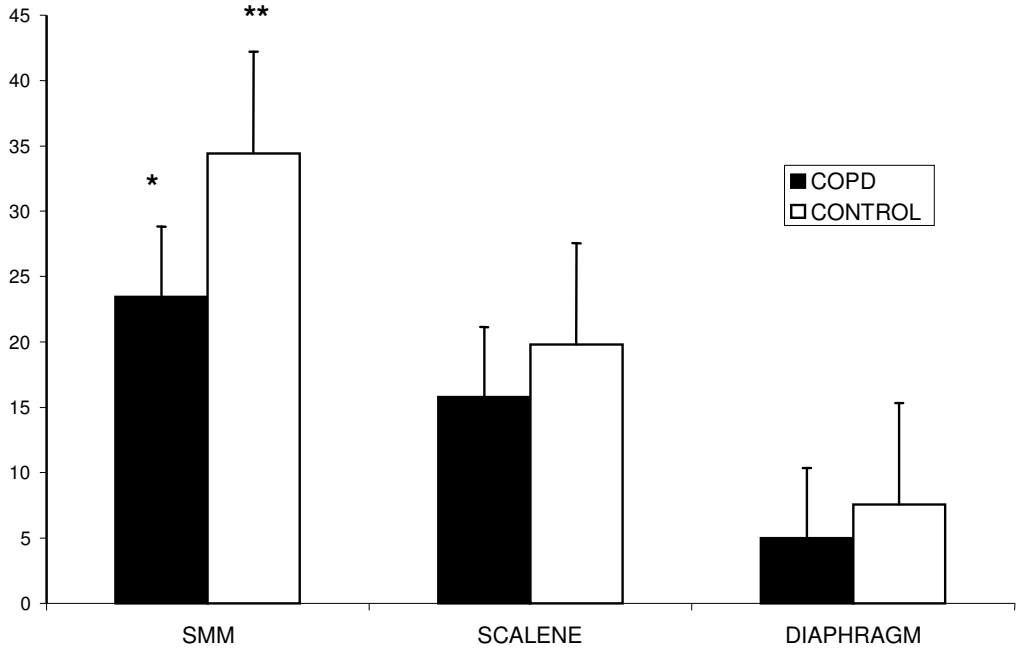
CONTROL
COPD

**Figure 3:**



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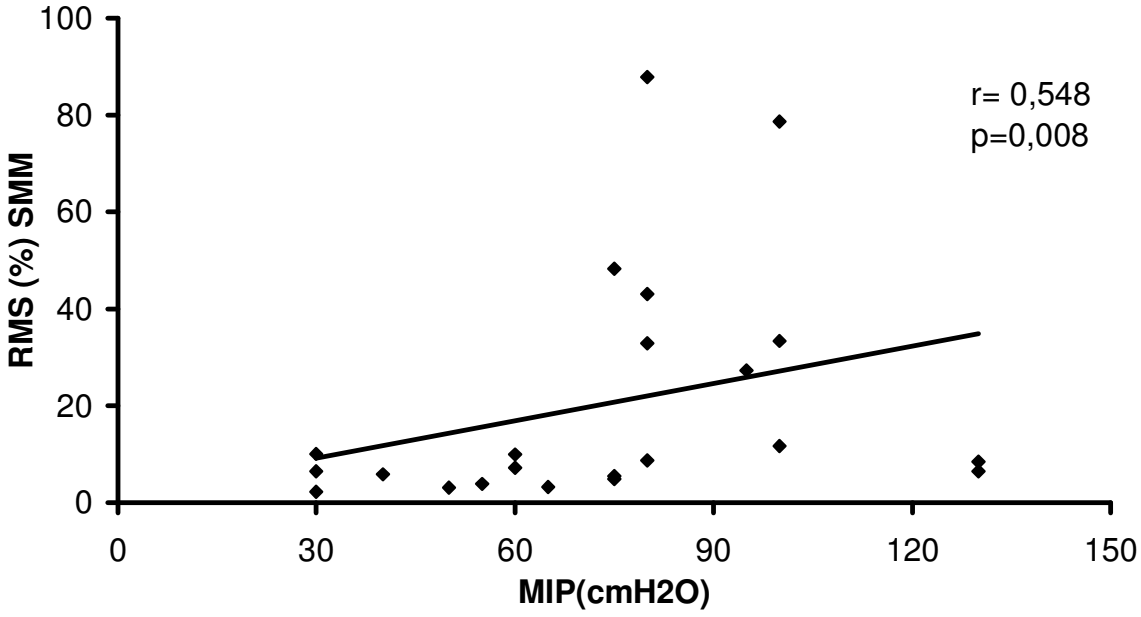

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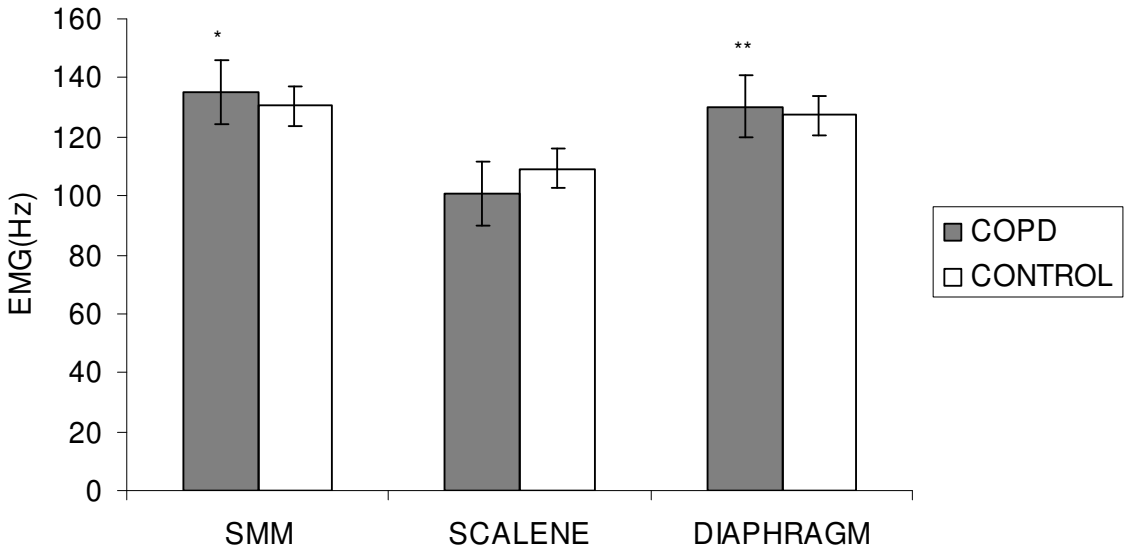
160
140
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100
80
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EMG(Hz)
*
**
SMM
SCALENE
DIAPHRAGM
COPD
CONTROL

**Figure 6: (A)**

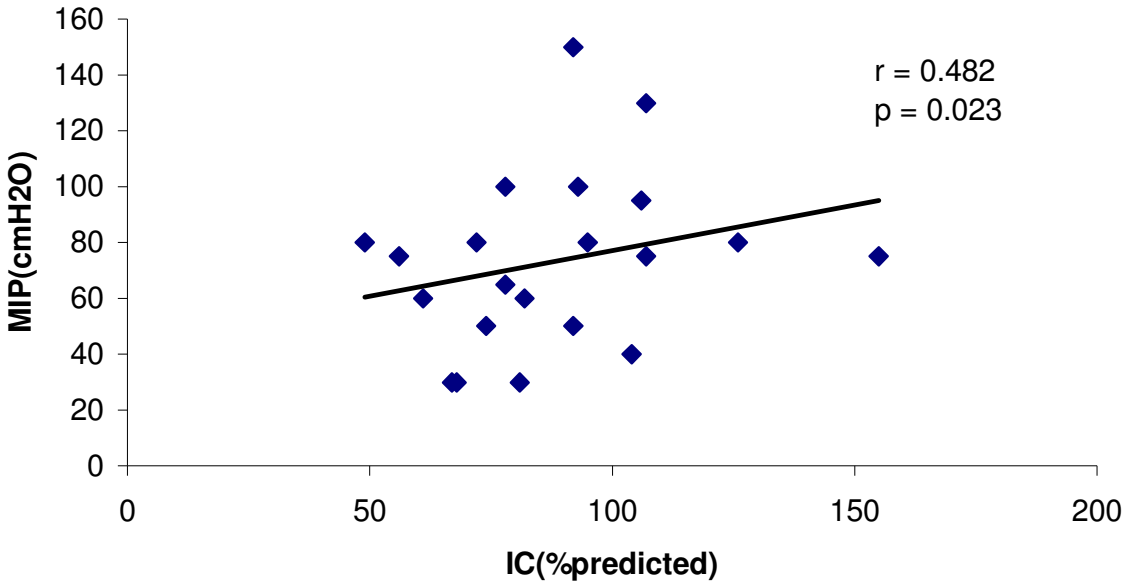

160
140
120
100
80
60
40
20
0
MIP(cmH2O)
0
50
100
150
200
IC(%predicted)
r = 0.482
p = 0.023

**Figure 6: (B)**

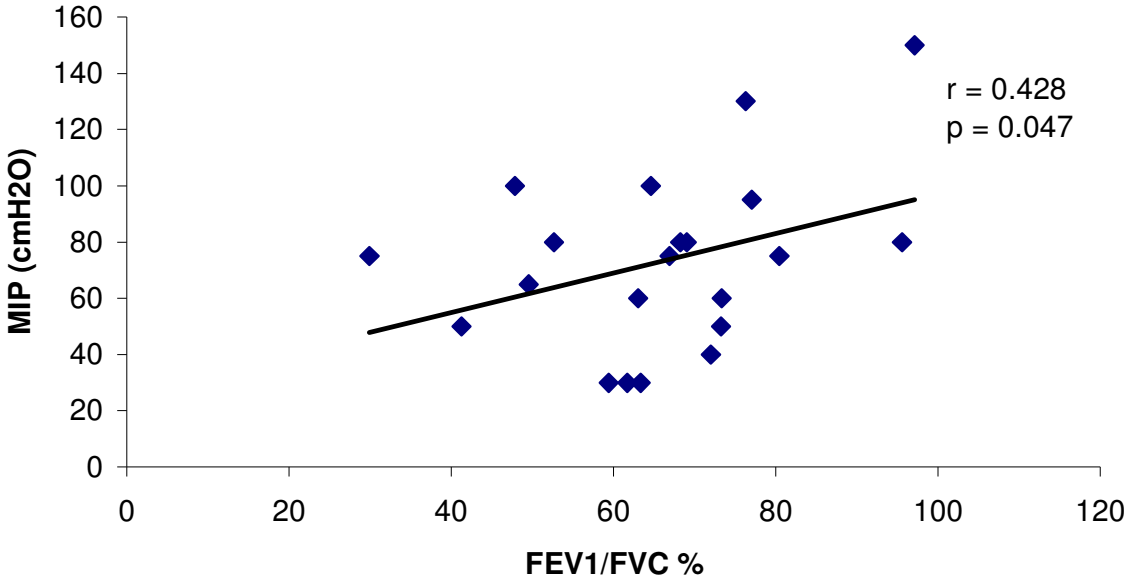

160
140
120
100
80
60
40
20
0
MIP (cmH2O)
0
20
40
60
80
100
120
FEV1/FVC %
r = 0.428
p = 0.047

**Figure 7:**

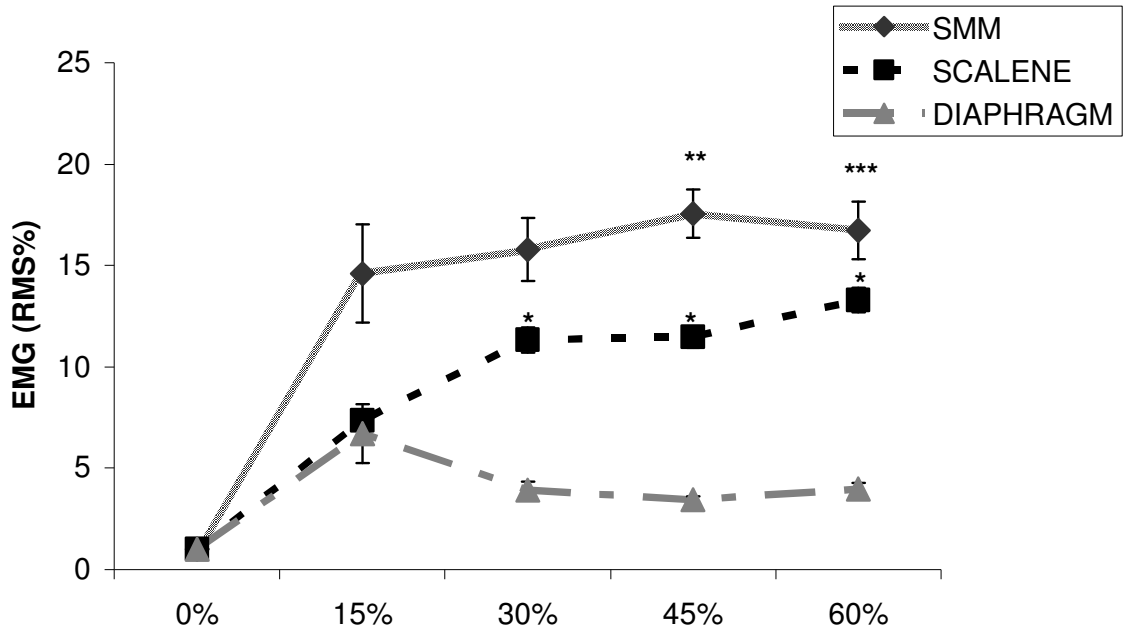
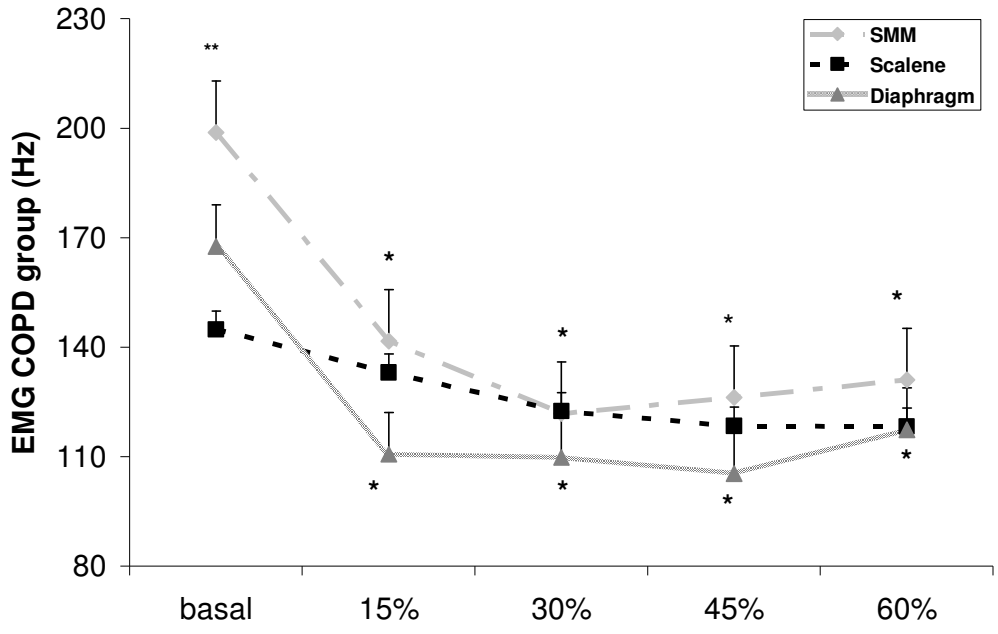


**Figure 8:**


230
200
170
140
110
80
EMG COPD group (Hz)
SMM
Scalene
Diaphragm
basal
15%
30%
45%
60%

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# Inspiratory muscular activation during threshold® therapy in elderly healthy and patients with COPD

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**Abstract**

Inspiratory muscles training in COPD is controversial not only in relation to the load level required to produce muscular conditioning effects but also in relation to the group of patients benefiting from the training. Consequently, inspiratory muscular response assessment during Threshold® therapy may help optimizing training strategy. The objective of this study was to evaluate the participation of the diaphragm and the sternocleidomastoid (SMM) muscle to overcome with a 30% Threshold® load using surface electromyography (sEMG) and to analyze the correlation between SMM activation, maximum strength level of inspiratory muscles (MIP) and obstruction degree in COPD patients ($FEV_1$). We studied seven healthy elderly subjects, mean age of $68 \pm 4$ years and seven COPD patients, $FEV_1$ $45 \pm 17\%$ of the predicted value, with mean age $66 \pm 8$ years. sEMG analysis of SMM muscles and diaphragm were obtained through RMS (root-mean-square) during three stages: pre-loading, loading and post-loading.
*Results:* In the COPD group, the RMS of the SMM increased 28% during load ($p < 0.05$) while the RMS of the diaphragm remained constant. In the elderly there was a trend of a 11% increase in diaphragm activity and of 7% in SMM activity but, without reaching significance levels. SMM activity demonstrated good correlation with the obstruction level ($r = -0.537$).
*Conclusion:* To overcome the load required by Threshold® therapy, COPD patients demonstrated an increase of accessory muscles activity, represented by SMM. For the same relative load this increase seems to be proportional to the degree of pulmonary obstruction.


*Keywords:* Electromyography; Respiratory muscles; COPD; Inspiratory muscle training

## 1. Introduction

Chronic obstructive pulmonary disease is defined as a pathology characterized by the presence of airflow obstruction due to chronic bronchitis or emphysema [4]. In patients with advanced COPD, dyspnea is reported as a limiting factor during exercise testing and as a common complaint during daily activities. In addition, studies investigating dyspnea suggest that the degree of shortness of breath subjectively reported by patients is related to the activity and strength of inspiratory muscles [15].

Respiratory muscle function is profoundly affected by COPD because of the effort increase in the act of breathing and also in muscular capacity decrease to overcome ventilation load [21]. The major problem is the adverse

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effects on the inspiratory muscles function resulting from pulmonary hyperinflation. Such hyperinflation shortens and flattens the diaphragm, altering the length of the diaphragm muscle fibers as well as their ability to produce strength [21]. In addition, it has been demonstrated in animals, in healthy humans and in COPD patients, that hyperinflation increases the demand of rib cage and neck muscles decreasing the relative contribution of the diaphragm to chest wall motion [7].

The inspiratory muscle training (IMT) increases inspiratory muscle performance thus increasing the capacity of activities tolerance [10,11]. Two methods are described in the literature for inspiratory muscles overloading: non-linear inspiratory resistive loading and linear loading through Threshold® [9]. IMT through resistive devices can alter the loading degree if any change in the breathing pattern is produced. On the other hand, Threshold® training has been recommended because of its independent flow feature and ability to maintain the same flow with different inspiratory flow rates. The Threshold® [9] IMT device is commercially available with a spring-loaded valve connected to a mouthpiece. The system's valve opens at a critical adjustable pressure and when this occurs, the system's pressure remains constant [9].

However, the efficacy of IMT in COPD patients is controversial and its clinical use limited [1]. Lisboa et al. [11], observed a walking capacity increase, dyspnea reduction, reduction of the metabolic cost of more significant sub-maximum exercises with a MIP 30% load than at a 10% load.

Various authors [10,17] have demonstrated that strength enhancement of respiratory muscles and dyspnea reduction in moderate to severe COPD patients are accomplished when load levels above 30% of the maximal inspiratory pressure (MIP) are applied. For this reason loading level specifications are essential for treatment success.

On the other hand, a study performed by Berry et al. [2] did not find additional benefits to general reconditioning exercises with IMT, neither did Smith et al. [24] who through meta-analysis suggested that the studies performed had not proven IMT to be clinically useful.

Recently, Lotters et al. [12] also through meta-analysis, have demonstrated that IMT is one of the important phases in pulmonary rehabilitation programs for CPOD and that results obtained are directly proportional to disease severity in other words, weak inspiratory muscles enhances IMT efficacy.

Several authors [11,12] have suggested that the best inspiratory muscles training system still remains to be defined. Many are the factors that may interfere in the results of different training protocols such as: load level and modulation, muscles shortening speed and respiratory pattern. Therefore, the use of different ventilation modalities could explain the still controversial results obtained from CPOD patients.

Despite the controversial points presented above, especially related to few studies correlating inspiratory muscular activity and IMT, the objectives of this study were to asses the activation pattern able to overcome with a 30% MIP equivalent load through surface EMG, to compare SMM activation against pulmonary obstruction degree ($FEV_1$) and the maximum force of inspiratory muscles (predicted MIP%).

## 2. Methods

### 2.1. Sample

Fourteen volunteers from both sexes were selected:

- Seven patients with COPD and stable clinical condition (mean age 66.4 ± 8.7 years); forced expiratory volume in one second ($FEV_1$): 45.8 ± 17.1% predicted [18]; peak expiratory flow (PEF): 59.7 ± 9.7% predicted; oxygen saturation ($SaO_2$): 93 ± 1.63%; maximal inspiratory pressure (MIP): 75.3 ± 14.4% predicted; weight: 72.9 ± 21.1 kg; height: 1.7 ± 0.1 m; body mass index (BMI): 24.8 ± 5.3; breathing rate(BR): 18.8 ± 3.0 ipm, without signs of cardiovascular, neuroendocrinal and osteomuscular diseases, and who had not undergone previous treatment (<6 months) involving physical exercises. Bronchodilator therapy in the COPD group was not interrupted during this study;
- Seven healthy elderly (mean age 68.1 ± 4.2 years; PEF: 97.3 ± 14.4% predicted [18]; $SaO_2$: 97 ± 0.1%; MIP: 104.2 ± 15.8% predicted; weight: 59.7 ± 10.6 kg; height: 1.58 ± 0.1 m; BMI: 24.2 ± 3.8; breathing rate: 14.2 ± 3.1 ipm).

This study was submitted and approved by the ethical review committee and permission from patients was obtained after a prior explanation about the research.

### 2.2. Material and methods

#### 2.2.1. First assessment

All patients were submitted to a first assessment comprising medical history, vital signal measurements and cardiopulmonary examination as follows: blood pressure measurement (Tycos® Welch Allyn Company USA-7050-14), oxygen saturation, cardiac rate (digital oximetry), breathing rate, ventilometry (Wright Respirometer Mark 8, Ferraris Medical Limited, England), peak expiratory flow (PEF) – Astech Peak Flow Meter, Center Laboratories, NY, USA, maximal inspiratory pressure (MIP) – Marshal Town Instrumentation

Industries, model MV-150 and pulmonary function test (Jones Satellite Spirometer).

PEF and MIP were taken from the best values, after three measurements with one-min interval between them. The PEF measurement was obtained from the total lung capacity (TLC), and MIP from the functional residual capacity (FRC), both with the patient seated. The pulmonary function was performed considering FVC and the $FEV_1$.

Threshold® IMT device (Fig. 1), is a commercially available lightweight clear plastic cylinder (weight, 36.4 g; diameter, 4.06 cm) with a spring-loaded valve at one end and a mouthpiece on the other. The valve blocks air flow until the patient generates sufficient inspiratory pressure to overcome the resistance provided by the spring-loaded valve. The threshold pressure is independent of airflow rate or respiratory frequency. The pressure settings are adjustable in −2 cm $H_2O$ increments (range, −7 cm $H_2O$ to −41 cm $H_2O$) [10,17].

### 2.2.2. Electromyography

Biological signals were obtained using an 8 channel module (EMG System do Brasil LTDA), consisting of a signal conditioner with a band pass filter with cut-off frequencies at 20–500 Hz, an amplifier gain of 1000× and a common mode rejection ratio >120 dB. All data were processed using specific software for acquisition and analysis (AqData), a converting plate for A/D 12 bits signal to convert analog to digital signals with a sampling frequency of anti-aliasing 2.0 kHz for each channel and an input range of 5 mV. Active bipolar superficial electrodes consist of two rectangular parallel bars of Ag/AgCl (1 cm in length, 0.2 cm in width and separated by 1 cm). These bars are coupled to a rectangular acrylic resin capsule 2.2 cm in length, 1.9 cm in width and 0.6 cm high with an internal amplifier in order to reduce the effects of electromagnetic interferences and other noises.

Electrodes were fastened to the skin where it was previously cleaned with alcohol and guided by bone prominences and the route of the muscle fibers. The electrode intended to capture electromyographical signals from the diaphragm was placed on the 7th or 8th anterior inter costal space in accordance to the best signal capture between the axillary and hemiclavicular right line. In the case of the sternocleidomastoid muscle, the electrode was placed on the muscular body, at 5 cm from the mastoid process.

The skin underlying the electrode sites was cleaned with rubbing alcohol prior to electrode placement. Also, palpation of the abdominal muscle with the subject in the testing position was used to determine electrode placement. The electrodes were then coated with a thin film of conductive gel were fixed with micropore adhesive tape at the midline of the muscle belly with their detection surface perpendicular to the muscle fibers [8,25,26,28]. In all procedures the capture and analysis of EMG signals were carried out as recommend by the International Society Electrophysiology Kinesiology (ISEK) [28].

The EMG was obtained from a completely rectified wave using a linear wrapper Butterworth filter (4th order), at a rate of 5 Hz normalized at a base of time and amplitude. EMG signals which were then compared from different muscles.

### 2.2.3. Ventilometry

Ventilometry during the loading was carried out by connecting the mouthpiece of the equipment to the same orifice where the silicone mask is adjusted, and in which the inspired tidal volume ($V_T$) and basal ventilometry is recorded. The threshold device was connected to the second orifice thus avoiding any entrance of air. Nasal clips were used during the measurements and the values were recorded according to the experimental protocol over a 1-min interval.

This study was performed on six consecutive days for each patient, with an initial phase consisting of learning and adapting to the basic procedures, and a second phase on which the data were collected.

During the recording of electromyographical signals, the volunteers were seated in a comfortable reclining chair (approximately 60°), with the arms in a resting position. The resisted breathing was carried out through a device attached to the mouthpiece providing a pre-fixed (7–41 cm $H_2O$) linear loading Threshold®, established according to the MIP previously obtained. Nasal clips were used during the threshold process.

The electromyographical signals from the muscles were recorded during 7 min on the first, fourth and sixth day, divided into three stages:

- One minute breathing through the device without the resistive membrane, resulting in a null loading. This represented the pre-loading resting period.
- Five minutes breathing with the resistive membrane through the Threshold® with loading. This represented the loading period. On the first three days, the loading was 15–20% of the MIP (learning and training period), and on the fourth and sixth days, approximately 30%.

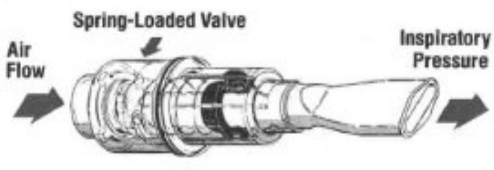


Fig. 1. The IMT device used in the study (Threshold IMT® Inspiratory Muscle Trainer).

- One minute breathing through the Threshold® without the resistive membrane, resulting in a null loading. This represented the post-loading resting period.

The oxygen saturation was measured during the experiment, and the arterial pressure was assessed at the beginning and at the end of the study.

#### 2.2.4. Data analysis

As a primary object of this study, the electromyographical signal processing was achieved by the time-domain, aiming at measuring the signal intensity during the span of muscular contraction. The data were processed using The AqData program, which does data filing, and statistical and mathematical processing.

Measurements and recordings obtained on the sixth day were used for data analysis. From the results of the program, the RMS (root-mean-square) was used to evaluate the intensity of the muscular contraction.

For the analysis, an inspiratory cycle was selected, according to the following:

- Pre-loading period: RMS values from diaphragm and sternocleidomastoid muscles were obtained from the inspiratory cycle of major amplitude in the final 10 s from 1 min recording.
- Loading period: RMS values from diaphragm and sternocleidomastoid muscles (in both groups) were obtained from the inspiratory cycle of major amplitude in the final 10 s, of the second minute, from 5 min recording.
- Post-loading period: RMS values from diaphragm and sternocleidomastoid muscles (in both groups) were obtained from the inspiratory cycle of major amplitude in the final 10 s of a 1 min recording.

Ventilometry and oxygen saturation parameters during the 30% loading were compared to the recorded values at the initial evaluation.

For a comparative analysis between muscles and individuals, normalization of the electromyographical signal amplitude was calculated for the RMS values by converting absolute (liable to constitutional interferences) into relative values.

A 100% reference value was calculated. This reference value was the pre-loading resting, which was considered to be a value of 1. Values during the loading period resulted from the mathematical ratio between the absolute values of the loading period value and the absolute values of the pre-loading period. The post-loading values were obtained from the mathematical ratio between the absolute values of the post-loading period and those of the referential pre-loading period.

Results from RMS values greater than 1 represented an increase in muscle activity and values lower than 1 represented a decrease in muscle activity.

### 2.3. Statistical analysis

Data analysis was carried out using a non-parametric test with independent samples of Mann–Whitney to compare groups (COPD/elderly), and the Wilcoxon Test in the paired measurements (relation between loading period × pre-loading period, and post-loading period × pre-loading period). All tests were analyzed with a significance level of 95% ($p < 0.05$). The software used was the SPSS, version 8.0.

## 3. Results

### 3.1. Ventilometry and oxymetry

Comparisons were made between the loading period and basal values of initial assessment (mean ± SD). Breathing rate (BR) demonstrated a significant reduction ($p = 0.018$) with the mean frequency being reduced from 18.9 to 14 bpm. Tidal volume increase from 584.1 to 960.1 ml ($p = 0.018$). Minute volume increased from 10.9 to 12.7 l/min, but without reaching significance levels ($p = 0.168$), as shown in Table 1.

The load effect in the $O_2$ saturation, studied in both groups, showed a significant increase. In the COPD group $O_2$ mean saturation ranged from 93% to 97.1% ($p = 0.017$), in the elderly group $O_2$ saturation ranged from 96.6% to 98.1% ($p = 0.016$) as shown in Fig. 2.

Table 1
Variation between breathing rate (BR), tidal volume ($V_T$) and minute volume (MV) when compared to rest basal values and to the loading period in the COPD group

| | Basal value | With loading (30% MIP) |
|---|---|---|
| Breathing rate (ipm) | 18.9 | 14[a] |
| Tidal volume (ml) | 584.1 | 960.1[a] |
| Minute volume (L/min) | 10.9 | 12.7 |

[a] $p < 0.05$.

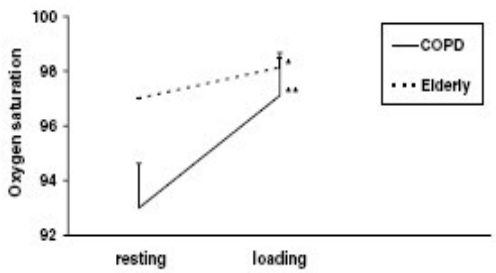


Fig. 2. Oxygen saturation (mean ± SD) in the COPD and elderly groups during loading compared to basal resting period (*$p < 0.05$).

### 3.2. Sternocleidomastoid and diaphragm activity analysis

Sternocleidomastoid activity represented by RMS value, as shown in Fig. 3, indicated a increase of 28% ($p = 0.04$) during the loading period in the COPD group. In the elderly group there was a tendency of a 7% increment but, without reaching the significance level ($p = 0.09$). Post-loading muscular activity in the COPD group tended to remain high, but in the elderly group post-loading activity was reduced in 10% ($p = 0.027$). The Fig. 4 shows the pattern of electric of the SMM in the COPD group.

Diaphragmatic activity in the elderly group, considering the relative RMS value in the pre-loading period indicated an increase tendency of 11% during the loading period ($p = 0.149$) and reduction of 12% during post-loading ($p = 0.390$). Nevertheless, no statistical significance was established. In the CPOD group there was no significant variation during the loading and post-loading period, as shown in Fig. 5. Fig. 6 shows the pattern of electric of the diaphragm in the elderly group.

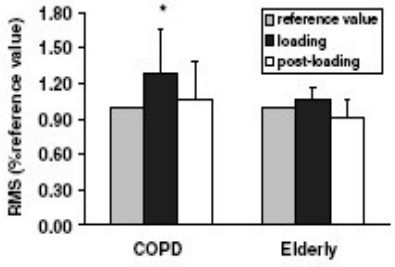


Fig. 3. Sternocleidomastoid activity measured by the RMS (% reference value) in the COPD group and in the elderly group during loading and post-loading periods (*$p < 0.05$).

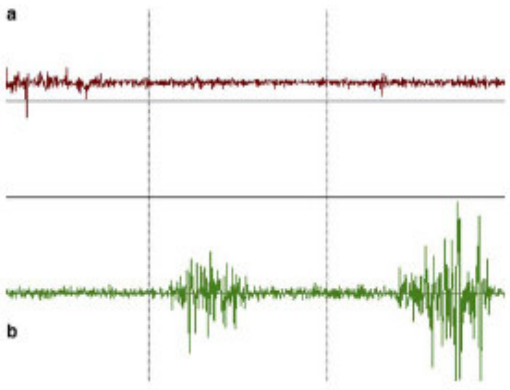


Fig. 4. EMG recordings of sternocleidomastoid muscle in COPD patient during (a) pre-loading and (b) loading periods using Threshold® therapy (load 30% maximal inspiratory pressure).

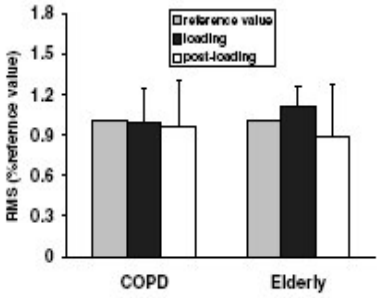


Fig. 5. Diaphragm activity measured by the RMS (% reference value) value in the CPOD group and in the elderly group during loading and post-loading.

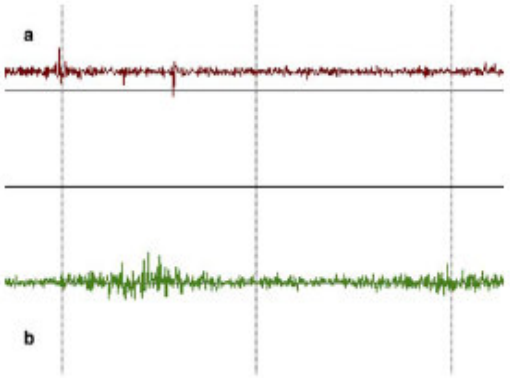


Fig. 6. EMG recordings of diaphragm muscle in healthy elderly during (a) pre-loading and (b) loading periods using Threshold® therapy (load 30% maximal inspiratory pressure).

#### 3.2.1. Comparison between the RMS value of the sternocleidomastoid muscle during loading and spirometric index $VEF_1$ in the COPD group

Through correlation analysis between the RMS value of the sternocleidomastoid muscle during loading, and spirometric index $VEF_1$, an inverse correlation tendency was noted considering that sternocleidomastoid muscle activity was higher in patients with lower $VEF_1$ ($r = -0.537$, $p = 0.214$), as shown in Fig. 7.

#### 3.2.2. Comparison between the RMS value of the sternocleidomastoid muscle during loading and MIP force index (predicted %) in the COPD and elderly groups

Through correlation analysis between the RMS value of the sternocleidomastoid muscle during loading and the level of MIP force (predicted %) no correlation was established between muscular activity in response to the applied load and the level of basal force of CPOD patients and elderly subjects ($r = -0.013$, $p = 0.965$).

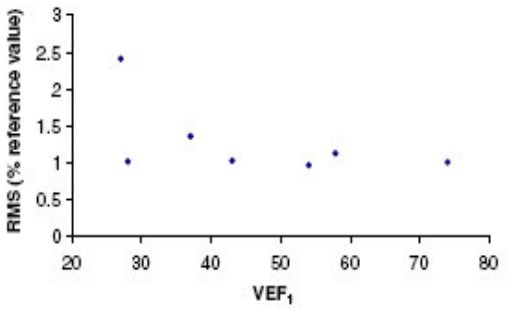


Fig. 7. Correlation between sternocleidomastoid muscular activity during loading indicated by the RMS(root mean square) value and $VEF_1$ spirometric index in COPD patients ($r = -0.537$, $p = 0.214$).

## 4. Discussion

### 4.1. Inspiratory muscular activity in response to IMT through Threshold

This study suggests that to overcome with the Treshhold® load there is an increase in inspiratory muscles activity. In CPOD patients, this increase occurs predominantly in the accessory muscles as in the sternocleidomastoid (SMM) muscle. In elderly subjects there is participation of the diaphragm and SMM.

The results indicate that the sternocleidomastoid muscle is the principal muscle responsible for the response to Threshold® load in CPOD patients because while its activity showed a 28% increase, diaphragm activity remained practically constant. In the elderly group, load response was present not only in the sternocleidomastoid muscle but in the diaphragm as well, with increments of 7% and 11%, respectively, therefore, demonstrating a higher tendency of diaphragm activation.

In healthy individuals the diaphragm is responsible for 60–70% of the tidal volume during rest and diaphragm activation occurs only in adverse conditions [29], but in individuals with CPOD, pulmonary hyperventilation, a characteristic of the condition, affects the force generating ability of the diaphragm due to shortening and loss of contractile elements [1,5,29].

Some studies [13,14] have reported increased activity of accessory muscles in COPD patients during both rest and exercises. Mananas et al. [14] in a electromyography study reported that in normal individuals the sternocleidomastoid muscle is active only when high ventilation levels are required. Nevertheless, in COPD patients the activity of this muscle plays an important role in the respiratory function including respiration at low flow rates [14].

According to different studies [5,6,14] there is no consensus related to the SMM activity during rest. In opposition to Mananas assumption, De Troyer et al. [6] while studying accessory muscles activation in the COPD condition, were unable to find evidence of SMM inspiratory activity during rest. They further suggested that this muscle has a high activation threshold and activation is restricted to respiratory deficiency or severe muscular weakness.

Another possible theory to explain prevalent SMM activation in relation to the non-additional increment of diaphragmatic activity in patients with COPD may be related to the respiratory drive increase present during rest to overcome the intrinsic load of the respiratory system. As noted by De Trover [5] through needle electrodes inserted in the costal diaphragm a frequency of $17.9 \pm 4.3$ Hz in normal subjects was registered, representing a respiratory drive increment in individuals with COPD. Although the technique employed may be different from the one we used, which could limit our comparison, we suggest that individuals with CPOD already had increased inspiratory muscle activity during rest.

Still related to diaphragm activity, Sinderby et al. [23] studying voluntary diaphragm activation noted that healthy individuals breathed at 8% of maximal RMS, while CPOD patients breathed at 43% without additional gain in generating pressure which corroborates our suggestions that the diaphragmatic activity of individuals with CPOD is already increased during rest.

Therefore, data suggest that to overcome the obstructive component and mechanical disadvantage the diaphragm of CPOD patients requires high activation levels which are already there even during rest. This is certainly in agreement with the data of this study indicating that the diaphragm does not change contraction intensity as reflected by the RMS value in order to overcome the additional load of the Threshold®.

### 4.2. Relation between SMM activity, obstruction level and predicted MIP%

Lotters et al. [12] in recent meta-analysis suggested that in addition to training, strategy differences and methodological characteristics of patients such as the degree of hyperventilation, airways obstruction severity and weakness of the respiratory tract could influence IMT [12]. This study demonstrates an initial divergence in the comparison of CPOD patients' muscular activities who showed different muscular recruitment levels notwithstanding the use of the same training load (30% MIP equivalent load). $VEF_1$ is a spirometric parameter related to the degree of COPD severity: a low percentage value of the $VEF_1$ parameter corresponds to a high obstruction level. In our study, correlation analysis demonstrated an inverse tendency: SMM muscular activation of the RMS value was higher in patients with lower $VEF_1$.

Other studies [6,13,14] were performed equally comparing SMM activity during rest and during increasing

loads with the obstruction level ($VEF_1$) in adults and children, indicating an increase of muscular activity according to the obstruction degree. The obstruction component of the patients associated to the loss of elastic recoil results in pulmonary hyperventilation. Larson et al. [10] in their study related to ITM with MIP loads ranging from 15% to 30% noted that in patients using MIP loads at 30%, RFC was positively associated to increased exercise tolerance. This is suggestive that hyperinflation factors could influence the results in patients undergoing IMT [10]. They further suggest more research to determine what group of patients could benefit from the program [10].

SMM activation values were compared with the predicted MIP% and with the obstruction level obtained through $FEV_1$ with the purpose of studying the current training strategy. However, no significant correlation was determined. The recommendation is that the current strategy should consider not only the MIP but also the obstruction level of each patient.

### 4.3. Assessment through surface EMG

The absolute value of the sEMG signal suffers the effects of constitutional individual variables and different muscles therefore, offering poor comparison information [3,22]. One of the ways of compensating this constraint is to normalize EMG curves amplitude to take into account the study of individual differences. This technique consists in turning absolute values into relative values using a reference EMG considered at 100% [3,22].

There are different ways of determining the reference value [3,22]: maximum voluntary isometric contraction using the highest activity peak found during various repetitions of what is to be compared, with the rest signal, among others. In our study, we used the preload value as the 100% reference.

sEMG was used in our study because it is a non-invasive method reflecting muscular activity of the large surface muscles through the time and space adding of motor unit signals [7,16,19,20]. Nevertheless, EMG analysis and interpretation can be easily misled by non-physiological signals, ECG signals or by signals of adjacent muscles [23]. The interference from ECG signals was attenuated by placing electrodes in the right hemithorax, moreover our objective was not quantitative analysis of muscular activity but to assess this activity during loading proportionally to the period without loading. Therefore, in our opinion this was not a constraining factor to the study.

Interference of the abdominal and intercostal muscles can be detected by diaphragm sEMG due to its deep location [23]. Interference of intercostal muscles can be minimized by changing electrodes position considering that intercostal inspiratory action is stronger in the superior dorsal regional of the rib cage. In other words, the action of intercostal and abdominal muscles adjacent to the electrodes is predominantly expiratory and considering that the diaphragm is an inspiratory muscle this interference should be minimal.

### 4.4. Ventilometry and oximetry response to Threshold® load

In addition to the electromyography study we evaluated oxygen saturation and ventilometry. Ventilometry analysis during loading was performed in COPD subjects and resulted in small MV variation, $V_T$ increase and BR decrease. Respiratory response to linear inspiratory loads has been studied by various authors. A significant increase of MV and in $V_T$ with practically constant BR has been demonstrated which is suggestive of load induced hyperventilation [29].

It is also well known that the introduction of a mouthpiece together with the load changes the respiratory pattern responsible for the $V_T$ and EMG of the sternocleidomastoid muscle [6,29]. That is why, to avoid this, registration of electromyography activity during rest, pre-loading and post-loading was accomplished with the Threshold® without the resistive membrane. Thus, only the effect of the load itself was assessed.

Increased $O_2$ saturation parameter was noted in both groups, but it returned to basal levels when the device was removed. In a different study with the same device, during an incremental test, there was a proportional increase of $O_2$ saturation returning to rest following interruption [10].

According to the properties of the Hemoglobin dissociation curve, an induced $CO_2$ reduction by hyperpnoea, for example, results in a curve deviation to the left, that is, there is an increase of hemoglobin affinity caused by $O_2$ which is related to saturation increase during Threshold® considering it was followed by tidal volume increase [27].

## 5. Conclusion

This study suggests that to overcome with the Threshold® load there is an increase of inspiratory muscles activity. In COPD patients this increase occurs principally in the accessory muscles represented by SMM. We have also noted that the activation level increases according to the obstruction degree. Nevertheless, no significant correlation between activation levels and individual force (MIP) was found. At last, it is our suggestion that obstruction level and muscular recruiting in response to the load should be considered when planning inspiratory muscles training strategies.

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# Inspiratory muscle endurance testing: Pulmonary ventilation and electromyographic analysis

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**Abstract**

This study analyzed regional pulmonary ventilation and electromyographic (EMG) activity of the respiratory muscles during an inspiratory muscle endurance (IME) test in 10 young women. Radioaerosol (99mTc-DTPA) was generated using a jet nebulizer connected to a linear inspiratory loading system. The lung scintigraphic analysis showed an increase in the radioaerosol deposition using loads of 20 and 30 $cmH_2O$ ($p < 0.01$). The vertical gradient showed a larger radioaerosol deposition in the medium third of the lungs during the control period ($p < 0.001$). There were larger amounts of radioaerosol deposition in the medium third when compared with the upper and lower third at 30 $cmH_2O$ ($p < 0.001$). The horizontal gradient showed a larger deposition in the intermediate and central segments during all phases ($p < 0.00$). Electromyographic activity from the muscles of the lower rib cage increased with loads of 20 and 30 $cmH_2O$ ($p < 0.03$). There was an increase in deposition of radioaerosol when the load increased ($r = 0.584$, $p = 0.000$ for the left lung and $r = 0.609$, $p = 0.000$ for right lung). These findings suggest that during the IME test, EMG activity in the muscles of the lower rib cage increase during progressive respiratory workloads is associated with a greater radioaerosol deposition in the medium third and intermediate and central segments of the lungs.


*Keywords:* Respiratory function; Respiratory muscles; Pulmonary ventilation; Electromyography

## 1. Introduction

Regional pulmonary ventilation has been observed to be a function of regional pulmonary compliance (Alderson and Line, 1980), respiratory rate (Chamberlain et al., 1983), ventilatory pattern and a subject's posture (Nield et al., 2003; Roussos and Macklem, 1982; Takahashi et al., 2005). During physical exercise or episodes of respiratory obstruction, the inspiratory muscles must overcome resistive loads to maintain ventilation (Wells et al., 2005). Optimal pulmonary ventilation depends on the efficiency of the breathing muscles, which work to overcome the elasticity of the lungs and rib cage and the resistance to flow from the airways. These resistive loads can lead to respiratory muscular fatigue (Yan and Kayser, 1997; Chen and Yan, 1999).

The strength and endurance of the inspiratory muscles have been measured using several different methods. Strength can be assessed by measuring maximal inspiratory pressure through manovacuometry (Bruschi et al., 1992; Eastwood et al., 2001). Inspiratory muscle endurance (IME) is often measured as the duration an inspiratory resistive load can be maintained (Eastwood et al., 2001; Lotters et al., 2002). Using the webbight plunger principle proposed by Nickerson and Keens (1982). Martyn et al. (1987) developed an incremental threshold loading (ITL) protocol as an endurance test for the inspiratory muscles. The technique has the advantage of not being affected by changes in the breathing rate and offers the same results when used with different groups of individuals (McElvaney et al., 1989; Nickerson and Keens, 1982).

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Based upon the weight plunger principle, Larson et al. (1988) developed a spring-load valve to evaluate and strengthen the inspiratory muscles of patients suffering from chronic obstructive pulmonary disease (COPD). Johnson et al. (1996) evaluated the spring-load valve during inspiratory muscle training and compared it to the weighted plunger method and found no significant difference between the two systems. A protocol for the IME test was proposed based on the use of standard pressure increments (Johnson et al., 1997).

Currently, it is unknown how regional pulmonary ventilation behaves in a situation of ITL and which respiratory muscles are active during IME testing. The aim of this present study was to analyse the regional pulmonary ventilation and electrical activity of the respiratory muscles in normal individuals during an IME test.

## 2. Methods

### 2.1. Subjects

A sample of convenience of 10 apparently healthy female volunteers were recruited for the study (mean age of $25.3 \pm 1.4$ years, weight of $54.9 \pm 7.2$ kg and height of $1.62 \pm 0.08$ m). Exclusion criteria were: history of smoking or respiratory problems, pregnancy, breathing rate >20 bpm, heart rate <50 or >100 bpm, oxygen saturation ($SpO_2$) ≤90%, maximal inspiratory pressure ≤50 $cmH_2O$, $V_t \leq 6$ ml/kg, or forced vital capacity FVC < 81% and forced expiratory volume on the first second $FEV_1$ < 85% of predicted values. The protocol was approved by the Ethical Committee from and all the subjects gave written informed consent.

### 2.2. Experimental procedure

Each subject was examined at three different occasions: the initial evaluation included obtaining measurements of resting pulmonary function, respiratory muscle function, oxygen saturation, and heart rate. In addition to this, a pulmonary scintigraph exam was performed during the second visit and a respiratory EMG activity was performed during the IME test (last day). The remaining examination included the measurement of electromyography (EMG) and was performed 1 day after the pulmonary scintigraph.

#### 2.2.1. Preliminary tests at rest

Maximal inspiratory pressure (MIP) was obtained using a manovacuometer model MV-150 (Marshall-Town Instrumentation Industries) according to the Black and Hyatt protocol (1969).

Minute ventilation (tidal volume × breathing rate) was verified through the Wright Respirometer MARK 8 (Ferraris Medical Limited, Middlesex, England) ventilometer model, and spirometry was performed with the Jones Satellite Spirometer (Jones Medical Instruments Company, IL, USA). The oxygen saturation (Sat%O2) and heart rate (HR) were verified through the pulse oximeter (Moriya 1001, J.G. Moriya, Ind. Com. de Equip. Médicos Hosp. LTDA, SP, BR).

#### 2.2.2. Pulmonary scintigraph examination during incremental threshold loading

The pulmonary scintigraph examination was carried out using the jet nebuliser for radioisotopes Venticis II (Ventibox/CIS Bio International, France) coupled to the linear respiratory loading system—spring-load valve (Threshold® IMT, Healthscan Products Inc., NJ, USA). The scintigraph record was taken by the Vertex-dual (Head/ADAC Labor) gamma camera model at $128 \times 128 \times 16$, in the posterior incidence. Only posterior lung images were analyzed due to the fact that the posterior lung received the major portion of radioaerosol during inhalation and because other lung images could be contaminated by stomach activity.

The pulmonary scintigraph procedure was performed with the volunteer in a sitting position and wearing a noseclip. The volunteers sat for 20 min prior to testing and were advised to not alter their breathing pattern and were asked to breathe comfortably through the ITL system (Threshold® spring-load valve). The Threshold® device consists of a spring-loaded valve that blocks airflow until the subject generates sufficient inspiratory pressure to overcome the resistance provided by the spring-loaded valve.

The volunteers breathed through the apparatus for 16 min and scintigraphic images were taken every 4 min. The 16 min ITL duration was used to optimize scintigraphic analyses. The images were considered as independent stages of the experiment. The first image was considered as the volunteer's control image—zero load (control phase). In this image, the volunteers breathed through the same system, but the spring-load valve membrane which controls the loading from this apparatus was inverted to prevent respiratory loading.

After the control phase the resistance of the spring-load valve was incrementally increased every 4 min to 10, 20 and 30 $cmH_2O$. A brief apneusis period was experienced by each subject during the incremental adjustment of the resistance when a pre-fastened spring-load valve was exchanged and coupled quickly to the system. The breathing rate, heart rate and oxygen saturation were recorded each minute during this procedure.

The subsequent images from each lung were analyzed during the control phase and during the three levels of respiratory loading. The first image obtained at 4 min of respiration was the individual's control image (zero load). The three images generated after 8, 12 and 16 min with loads of 10, 20 and 30 $cmH_2O$, respectively, were treated by the method of image subtraction.

Three vertical (upper, middle, lower) and three horizontal (central, intermediate and peripheral) regions of interest (ROI) were drawn for each lung, as illustrated in Fig. 1(A) and (B), respectively, following the protocol described by Chamberlain et al. (1983), Graham et al. (1990) and Franca et al. (2006). A comparison between pulmonary deposition in each lung was taken considering the number of counts (pixels) captured by the scintigraphy camera in each ROI.

#### 2.2.3. Respiratory muscle activity by EMG surface

The EMG was obtained under the same experimental conditions (the day after pulmonary scintigraph exam) with the volunteers repeating the test of incremental loading and

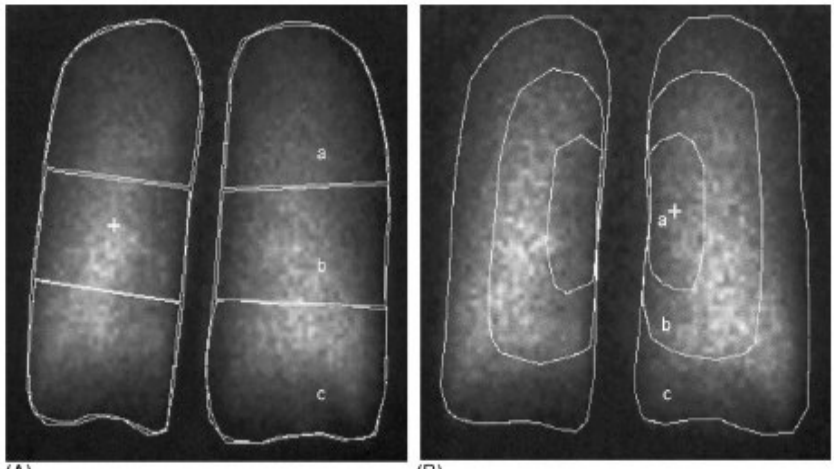


Fig. 1. Pulmonary deposition of radioaerosol in control phase (posterior incidence). Delimitation of the regions of interest (ROIs). (A) By strata (vertical gradient): upper (a), medium (b) and lower (c) thirds, and (B) by segments (horizontal gradient): central (a), intermediate (b) and peripheral (c) regions.

undergoing an analysis of the inspiratory muscle activity during and after the test (1 min of breathing through the Threshold® without loading which represented the recovery phase).

Electromyography: Biological signals were obtained using an eight channel module (EMG System do Brasil LTDA), consisting of a signal conditioner with a band pass filter with cut-off frequencies at 20–500 Hz, an amplifier gain of ×1000 and a common mode rejection ratio >120 dB. All data were processed using specific software for acquisition and analysis (AqData), a converting plate for A/D 12 bits signal to convert analog to digital signals with a sampling frequency of anti-aliasing 2.0 kHz for each channel and an input range of 5 mV. Active bipolar superficial electrodes consisting of two rectangular parallel bars of Ag/AgCl (1 cm in length, 0.2 cm in width and separated by 1 cm) were used and were coupled to a rectangular acrylic resin capsule 2.2 cm in length, 1.9 cm in width and 0.6 cm high with an internal amplifier in order to reduce the effects of electromagnetic interference and other noise.

Electrodes were fastened to the skin where it was previously cleaned with alcohol and guided by bone prominences and the route of the muscle fibers. The EMG activity was measured in the upper and lower parts of the thorax following the protocol described by Dornelas de Andrade et al. (2005). The sternocleidomastoid was used to evaluate the performance from the superior rib cage and the electrode was placed on the muscular body, at 5 cm from the mastoid process. The electrode intended to capture electromyographical signals from the lower parts of the thorax was placed on the 7th or 8th anterior intercostal space in accordance to the best signal capture between the axillary and hemiclavicular right line. In all procedures the capture and analysis of EMG signals were carried out as recommend by the International Society Electrophysiology Kinesiology (ISEK) (Solomonow, 1995; Williams, 1987).

The EMG was obtained from a completely rectified wave using a linear wrapper Butterworth filter (4th order), at a rate of 5 Hz normalized at a base of time and amplitude. EMG signals were then compared from different muscles. The electrical activity was measured using the root mean square (RMS) values.

### 2.3. Statistical analysis

The data were coded and stored using statistics Stat software and analyzed by ANOVA and the Tukey HSD post hoc test. A $p$-value of less than 0.05 was considered to be statistically significant. Results are given as the mean ± standard deviation.

To analyze radioaerosol deposition, the lung segments were independently compared with each other during each phase.

## 3. Results

Table 1 shows the anthropometric parameters, MIP and TV from the 10 volunteers. Two of the subjects presented with a discreet reduction in the forced vital capacity (FVC) with 75% of the spirometrical value predicted for both. Three volunteers

Table 1
Characteristics antropometrics and spirometrics

| Variable | Mean (±S.D.) |
|---|---|
| Age (years) | 25.3 ± 1.4 |
| Height (cm) | 54.9 ± 7.2 |
| Weight (kg) | 1.6 ± 0.08 |
| BMI | 21.5 ± 2.2 |
| MIP ($cmH_2O$) | 85.7 ± 12.9 |
| $V_t$ (ml) | 511 ± 114.2 |
| BR (ipm) | 18.9 ± 5.4 |
| $SpO_2$ (%) | 97.6 ± 0.6 |
| FVC (% predicted) | 95 ± 11 |
| $FEV_1$ (% predicted) | 94 ± 10.5 |
| PEF (l/s) | 412 ± 81 |

Data are expressed in mean ± S.D. BMI: body mass index; maximal inspiratory pressure (MIP); tidal volume ($V_t$); breath rate (BR); FVC: forced vital capacity; $FEV_1$: forced expiratory volume in the first second; PEF: peak expiratory flow. FVC and $FEV_1$ are expressed as percentage of predicted values.

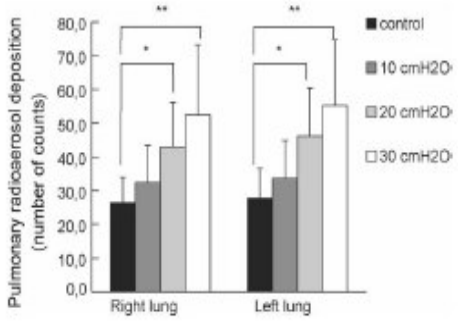


Fig. 2. Pulmonary radioaerosol deposition (number of counts—mean ± S.D.) in both lungs in the control phase (zero load) and with 10, 20 and 30 $cmH_2O$ loads ($^{*}p < 0.01$ and $^{**}p < 0.001$).

were unable to breathe at 30 $cmH_2O$ load due to fatigue, and stopped the IME test in the 12th min.

### 3.1. Respiratory rate, heart rate and oxygen saturation

Breathing rate in the control phase was of (18.9 ± 5.4 breaths/min) and decreased during the incremental 20 and 30 $cmH_2O$ loadings (14.9 ± 2.2 and 15.5 ± 3.2 breaths/min, respectively, $p = 0.03$) and remained lower during the recovery phase (16.4 ± 2.7 breaths/min). However, there was no difference between the control (zero load) and the recovery phases.

For the oxygen saturation, we observed a slight decrease during ITL, but the decrease was not significant. There was no significant difference in heart rate between the ITL phases.

### 3.2. Radioaerosol deposition

The analysis of the radioaerosol deposition in both the right and left whole lungs indicated a higher proportion of deposition at 20 cm ($p < 0.01$) and 30 cm ($p < 0.001$) $H_2O$ load increments than either at the control (zero load) or the 10 $cmH_2O$ loads. No statistically significant differences were found among the lungs (Fig. 2).

The vertical gradient of radioaerosol deposition for the right lung showed the middle third with a greater radioaerosol deposition (30.87 ± 5.68, 42.01 ± 7.65, 55.21 ± 11.46 and 72.82 ± 17.51 for the control, 10, 20 and 30 $cmH_2O$ loads, respectively) when compared with the upper third (22.81 ± 4.39, 26.81 ± 7.0, 35.58 ± 4.17 and 41.28 ± 12.1 for the control, 10, 20 and 30 $cmH_2O$ loads, respectively) for all phases ($p < 0.05$ for the control phase and $p < 0.001$ for the other phases). When compared with the lower third the same deposition was found, except at the 30 $cmH_2O$ load, in which the middle third presented a larger deposition (72.82 ± 17.51 for the middle third and 43.37 ± 17.02 for the lower third, with $p < 0.001$), as shown in Fig. 3(A)).

For the left lung, the radioaerosol deposition was homogeneous in the control phase. During the increasing workload increments, the medium third presented with a larger radioaerosol deposition (43.21 ± 9.72, 59.28 ± 14.02 and 72.65 ± 16.59 for the 10, 20 and 30 $cmH_2O$ loads, respectively) when compared to the upper third (28.04 ± 7.59 for the 10 $cmH_2O$ load with $p < 0.02$ and 38.71 ± 7.62 and 43.95 ± 11.63 for the 20 and 30 $cmH_2O$ loads, respectively, with $p < 0.001$). When compared to the lower third, the same deposition was found, except at the 30 $cmH_2O$ load, in which the medium third presented a larger radioaerosol deposition (72.65 ± 16.5951 for the middle third and 49.44 ± 17.07 for the lower third with $p < 0.02$) as shown in Fig. 3(B).

The horizontal gradient for the right lung showed a larger radioaerosol deposition in the intermediate (34.48 ± 7.43, 46.97 ± 10.75, 62.95 ± 13.66 and 74.92 ± 19.31 for the control, 10, 20 and 30 $cmH_2O$ loads, respectively) and central segments (33.45 ± 5.52, 45.51 ± 9.43, 57.68 ± 7.76 and 76.81 ± 18.52 for the control, 10, 20 and 30 $cmH_2O$ loads, respectively), compared with the peripheral segment (17.41 ± 5.57, 20.62 ± 8.48,

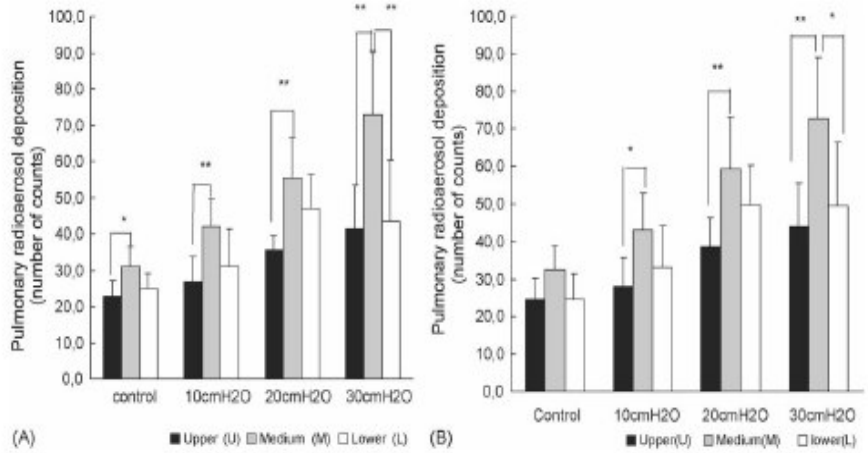


Fig. 3. Pulmonary radioaerosol deposition (number of counts—mean ± S.D.) in the right lung (A) and left lung (B) when considering the division of the lung in the vertical gradient, for the upper, medium and lower thirds in the control phase (zero load) and with 10, 20 and 30 $cmH_2O$ loadings ($^{*}p < 0.05$, $^{**}p < 0.02$ and $^{***}p < 0.001$).

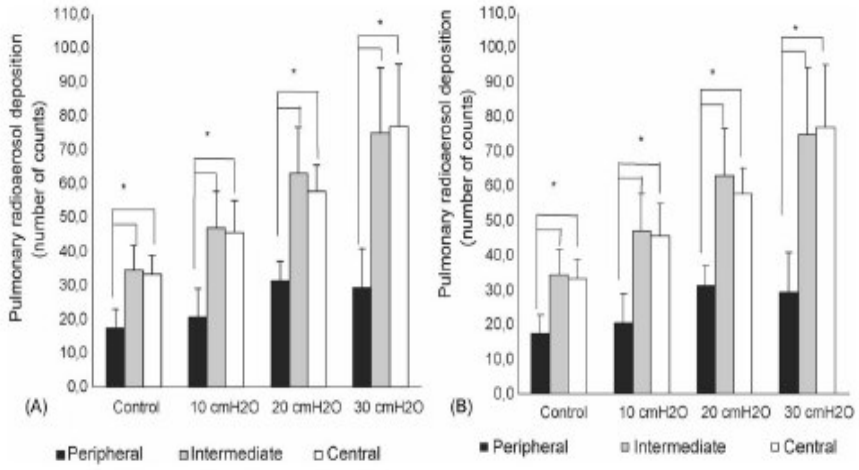


Fig. 4. Pulmonary radioaerosol deposition (number of counts—mean ± S.D.) in the right lung (A) and left lung (B), when considering the division of the lung segments into the horizontal gradient, for the cortical, intermediate and central segments, in the control phase (zero load) and with 10, 20 and 30 $cmH_2O$ loads ($^*p < 0.001$).

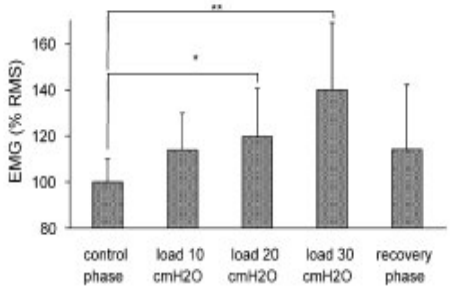


Fig. 5. Electromyographic activity of the lower rib cage muscles. Values in root mean square (RMS) ±S.D. in the control phase (zero load) and with 10, 20 and 30 $cmH_2O$ loads. It has been observed a significant increase in the electric activity for the incremental 20 $cmH_2O$ ($^*p < 0.02$) and 30 $cmH_2O$ ($^{**}p < 0.03$) loads in relation to the control phase.

$31.30 \pm 5.94$ and $29.34 \pm 11.59$ for the control, 10, 20 and 30 $cmH_2O$ loads, respectively, with $p < 0.001$), was observed during all phases of the IME test (Fig. 4(A)). The left lung had a larger deposition in the intermediate and central segments ($p < 0.001$), without a significant difference between the two, during all phases of the test. This behavior was similar to the one presented in the right lung (Fig. 4(B)).

### 3.3. Surface EMG

The electromyographic analysis of the superior rib cage, for the sternocleidomastoid, did not find a significant difference among the control phase ($11.8 \pm 1.31$) and the loaded or recovery phases ($13.5 \pm 2.70$, $14.2 \pm 2.9$, $16.6 \pm 5.9$, and $13.5 \pm 3.5$ for 10, 20 and 30 $cmH_2O$, and the recovery phases, respectively).

The electromyographic analysis of the lower rib cage muscles showed a significant increase in electrical activity during the 20 $cmH_2O$ ($9.7 \pm 3.9$, with $p = 0.02$) and 30 $cmH_2O$ ($10.0 \pm 2.7$, with $p = 0.03$) incremental loads, compared to the control phase, without a load ($4.6 \pm 1.4$) (Fig. 5).

Fig. 6(A) and (B) show correlation between load and pulmonary deposition of radioaerosol. There was an increase in deposition of radioaerosol when the load increased ($r = 0.584$, $p = 0.000$ for the left lung and $r = 0.609$, $p = 0.000$ for right lung).

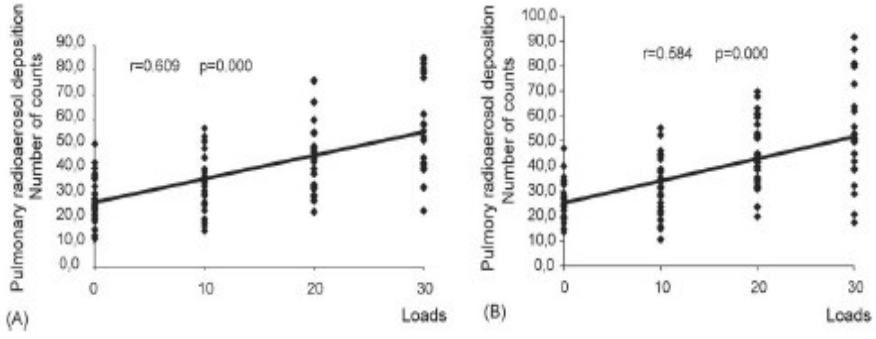


Fig. 6. Correlation between loads and pulmonary deposition of radioaerosol. There was a correlation between deposition of radioaerosol and loads ($r = 0.609$, $p = 0.000$ for right lung (A) and $r = 0.584$, $p = 0.000$ for the left lung (B)).

## 4. Discussion

We have found that during the test of IME using a test of ITL that the breathing rate decreased with accompanying changes in the activity of the respiratory muscles that likely occured to minimize ventilatory work. We observed an increase in EMG activity in the muscles of the lower rib cage during progressive respiratory workloads that is associated with a greater radioaerosol deposition in medium third and intermediate and central segments in both lungs.

Loads imposed on the respiratory muscles are commonly used in the evaluation of endurance and for respiratory muscle training (Klefbeck and Hamrah, 2003; Nield, 1999). Using a spring-loaded valve, Bardsley et al. (1993) evaluated the endurance of the inspiratory muscles with increasing workloads and showed that the test was not influenced by the ventilatory pattern. Larson et al. (1999) used ITL in patients with COPD and found moderate breathing difficulty with a decrease in the tidal volume and increase in the breathing rate that was needed to complete the final stage of the test. The ITL in this study was observed to be reproducible for the evaluation of respiratory muscle endurance.

Eastwood et al. (2001) investigated the effects of incremental resistance breathing in athletes and sedentary individuals and verified that during progressive ITL, both groups maintained a low breathing rate, high tidal volume and an extended inspiration and expiration time. They also observed a decrease in arterial oxygen saturation at the maximum loads. The efficiency of the breathing muscles was found to be similar for both groups.

Under normal conditions the additional expenditure of oxygen can be ascribed to the metabolism of the respiratory muscles. During breathing with increasing resistive loads, the demand for oxygen is progressively increased, due to the increase in respiratory work (Roussos and Macklem, 1982; Kyroussis et al., 2000; Polkey et al., 1997). Our study of apparently healthy females found a slight decrease in the hemoglobin saturation during ITL at 20 and 30 $cmH_2O$ loads, but without reaching significance levels. This finding is suggestive of greater metabolic activity of the breathing muscles. Indeed, the greater metabolic activity has been substantiated by surface EMG analysis, in which an increase in the muscle activity of the lower rib cage was recorded for the last two loads. Future studies of pulse oximetry and EMG analysis during ITL should be performed in patients with lung disease to better understand the changes in oxygen saturation and EMG activity during ITL in various forms of lung disease.

In our study, three volunteers were unable to maintain the airflow during the 30 $cmH_2O$ inspiratory loads due to respiratory muscular fatigue and the muscle's incapacity to exert force under load. Roussos and Macklem (1982), working with non-linear inhale resistive loads, demonstrated that the breathing muscles become fatigued when exceeding the critical level of energy consumption. However, the muscles are often coordinated to avoid this fatigue. Roussos and Macklem (1982) found that the inability to continue breathing during an IME test is related to hypoxemia and subsequent respiratory muscle fatigue.

The topographical distribution of lung ventilation has been attributed mainly to the vertical gradient of the existing pleural pressure between the upper and lower portions of the lungs (West, 1990). Many factors influence ventilation distribution (Medeiros et al., 1994; Chamberlain et al., 1983), of which the most important are the local alveolar compliance and the resistance of peripheral airflow. Other factors that influence the distribution include minute ventilation inspiratory volume, pre-inspiration lung volume, the individual's position (Alderson and Line, 1980), contraction of different muscle groups (Roussos and Macklem, 1982; Decramer, 1997; Marchand and Decramer, 2000; De Troyer and Estenne, 1988), changes in the inspiratory flow (Aliverti et al., 1997; Pavia et al., 1985) and breathing rate (Chamberlain et al., 1983; Gandevia et al., 1999). Greater radioaerosol deposition occurred in both lungs during ITL. It is possible that these findings were a consequence of the breathing pattern adapted by volunteers, although they had been instructed to maintain pre-established specific patterns of a ventilation.

In a simplified way, the analysis of the vertical gradient of the radioaerosol deposition demonstrated a larger deposition in the middle third. Several factors that might have affected the deposition would be: (1) in the posterior incidence, for radioactivity reception by the gamma camera, the third section includes parts of anterior basal regions, (2) in the sitting position, the intrapleural pressure is progressively more subatmospheric from the base (about $-2.5$ $cmH_2O$; where the lung is compressed by it's weight) to the apex ($-10$ $cmH_2O$; where the lung's weight is less of an influence) (Alderson and Line, 1980) which enables the alveoli at the base to be more compliant with considerable variation in volume during inhalation and exhalation (West, 1990), (3) the pattern of muscle contraction may affect lung ventilation such that the greater EMG activity of the lower rib cage muscles suggests that ventilation was mainly directed to the middle and inferior thirds, and (4) the localization of the large bronchial tubes in the third section may account for most of the radioaerosol inertial impact, due to the turbulence in these parts of the respiratory system. Radioaerosol deposition is dependent on the above physical properties (Dolovich, 2001). According to O'Doherty and co-workers (Miller and O'Doherty, 1992), particles of medium mass of aerodynamic diameter of the radioaerosol of $^{99m}$Tc-DPTA (<1.0 μm), have an adequate periferal penetration in normal individuals. However, it is possible that such an impact on the large bronchial tubes seen in individuals with chronic respiratory limitations may have occurred in the subjects of our study as a result of ITL.

The horizontal gradient provides another view for the evaluation of the radioaerosol deposition. In general, the largest deposition occured in the intermediate and central areas, with the peripheral segment presenting with the smallest deposition. The following factors may be related to this pattern of horizontal deposition including: high flows favor the deposition in the large airways, owing to the inertial impact (Levitt et al., 1995; Dolovich, 2001) and possibly, the greater radioaerosol deposition in those areas is related to the size of the generated particles.

Due to some limitations in the methods used in this study, it cannot be confirmed that areas with reduced radioaerosol deposition necessarily correspond to those that are poorly ventilated. Further investigation of the interactive relationship between pulmonary deposition and ITL is needed. Future

study of simultaneous radioisotope deposition with the ventilation/perfusion ratio during ITL would provide a better understanding of these relationships.

The EMG evaluation enabled an additional interpretation of our results which found increasing EMG activity in the lower rib cage muscles throughout the course of ITL. That is, the larger the load, the greater the lower thoracic muscle activity. However, at the same time, the stemocleidomastoid muscle activity did not differ throughout the phases of the test, thus raising the question of the effect of posture maintenance during ITL. Ratnovsky and Elad (2005) in a study with a realistic two-dimensional model, showed the role of the sternocleidomastoid muscle increases at high efforts and may reach almost 10% of inspiratory work. In our study the maximal ITL was 30 $cmH_2O$ which may not have been great enough to increase sternocleidomastoid muscle activity in our subjects without a previous history of pulmonary disease. Previously, we reported that it is necessary to increase inspiratory muscle activity to overcome ITL with the Treshhold® device (Dornelas de Andrade et al., 2005). In patients with COPD this increase occurs predominantly in the accessory muscles such as the sternocleidomastoid muscles while in elderly subjects (without any previous history of pulmonary disease) there was combined sternocleidomastoid and diaphragmatic muscle activity. For this reason, future studies of patients with lung disease are needed to clarify the effects of ITL and better understand the role of these muscles and lung ventilation especially when hyperinflation is present.

Due to the scarcity of literature about lung ventilation during the ITL test or during the training of the breathing muscles, it is difficult to compare these results with other studies. However, our results suggest that during an IME test via ITL, adjustments in the breathing frequency and respiratory muscle activity occurred which likely minimized the work of the breathing muscles. The increase in EMG activity in the lower rib cage muscles was observed as the respiratory workloads increased and there was a greater radioaerosol deposition in the medium third of the lungs and in the intermediate and central segments of the lungs during the IME test.

In summary, our findings reveal that apparently healthy young women experience a decrease in the breathing rate combined with changes in respiratory muscle activity during ITL that are likely to minimize ventilatory work. An increase in EMG activity in the muscles of the lower rib cage during progressive respiratory workloads is associated a greater radioaerosol deposition in medium third and intermediate and central segments in both lungs. Further studies analyzing patients with lung disease are needed to clarify the effects of ITL since greater resistance to airflow in COPD patients leads to important alterations in their pulmonary volume and, consequently, in their respiratory muscle performance.

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## 7. CONCLUSÃO E PERSPECTIVAS FUTURAS

Nossos resultados demonstram, primeiramente, que o teste de força dos músculos respiratórios realizado através da manobra voluntária de Pimáx parece subestimar a ação global dos músculos inspiratórios, visto que a manobra é realizada principalmente pela musculatura do pescoço, com o diafragma apresentando pouca atividade em resposta ao teste, mesmo no grupo controle. Além disso, a interpretação dos baixos resultados encontrados parece não refletir falta de atividade dos músculos respiratórios, pois a atividade eletromiográfica foi similar em ambos os grupos.

Da mesma forma, a avaliação da resistência muscular inspiratória com o teste incremental parece confirmar o comportamento similar entre os grupos. No entanto, sugerimos que a investigação da fadiga muscular através da variação do espectro de freqüência seja realizada através de dispositivos com maiores níveis de carga que permitam induzir alterações eletromiográficas comuns à fadiga.

Os menores volumes mobilizados durante o teste incremental pelo grupo DPOC, apesar da atividade eletromiográfica similar ao grupo controle, sugere que o déficit funcional na DPOC é resultado de uma mecânica respiratória prejudicada em função da obstrução e hiperinsuflação pulmonar.

Assim, sugerimos a necessidade de testes mais acurados e de interpretações mais criteriosas a fim de direcionar o diagnóstico e tratamento das disfunções dos músculos respiratórios.

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# ANEXOS

**TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO**

**TÍTULO: INFLUÊNCIA DA OBSTRUÇÃO E HIPERINSUFLAÇÃO PULMONAR NA ATIVIDADE DOS MÚSCULOS RESPIRATÓRIOS E MOBILIZAÇÃO DE VOLUMES PULMONARES DURANTE TESTES DE FUNÇÃO MUSCULAR RESPIRATÓRIA**

**INVESTIGADOR:** Thayse Neves Santos Silva

**LOCAL DE ESTUDO:** Laboratório de Fisioterapia cárdio-respiratória do Departamento de Fisioterapia da Universidade Federal de Pernambuco.

**ENDEREÇO:** Av. Prof. Morais Rego, nº1235, Cidade Universitária, Recife-PE tel:2126-8496.

**OBJETIVO E DESCRIÇÂO DO ESTUDO**

Este trabalho tem como objetivo analisar a resposta muscular de pacientes DPOC aos testes de força e resistência dos músculos respiratórios. Os voluntários realizarão testes de força máxima dos músculos respiratórios e respiraram através de um aparelho que dá pequenas cargas contrárias à respiração. Serão coletados dados através de eletrodos colocados sobre a pele para avaliar a participação dos músculos respiratórios durante os testes.

## RISCOS E BENEFÍCIOS

Por se tratar de um estudo sobre avaliação muscular através de métodos não invasivos, os riscos são praticamente desprezíveis. Os benefícios serão direcionados a pacientes e fisioterapeutas através do melhor conhecimento e utilização dos testes de função muscular inspiratória.

**CONFIDECIALIDADE E PARTICIPAÇÃO VOLUNTÁRIA/ RETIRADA**

**As informações obtidas através deste estudo serão tratadas rigorosamente com confidencialidade. Os resultados dessa pesquisa serão divulgados publicamente,porém sua identidade não será revelada.**

A participação neste estudo é voluntária. Podendo o(a) senhor(a) recusar-se ou deixar de participar a qualquer momento da realização deste estudo.

**CONSENTIMENTO LIVRE E ESCLARECIDO**

Li e entendi as informações procedentes descrevendo este estudo. Dou livre meu consentimento para a participação do estudo até que descida pelo o contrário.

| | | |
|---|---|---|
| Nome | Assinatura | Data |
| Nome da testemunha | Assinatura | Data |
| Nome da testemunha | Assinatura | Data |
| Nome do investigador | Assinatura | Data |