

Physical Activity as a Mediator Between Dyspnea and Fatigue in Patients with Chronic Obstructive Pulmonary Disease

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Une étude transversale a été menée pour examiner l'effet médiateur de l'activité physique entre la dyspnée et la fatigue chez les patients atteints de bronchopneumopathie chronique obstructive (BPCO). La dyspnée a été mesurée à l'aide d'une échelle analogique verticale visuelle, et la fatigue à l'aide d'une échelle graduée des profils de l'humeur et de la fatigue (Profile of Mood States-Fatigue) et d'une activité physique, soit le test de la marche de six minutes (6MW). Un échantillon de commodité composé de 17 patients et 22 patientes atteints de BPCO a produit les données pour analyse. L'échantillonnage était caractérisé par un volume expiratoire avec effort relativement élevé en une seconde (FEV1) de valeurs normales prévues, indiquant une légère atteinte pulmonaire et un taux moyen de fatigue et de dyspnée élevé. Les contrôles sur l'âge et le FEV1, la dyspnée, l'activité physique et la fatigue étaient relativement interreliés. Les résultats de l'analyse de régression indiquaient une fonction médiatrice de l'activité physique entre la dyspnée et la fatigue. Les limites et les suggestions en ce qui a trait à la pratique et à la recherche future sont présentées.

A cross-sectional design was used to examine the mediating effect of physical activity between dyspnea and fatigue in patients with chronic obstructive pulmonary disease (COPD). Dyspnea was measured using a vertical visual analogue scale, fatigue using the Profile of Mood States–Fatigue subscale, and physical activity using the 6-minute-walk (6MW) test. A convenience sample of 17 male and 22 female patients with COPD provided data for analysis. The sample was characterized by relatively high forced expiratory volume in 1 second (FEV1) of predicted normal values, indicating mild lung impairment and high mean levels of fatigue and dyspnea. Controlling for age and FEV1, dyspnea, physical activity, and fatigue were significantly interrelated. Results of the regression analysis suggested the mediating function of physical activity between dyspnea and fatigue. Limitations and suggestions for practice and future research are presented.

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Introduction

Chronic obstructive pulmonary disease (COPD), a term that can apply to emphysema, bronchitis, or a combination of the two, is a progressive debilitating condition (Lacasse, Brooks, & Goldstein, 1999). In Canada, COPD accounted for 4.1% of all deaths in 1995 and is the fourth and seventh leading cause of death among men and women, respectively (Lacasse et al.). COPD patients experience myriad symptoms (Gift & Pugh, 1993), one of the most distressing and prevalent of which is fatigue (Graydon, Ross, Webster, Goldstein, & Avendano, 1995). In a study with 146 COPD patients, 91% reported that they experienced fatigue anywhere from "sometimes" to "always" (Kinsman et al., 1983). Fatigue has been shown to be associated with impaired quality of life in COPD patients (Breslin et al., 1998). It is a significant problem.

Fatigue is an enduring, subjective feeling of generalized tiredness or exhaustion (Aaronson et al., 1999) that can be differentiated as acute or chronic (Piper, 1993). Acute fatigue is localized and temporary, has been suggested as a protection against over-exertion and muscle damage, and can be mitigated by such strategies as a good night's sleep, adequate rest, or proper diet. In contrast, chronic fatigue is general, pervasive, and continuous, may last for long periods, and cannot be mitigated by sleep or rest (Piper). The mechanisms that lead to chronic fatigue in COPD remain elusive in light of the complexity of COPD and the paucity of research on fatigue in this patient population (Woo, 1995).

Review of the Literature

Dyspnea and Fatigue

Fatigue is identified as a common experience in COPD patients, second only to dyspnea in prevalence (Graydon, Ross, et al., 1995; Guyatt, Townsend, Berman, & Pugsley, 1987; Kinsman et al., 1983). Janson-Bjerklie, Carrieri, and Hudes (1986) report that up to 45% of their research participants, when asked to describe dyspnea, included fatigue as a descriptor. Dyspnea and fatigue are not only commonly experienced by COPD patients, but have been shown to be related. Pearson correlation coefficients for the relationship between the two range from 0.69 (Woo, 2000) to 0.76 (Kinsman et al.). Various explanations have been offered for both dyspnea and fatigue. However, the mechanism that relates dyspnea to fatigue is not well understood. Dyspnea can be evoked in COPD as a result of decreased pulmonary function due to progressive destruction of the alveolar structure and inadequate alveolar gas exchange (Killian & Jones, 1988). With decreased pulmonary

function, oxygenation of locomotive muscles and the energy-producing mechanism of the muscle are impaired, leading to fatigue.

Physical Activity and Fatigue

Chronic fatigue in COPD may also arise from patients decreasing their physical activity in order to avoid the distressing experience of dyspnea (Sassi-Damborn, Eakin, Ries, & Kaplan, 1995). Dyspnea may be precipitated by muscle use during physical activity, with its increased ventilatory demand and ribcage and accessory muscle recruitment (Gift & Pugh, 1993). In COPD patients it may be associated mainly with physical activity. According to Leidy and Haase (1996), dyspnea is one of the major hindrances to physical activity among COPD patients. As a result of decreased physical activity and immobility, the locomotive muscle undergoes morphological changes. Losses in skeletal muscle fibre, contractile protein, energy-generating enzymes, and energy store (e.g., glycogen) have been seen secondary to reduced physical activity due to limb immobilization (Appell, 1990; Mobily & Kelley, 1991). These changes lead to decreased endurance, performance, power output, and force generation of the muscles (Brooks & Faulkner, 1994; Karlsson, Diamant, & Folkers, 1992). Muller (1970) reports that 5.5% of muscle strength could be lost each day as a consequence of immobility. Reduced muscle strength and endurance as a result of deconditioning is one factor leading to fatigue with activity (Breukink et al., 1998). Patients with rheumatoid arthritis (Belza, Henke Yelin, Epstein, & Gillis, 1993) and postoperative patients (Christensen, Nygaard, Stage, & Kehlet, 1990) have reported increased fatigue with activity as a result of decreased physical fitness. Also, COPD patients who are physically deconditioned may experience a higher level of fatigue with activity than COPD patients who are physically active. Kinsman et al. (1983) found that COPD patients ($n = 146$) who experienced more difficulty with physical activities due to shortness of breath complained more frequently of fatigue ($p < 0.001$).

As compensation for fatigue, COPD patients may further restrict their physical activity. The resultant increased muscle disuse and degeneration may promote further fatigue. The result is a downward spiral of physical inactivity, muscle degeneration, deconditioning, and fatigue (Carter et al., 1988).

The purpose of the present study was to examine the relationships among dyspnea, physical activity, and fatigue. The specific research questions were: (1) *Are dyspnea, physical activity, and fatigue related in patients with COPD?* and (2) *Does physical activity play a mediating role in the relationship between dyspnea and fatigue?*

Table 1 *Demographic Characteristics of the Sample (N = 39)*

Characteristics	Range	Mean	Standard Deviation
Age	53–85 years	<i>M</i> = 69.9	<i>SD</i> = 8.23
Characteristics		Frequency	Percentage
Gender	male	17	43.6
	female	22	56.4
Marital status	single	5	12.8
	married	20	51.3
	widowed	11	28.2
	divorced	3	7.7
Education	<high school	15	38.5
	high school	12	30.8
	community college	9	23.1
	university	3	7.7
Employment	not employed	35	89.7
	employed part-time	4	10.3
Oxygen use	not used	31	79.5
	continuous	2	5.1
	at night only	4	10.3
	during exercise	2	5.1

Methods

Subjects and Setting

A convenience sample of 39 outpatients with COPD were recruited from the respiratory clinic of metropolitan acute-care hospitals. In anticipation of a moderate effect size, the sample size was considered adequate with approximately 10 data sets for each variable in multiple regression analysis (Norman & Streiner, 1998). Since three variables were considered in this study, a sample of more than 30 subjects was required. Demographic characteristics of the sample are summarized in Table 1. To be eligible, the subjects had to: (1) report dyspnea and fatigue, (2) be diagnosed with COPD with a FEV1 of less than 60% of predicted normal values, and (3) be ambulatory without the assistance of another person. Patients with concomitant neuromuscular disease that might affect performance of the walking test were excluded.

Procedure

The study was approved by the appropriate institutional review committees. Eligible patients were initially approached by their physician in the pulmonary function laboratory. The total number of patients approached and the number who refused to participate is not available. The physicians indicated that the reasons for refusal were related to transportation arrangements, feeling sick, inconvenience, fatigue, and lack of time. Those patients who expressed an interest in the study were contacted by the investigator after their appointments at the pulmonary function laboratory. They were provided detailed written and verbal descriptions of the study, were encouraged to ask questions, and were informed that their future medical care would not be affected by whether or not they agreed to participate. Informed consent was obtained. Subjects were not compensated for their participation.

Subjects were asked to indicate their levels of fatigue using the Fatigue subscale of the Profile of Mood Sates (F-POMS) and their levels of dyspnea using the Vertical Visual Analogue Scale (VVAS). All patients were asked to fill out a demographic collection sheet that included questions about their age, gender, education, and number of years diagnosed with COPD. Patients' pulmonary functions within the previous 6 months were obtained from their medical records. At the end of the interview, the participants were asked to perform a 6-minute walking (6MW) test. Overall scheduling allowed for administration of the subjective measures (F-POMS and VVAS) prior to the more objective measure (6MW test). The F-POMS was administered before the VVAS in order to avoid alteration of the patient's perception of fatigue due to the length of the interview.

Measures

Profile of Mood States (POMS). The POMS was developed by McNair, Lorr, and Droppleman (1981) as a means of measuring the mood states of tension-anxiety, anger-hostility, vigour-activity, fatigue-inertia, depression-dejection, and confusion-bewilderment. For the purpose of this study, only the Fatigue subscale of the POMS (F-POMS) was used. The F-POMS consists of seven items. Subjects are asked to indicate the degree or intensity of their feelings in the preceding few days on a five-point Likert scale, from 0 ("not at all") to 4 ("extremely"). Internal consistency reliability has been reported as 0.93 (Norcross, Guadagnoli, & Prochaska, 1984), test-retest reliability as 0.74 (McNair et al.). Concurrent validity has been investigated by comparing the F-POMS with

other instruments that measure fatigue, with good results reported. Reeves, Potempa, and Gallo (1991) found the Pearson correlation coefficient between F-POMS and fatigue subscale scores of the Fatigue/Stamina Scale to be 0.79 ($p < 0.001$) in pregnant women.

Vertical Visual Analogue Scale (VVAS). Dyspnea was measured using the Vertical Visual Analogue Scale (VVAS). This is a 100mm vertical-line rating scale with anchors of "no shortness of breath" at the bottom and "shortness of breath as bad as can be" at the top. Patients are asked to mark a line to indicate the degree of shortness of breath experienced. Since there is little to read or see on the scale, the VVAS can be used by people with some sight impairment (Gift, 1989). Using the VVAS, Gift observed significant differences between dyspnea scores obtained during severe obstruction (peak expiratory flow rate, or PEFR, less than 150 lpm) and mild obstruction (PEFR more than 150 lpm) in patients with asthma ($p < 0.01$) and COPD ($p < 0.01$). The Pearson product-moment correlation between the VVAS and PEFR was -0.85. Gift concluded that the results lent support to the construct validity of the VVAS.

Six-Minute Walk (6MW). The walking test is a simple, inexpensive, and safe method for assessing a subject's ability to engage in physical activity. Subjects are required to walk on a flat surface in an enclosed corridor of the pulmonary function laboratory from end to end for 6 minutes. At any time and for any reason, they are allowed to slow down or stop to rest. The investigator walks behind the subject to act as timekeeper. No encouragement is provided to the subject during the 6MW. Guyatt et al. (1985) contend that the 6MW imposes minimal stress and reflects the patient's ability to withstand the physical demands of day-to-day life, especially among those who are moderately or severely limited. The authors report that the repeated measurement of 6MW distance was consistent in the same subjects, supporting the reproducibility and reliability of the 6MW. Furthermore, studies with COPD patients have demonstrated that the 6MW distance is significantly correlated with the gas transfer index (T_{LCO}) ($r = 0.68$), FEV_1 ($r = 0.53$), breathlessness on the MRC scale ($r = -0.52$), and FVC ($r = 0.48$) (all p values less than 0.001) (Berstein et al., 1994), thus supporting the construct validity of the 6MW.

Data Analysis

Distribution of all variables was tested using the Kolmogorov-Smirnov goodness-of-fit test. Distribution of the variables was not significantly

different from normal distribution. Data were analyzed using the Statistical Package for Social Science (SPSS), 10.0 version, for personal computers. Correlation among dyspnea, fatigue, and physical activity was estimated using the Pearson correlation coefficient (r). T-testing for independent samples for all the variables revealed no significant difference between males and females.

Regression analyses were conducted to evaluate the role of physical activity as a mediator between dyspnea and fatigue. In the first regression equation, fatigue as an outcome variable was regressed on dyspnea, the predictor variable. In the second equation, physical activity as the mediator was regressed on dyspnea. In the last equation, fatigue was regressed on dyspnea and physical activity simultaneously. In order for physical activity to be established as a mediator, the relationship between fatigue and physical activity must be significant and between dyspnea and fatigue non-significant (Lindley & Walker, 1993). The influence of age and FEV1 as covariates was controlled in each regression equation by entering age and FEV1 to each equation before other independent variables. The level of significance for all statistical tests was set at 0.05.

Table 2 *Ranges, Means, and Standard Deviations on Illness Characteristics*

Measurement	Range	Mean	SD
FEV1	21–72	46.28	12.33
Fatigue	3–25	11.28	5.10
Dyspnea	21–97	53.08	18.70
6MW (in metres)	6.04–694.32	379.00	152.05

Results

The subject profile for this study was a 69-year-old woman or man who was married or widowed, was not employed, had received at least a high-school education, had a FEV1 of 46% of predicted normal values, and did not require oxygen. Using a t-test for independent samples, no significant gender difference was noted in levels of fatigue, dyspnea, or physical activity.

Fatigue

All questions on the F-POM were answered, with no missing data. The possible range of scores for fatigue was 0 to 28. The actual range was 3.00 to 25.00, with a mean of 11.28 and a standard deviation of 5.10 (see Table 2). The distribution of fatigue scores was normal, with an estimated skewness of 0.39. Cronbach's alpha for the F-POMS was 0.80, indicating strong internal consistency reliability. No significant correlation was found among total fatigue scores, age, and FEV1.

Dyspnea

Dyspnea was measured using the VVAS. The possible range of scores for dyspnea was 0 to 100. The actual range was 21 to 97, with a mean of 53.08 and a standard deviation of 18.70 (see Table 2). Dyspnea scores were evenly distributed, with a skewness of 0.45, and were negatively and significantly correlated with FEV1 level ($r = -0.33$; $P = 0.04$). The higher the dyspnea score, the lower the FEV1. No significant correlation was found between VVAS scores and age.

Physical Activity

The actual 6MW distance ranged from 6.04 to 694.32 metres, with a mean of 379.0 m and a standard deviation of 152.05 m. The calculated skewness for the distribution of walking distances was -0.28. One subject was able to walk only 6.04 m due to extreme shortness of breath, anxiety, and inability to follow instructions. Although the distance of 6.04 m was 2.5 standard deviations below the mean of 379.0 m, the subject was included in the sample for analysis after it was found that exclusion would not alter the result. No correlation was found among 6MW, age, and FEV1.

Relationship Among Dyspnea, Physical Activity, and Fatigue

Ability to perform physical activity can be affected by the patient's age and pulmonary function. To ensure that relationships among dyspnea, 6MW, and fatigue were not confounded by the influence of age and FEV1, both age and FEV1 were included as covariates in the analysis. As shown in Table 3, although the correlation coefficients were low, all variables were significantly correlated. Dyspnea and fatigue were negatively correlated to 6MW and dyspnea was positively correlated to fatigue. Results suggest that the more dyspnea the COPD patients felt, the more fatigue they experienced and the shorter the distance they

were able to complete in the 6MW. The relationships illustrated by the scatterplots depict linear relationships.

Physical Activity as Mediator Between Dyspnea and Fatigue

To reduce the problem of multicollinearity, the dependent and independent variables were centred for the following analysis. Controlling for age and FEV1, dyspnea was a significant predictor of fatigue, explaining 26% of variance (Table 3). High levels of dyspnea augmented fatigue in COPD. In the second equation, physical activity as the mediator was regressed on dyspnea; the relationship was also significant, explaining 25% of variance. Results of the first two regression analyses supported further testing of the mediating effect of physical activity between dyspnea and fatigue. In the third equation, fatigue was regressed on dyspnea and physical activity simultaneously. With both dyspnea and physical activity included, the explained variance in fatigue increased from 26% to 39%. The standardized coefficient for the relationship between fatigue and physical activity was significant, while the coefficient for the relationship between dyspnea and fatigue fell from a significant value of 0.41 to a non-significant value of 0.24 ($p = 0.14$). According to Lindley and Walker (1993), the results of the analysis would support the mediating effect of physical activity between dyspnea and fatigue. A summary of the regression analysis is presented in Table 3.

Table 3 Summary of Regression Analysis					
Regression Equations	Dependent Variable	Independent Variables	R Square	Beta	t-value
1	Fatigue	Age	0.02	0.09	0.60
		FEV1	0.11	-0.17	-1.08
		Dyspnea	0.26	0.41	2.65*
2	6MW	Age	0.02	0.16	1.08
		FEV1	0.11	0.16	1.05
		Dyspnea	0.25	-0.41	-2.61*
3	Fatigue	Age	0.02	0.16	1.14
		FEV1	0.11	-0.10	-0.68
		Dyspnea	0.39	0.24	1.53 [†]
		6MW		-0.43	-2.78 [‡]
* $p = 0.01$ [†] $p = 0.14$ [‡] $p = 0.009$					

Discussion

Consistent with the findings of other studies (Breslin et al., 1998; Breukink et al., 1998; Gift & Shepard, 1999; Woo, 2000), this study found that dyspnea, physical activity, and fatigue were significantly interrelated. The more dyspnea that subjects perceived, the less physical activity they were able to perform, as indicated by the 6MW, and the greater the fatigue they reported. Thus the findings of this study support physical activity as a mediator between dyspnea and fatigue. Although the cross-sectional nature of the study precluded an assumption of causality, dyspnea in COPD may lead to decreased physical activity and physical deconditioning, thus predisposing patients to fatigue. It follows that interventions aimed at alleviating fatigue in COPD patients should consider managing symptoms such as dyspnea first, so that patients can engage in physical activity.

Reducing or ceasing activity has been identified as a common strategy for relieving fatigue among patients receiving cancer treatment (Graydon, Bubela, Irvine, & Vincent, 1995). Although resting may alleviate fatigue temporarily, the findings of this study suggest that increased physical inactivity may actually contribute to physical deconditioning and thus worsen fatigue. Perhaps patients should be encouraged to try other strategies besides resting to alleviate their fatigue. COPD patients who exercised regularly reported that their fatigue was significantly less frequent (Perry, 1981) and less intense (Simpson, Killian, McCartney, Stubbing, & Jones, 1992) after they participated in a pulmonary rehabilitation program. Fatigue may be mitigated by enhanced muscle strength and exercise endurance, improved psychological coping, nutrition counselling, a social-support program, or increased desensitization of the symptom. Further study is needed to clarify these relationships.

The generalizability of the results of this study should be interpreted with caution. High mean levels of dyspnea and fatigue were reported. Dyspnea ranged from 21 to 97, with a mean of 53.08 ($SD = 18.70$). Fatigue ranged from 3 to 25, with a mean of 11.28 ($SD = 5.10$). In a study with 76 COPD patients (Alonso, Anto, Gonzalez, Izquierdo, & Morera, 1992), the subjects rated dyspnea between 0 and 64, with a mean of 25 ($SD = 16$). The mean dyspnea score and variability in distribution (SD) were lower than those found in the present study. Although Alonso and colleagues used the VAS to measure dyspnea and recruited a sample whose mean FEV1 was lower than that of the present study, their sample comprised only males and not all of their subjects experienced dyspnea. Other research has found gender differ-

ences in the rating of symptoms in COPD, with females reporting more symptoms (Leidy & Traver, 1995) and rating dyspnea higher and more distressing (Gift & Shepard, 1999) than males. Females may be more sensitive and attuned to their feelings and symptoms than males, or the high mean dyspnea score may be a reflection of the fact that more than half (56.4%) of the sample was female.

The over-representation of females in the sample may also explain the high levels of fatigue in this study. In a study by Prigatano, Wright, and Levin (1984), the mean F-POMS score for healthy subjects was below 5, as opposed to 10 for the COPD participants in the present study. Even for COPD patients who were oxygen-dependent due to severely impaired lung function, with a mean FEV1 of 26%, the reported mean fatigue score was 11.27 ($SD = 7.02$; ranging from 1 to 26) (Lee, Graydon, & Ross, 1991). However, not everyone recruited in these studies experienced fatigue. The mediating function of physical activity reported in the present study may be more specific for female than male COPD patients with high fatigue levels.

Limitations

Several limitations should be considered when interpreting the findings of this study. (1) The sample was small. (2) A non-probability sampling method was used. The available subjects may not be representative of the population. (3) The cross-sectional design precludes inferences of causality among dyspnea, physical activity, and fatigue. (4) Fatigue is a multidimensional concept. The use of a unidimensional instrument to measure fatigue may reflect only one aspect of it. (5) The sample consisted of a wide range of ages. As people age, their level of physical fitness may decline, thus affecting the relationship between fatigue and physical activity. Considering the potential confounding effect, age was controlled for in the analysis. (6) Walking distance may be influenced by various factors that could account for the measurement error. These factors are: unfamiliarity, motivation, comprehension, temperature and humidity on the day of data collection, endurance, weight, cardiovascular fitness, and neuromuscular function. The presence of measurement error in the mediator could account for the overestimate of the effect of the mediator and an underestimate of the effect of the independent variable on the dependent variable. To improve reliability, Larson and colleagues (1996) suggest that the results of the first two walking tests be discarded so that subjects can familiarize themselves with the test. These authors observed a 13% improvement in subjects' performances between the first 12MW test and the fourth. Repeated testing allowed

the subjects to learn the task and determine a strategy for optimal performance. However, repeated testing was not implemented in the present study.

Conclusion

This study used a descriptive cross-sectional design to examine how appraisal of fatigue relates to dyspnea and physical activity among patients with COPD. Fatigue, dyspnea, and physical activity were found to be significantly correlated. The greater the dyspnea, the lower the ability to perform physical activity, as indicated by the 6MW, and the greater the fatigue. Three regression equations were utilized to explore the role of physical activity in mediating between dyspnea and fatigue. The results suggest that physical activity does mediate the relationship between dyspnea and fatigue. This study should be replicated using a larger sample and among patients with various levels of FEV₁, in order to verify the function of physical activity in dyspnea and fatigue. Future studies should examine the effect of reduced dyspnea on physical activity and fatigue.

References

- Aaronson, L.S., Teel, C.S., Cassmeyer, V., Neuberger, G.B., Pallikkathayil, L., Pierce, J., Press, A.N., Williams, P.D., & Wingate, A. (1999). Defining and measuring fatigue. *Journal of Nursing Scholarship*, 31(1), 45-50.
- Alonso, J., Anto, J., Gonzalez, M., Izquierdo, J., & Morera, J. (1992). Measurement of general health status of non-oxygen-dependent chronic obstructive pulmonary disease patients. *Medical Care*, 30(suppl 5), MS125-MS135.
- Appell, H. (1990). Muscular atrophy following immobilization. *Sports Medicine*, 10, 42-58.
- Belza, B., Henke, C.J., Yelin, E.H., Epstein, W.V., & Gillis, C.L. (1993). Correlates of fatigue in older adults with rheumatoid arthritis. *Nursing Research*, 42, 93-99.
- Berstein, M., Despars, J.A., Singh, N.P., Avalos, K., Stanbury, D.W., & Light, R.W. (1994). Reanalysis of the 12-minute walk in patients with chronic obstructive pulmonary disease. *Chest*, 105, 163-167.
- Breslin, E., Van Der Schans, C., Breukink, S., Meek, P., Mercer, K., Volz, W., & Louie, S. (1998). Perception of fatigue and quality of life in patients with COPD. *Chest*, 114, 958-964.
- Breukink, S.O., Strijbos, J.H., Koorn, M., Koeter, G.H., Breslin, E.H., & Van Der Schans, C.P. (1998). Relationship between subjective fatigue and physiological variables in patients with chronic obstructive pulmonary disease. *Respiratory Medicine*, 92, 676-682.

- Brooks, S.V., & Faulkner, J.A. (1994). Skeletal muscle weakness in old age: Underlying mechanisms. *Medical Science in Sports and Exercise*, 26, 432-439.
- Carter, R., Nicotra, B., Clark, L., Zinkgraf, S., Williams, J., Peavler, M., Fields, S., & Berry, J. (1988). Exercise conditioning in the rehabilitation of patients with chronic obstructive pulmonary disease. *Archives of Physical Medicine and Rehabilitation*, 69, 118-122.
- Christensen, T., Nygaard, E., Stage, J.G., & Kehlet, H. (1990). Skeletal muscle enzyme activities and metabolic substrates during exercise in patients with postoperative fatigue. *British Journal of Surgery*, 77, 312-315.
- Gift, A.G. (1989). Validation of a vertical visual analogue scale as a measure of clinical dyspnea. *Rehabilitation Nursing*, 14, 323-325.
- Gift, A.G., & Pugh, L.C. (1993). Dyspnea and fatigue. *Nursing Clinics of North America*, 28, 373-384.
- Gift, A.G., & Shepard, C.E. (1999). Fatigue and other symptoms in patients with chronic obstructive pulmonary disease: Do women and men differ? *Journal of Gynaecologic Nursing*, 28, 201-208.
- Graydon, J.E., Bubela, N., Irvine, D., & Vincent, L. (1995). Fatigue-reducing strategies used by patients receiving treatment for cancer. *Cancer Nursing*, 18(1), 23-28.
- Graydon, J.E., Ross, E., Webster, P.M., Goldstein, R.S., & Avendano, M. (1995). Predictors of functioning of patients with chronic obstructive pulmonary disease. *Heart and Lung*, 24, 369-375.
- Guyatt, G., Townsend, M., Berman, L.B., & Pugsley, S.O. (1987). Quality of life in patients with chronic airflow limitation. *British Journal of Disease in Chest*, 81, 45-54.
- Guyatt, G.H., Sullivan, M.J., Thompson, P.J., Fallen, E.L., Pugsley, S.O., Taylor, D.W., & Berman, L.B. (1985). The 6-minute walk: A new measure of exercise capacity in patients with chronic heart failure. *Canadian Medical Association Journal*, 132, 919-923.
- Janson-Bjerklie, S., Carrieri, V.K., & Hudes, M. (1986). The sensations of pulmonary dyspnea. *Nursing Research*, 35, 154-159.
- Karlsson, J., Diamant, B., & Folkers, K. (1992). Exercise-limiting factors in respiratory distress. *Respiration*, 59(suppl 2), 18-23.
- Killian, K.J., & Jones, N.L. (1988). Respiratory muscles and dyspnea. *Clinics in Chest Medicine*, 9, 237-248.
- Kinsman, R.A., Yaroush, R.A., Fernandez, E., Dirks, J.F., Schocket, M., & Fukuhara, J. (1983). Symptoms and experience in chronic bronchitis and emphysema. *Chest*, 83, 755-761.
- Lacasse, Y., Brooks, D., & Goldstein, R.S. (1999). Trends in the epidemiology of COPD in Canada, 1980 to 1995. *Chest*, 116, 306-313.
- Larson, J.L., Covey, M.K., Vitalo, C.A., Alex, C.G., Patel, M., & Kim, M.J. (1996). Reliability and validity of the 12-minute distance walk in patients with chronic obstructive pulmonary disease. *Nursing Research*, 45, 203-210.

- Lee, R.N.F., Graydon, J.E., & Ross, E. (1991). Effects of psychological well-being, physical status, and social support on oxygen-dependent COPD patients' level of functioning. *Research in Nursing and Health*, 14, 323-328.
- Leidy, N.K., & Haase, J.E. (1996). Functional performance in people with chronic obstructive pulmonary disease: A qualitative analysis. *Advances in Nursing Science*, 18(3), 77-89.
- Leidy, N.K., & Traver, G.A. (1995). Psychophysiologic factors contributing to functional performance in people with COPD: Are there gender differences? *Research in Nursing and Health*, 18, 535-546.
- Lindley, P., & Walker, S.N. (1993). Theoretical and methodological differentiation of moderation and mediation. *Nursing Research*, 42, 276-279.
- McNair, D., Lorr, M., & Droppleman, L. (1981). *Profile of Mood States*. San Diego: Educational and Industrial Testing Service.
- Mobily, P.R. & Kelley, L.S. (1991). Iatrogenesis in the elderly: Factors of immobility. *Journal of Gerontologic Nursing*, 17(9), 5-10.
- Muller, E.A. (1970). Influence of training and of inactivity on muscle strength. *Archives of Physical Medicine and Rehabilitation*, 51, 449-462.
- Norcross, J.C., Guadagnoli, E., & Prochaska, J.O. (1984). Factors structure of the Profile of Mood States (POMS): Two partial replications. *Journal of Clinical Psychology*, 40, 1270-1277.
- Norman, G.R., & Streiner, D.L. (1998). *Biostatistics: The bare essentials*. Hamilton, ON: B.C. Decker.
- Perry, J.A. (1981). Effectiveness of teaching in the rehabilitation of patients with chronic bronchitis and emphysema. *Nursing Research*, 30, 219-222.
- Piper, B.F. (1993). Fatigue. In V. Carrieri-Kohlman, A.M. Lindsey, & C.M. West (Eds.), *Pathophysiological phenomena in nursing*, 2nd Ed. (pp. 279-302). Philadelphia: Saunders.
- Prigatano, G.P., Wright, E.C., & Levin, D. (1984). Quality of life and its predictions in patients with mild hypoxemia and chronic obstructive pulmonary disease. *Archives of Internal Medicine*, 144, 1613-1619.
- Reeves, N., Potempa, K., & Gallo, A. (1991). Fatigue in early pregnancy. *Journal of Nurse-Midwifery*, 36, 303-309.
- Sassi-Dambron, D.E., Eakin, E.G., Ries, A.L., & Kaplan, R.M. (1995). A controlled clinical trial of dyspnea management strategies. *Chest*, 107, 724-729.
- Simpson, K., Killian, K., McCartney, N., Stubbing, D.G., & Jones, N.L. (1992). Randomised controlled trial of weightlifting exercise in patients with chronic airflow limitation. *Thorax*, 47, 70-75.
- Woo, K. (1995). Fatigue in COPD. *Nurse Practitioner*, 20(10), 11-15.
- Woo, K. (2000). A pilot study to examine the relationships of dyspnea, physical activity, and fatigue in patients with chronic obstructive pulmonary disease. *Journal of Clinical Nursing*, 9, 526-533.