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Is Chronic Obstructive Pulmonary Disease a Risk Factor for Osteoporosis? A Structural Equation Modeling (SEM) Analysis

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Abstract

Background: Osteoporosis (OP) is reported to be far more prevalent in those with Chronic Obstructive Pulmonary Disease (COPD) than in healthy patients. While these two diseases share many common risk factors, studies suggest that COPD itself may be a contributing factor for poor bone health and thus could serve as a useful indicator to institute treatment for osteoporosis. Our study set out to further elucidate this correlation using structural equation modeling (SEM) in a population attending an academic family health team in Kingston, Ontario.

Methods: With ethics approval, data was collected from the existing electronic medical record system of the Queen's University Family Health Team in Kingston, Ontario. A path model with both structural and measurement components testing our hypothesis was constructed using the Structural Equation Modeling (SEM) software (SPSS AMOS 21©) using various latent and manifest variables that include the basic demographics, smoking status, alcohol usage and confirmed diagnoses of COPD and/or OP. Regression and covariance analyses were then performed and results were tabulated for discussions.

Results: Our proposed SEM model exhibited a goodness of fit index (GFI) of 0.88, which met the threshold (>0.85) of a good fit for our hypothesis. The correlation between poor lung function and poor bone health showed a statistically significant ($p<0.05$) positive regression coefficient of 5.753, indicating that poor lung function is indeed indicative of poor bone health. Alternatively, vitamin D and calcium intake in our population were found to have a statistically significant ($p<0.001$) negative regression coefficient of -0.342, -0.776 respectively, paradoxically implying that positive intake of both vitamin D and calcium is inversely correlated with poor lung function. Moreover, known risk factors for poor lung function such as age and smoking were confirmed with our model, and other factors like gender and alcohol intake were not. Limitations of our study included errors in documentation in the EMR and a biased sample that may not be representative for the general population.

Conclusions: Other studies have speculated a correlation between COPD and osteoporosis but definitive data is lacking. We performed a SEM analysis basing on electronic medical record data from an academic family health team in Kingston, Ontario, and our data supported a statistically significant correlation between poor lung function upon poor bone health with due regard to other factors including age, smoking, vitamin D and calcium intake.

Keywords: Osteoporosis; chronic obstructive pulmonary diseases; risks association; Structural equations modeling

Introduction

In Canada, Osteoporosis (OP) is a disease that affects approximately 1 in 4 women and 1 in 8 men over the age of 50 [1]. It is a condition characterized by low bone mass and micro-architectural changes that predispose to both silent and post-traumatic fractures [2,3]. As a result, untreated OP is associated with poor quality of life, decreased mobility, respiratory dysfunction, severe pain, and even increased mortality [2-5]. Current practice is to identify those at risks with bone mineral density (BMD) testing to institute early treatment to reduce morbidity and mortality of this debilitating disease [2,3].

Other risk factors have been identified for Osteoporosis. They include age, gender, low body mass index, cigarette smoking, alcohol abuse (≥ 3 units/day), current rheumatologic diseases, and history of steroid use (> prednisone 7.5 mg/day for 3 months). In addition, other chronic comorbidities have also been strongly correlated with OP that encourages early screening such as chronic obstructive pulmonary disease (COPD) [6].

COPD is a progressive debilitating lung condition characterized by chronic inflammation of the airways and alveoli, leading to airflow obstruction and decreased diffusion capacity of the alveoli. The leading causes of COPD include long-term exposure to cigarette smoke (both primary and secondary) and environmental toxins. Less often, COPD can be precipitated by a genetic predisposition known as alpha-1 anti-trypsin deficiency. COPD is a common disease that significantly decreases life expectancy and quality of life, due to lowered exercise tolerance, general deconditioning, increased heart strain, and iatrogenic sequels from short and long term use of steroids [2,3]. Not surprisingly, given the common risk factors shared by COPD and OP, a positive correlation between these two conditions has been recognized [2,3,5,7-10].

Several studies have reported a prevalence of OP-COPD dual diagnosis that varies from 4-60% [11-15], depending on the type of measurements used and the severity of COPD. This relationship is thought to be a result of risk factors that are shared by both OP and COPD: e.g., age, smoking, low BMI and steroid use. More recent evidence suggests that the shared risk factors may not fully explain the co-prevalence of COPD and OP, and that COPD *per se* may be a predisposing factor for poor bone health [9,11]. While the use of oral steroids for COPD may contribute to OP, studies have shown that steroids-naïve COPD patients had a significant lower bone mass when compared to age- and sex-matched non-COPD controls [5,16,17]. Regardless of the exact etiology, the correlation between OP and COPD prompted the 2010 Osteoporosis Guidelines to recommend that anyone between the ages of 50-64 with a history of COPD to undergo a bone mineral density (BMD) testing [6]. In practice, such recommendation is only infrequently followed [5], particularly for men [18].

One useful method to characterize correlations between measured and non-measurable variables in a defined system is Structural Equation Modeling (SEM). SEM is an excellent tool for examining multivariate relationships between variables in an integrated form that involves a rigorous mathematical method of analyzing correlations. This form of analysis assesses the correlations with respect to linear regression weights generated from a proposed path diagram. Moreover, one can also compare the inter-correlations between the proposed variables using covariance analysis. The path diagram is the kernel of SEM and defines the structural and measurement components as connected by arrows. The direction and placements of arrows define the schematic of hypothesized inter-relationships and therefore dictates the statistical comparisons [19].

In view of the fact that most of the published literature on the correlation between COPD and OP were based on European studies, it was one of our research aims to examine if the same correlation does exist for Canadian population.

Materials and Methods

Data extraction

For our study, ethics approval has been obtained from the Queen's University Health Sciences Research Ethics Board (HSREB). Relevant data was extracted from the Queen's University Family Health Team (QFHT) electronic medical record (EMR) system which was installed in July 2009. All patient records with a diagnosis of osteoporosis were first identified either via ICD-9 diagnostic codes or by text search in the medical notes using the terms "osteoporosis", "OP", "osteopenia", or "low BMD". Retrieved records from the initial search were then analysed for diagnosis of "chronic obstructive pulmonary disease", "COPD", "chronic obstructive pulmonary disease", "chronic bronchitis", "emphysema". In addition, the body-mass index, age, gender, alcohol abuse, smoking status, vitamin D intake, calcium intake, and prednisone use was entered for each record. All data was entered into an Excel spreadsheet and dichotomous results are transformed to a binary form ("1" for "Yes" and "0" for "No").

Structural equation model (SEM) analysis

A SEM path diagram was constructed with the SPSS AMOS 21© software to elucidate our proposed model of correlations (Figure 1). As per SEM convention, the variables denoted as rectangular boxes are manifest (measured) variables (i.e. with data), and those represented as ovals are considered as latent (non-measurable) variables. By definition, patients carrying a diagnosis of COPD and OP were considered to have Poor Lung Function (PLF) and Poor Bone Health (PBH) respectively, hence a regression weight of 1 were assigned respectively. All extracted data was then transported into an AMOS 21© spreadsheet. Using the built in functions of the AMOS 21© software, multiple linear regression analyses were then performed as per proposed path diagram. Comparisons were made between the measured variables and the latent variables, as well as our focus of interest: PLF as an indicator for PBH. Covariant analysis was also performed for all other measured variables. As per common practice in SEM, the relationship arrows in our path diagram were adjusted until the best goodness of fit of model was achieved to allow the best valid conclusions. Statistical significance of all data was considered with a p-value of <0.05.

Results

Population demographics

Out of a total of 16,992 patient records retrieved, 708 patients (4.2%) were identified with a diagnosis of osteoporosis (Table 1). The sample was found to be predominately women with 600 (84.7%) females and 108 males (15.3%). The average age was 69.5 years and average body mass index was 26.7. Out of these OP patients, 80 (11.3 %) were identified with a diagnosis of COPD. Moreover, 259 were documented smokers (36.6%), while only 7 (1%) were reported to have alcohol abuse. Those who had recorded vitamin D and calcium intake were 281 (39.7%), and 324 (45.8%) respectively, and 65 (9.2%) had been prescribed prednisone at least once.

Age	mean=69.5 yrs	COPD	n=80 (11.3%)	Vitamin D intake	n=281 (39.7%)
Gender	F=600 (84.7%) M=108 (15.3%)	Smoking	n=259 (36.6%)	Calcium intake	n=324 (45.8%)
Body Mass Index	mean=26.7 kg/m^2	Steroid use	n=65 (9.2%)	Alcohol use	n=7 (1%)

Table 1: Population demographics in those with osteoporosis.

Structural equation modeling (SEM)

Our proposed SEM path model (Figure 1) shows a statistically significant ($p<0.05$) correlation between poor lung function (PLF) leading to poor bone health (PBH) with a non-standardized regression weight of 5.753. In addition, other measured variables showing statistically significant correlations ($p<0.05$) towards PBH including smoker status (0.061), age (14.831), BMI (-0.255), and Vitamin D intake (0.344). Similar to PBH, age also had a statistically significant correlation with PLF with a regression weight of 12.637. Other

correlations seen with PLF were smoker status (0.889), vitamin D (-0.342) and calcium intake (-0.776). Unexpectedly gender, steroid use and alcohol abuse were not found to be statistically significant in their regressive correlations with PLF. Basing on both regression and covariance analysis described above, our proposed path model (Figure 1) shows a Goodness of Fit Index (GFI) of 0.88 (degree of fit considered good to excellent for GFI>0.85). When the path diagram was simply altered to show a reversed correlation between PBH and PLF, all the results were not statistically significant and our goodness of fit index returned an invalid model. This strongly suggests the unidirectional relationship of PLF upon PBH and not vice versa.

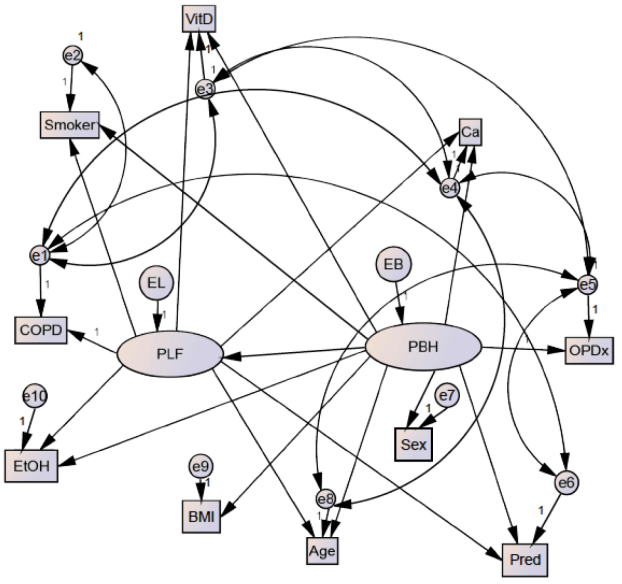

Figure 1: Proposed structural equation modeling (SEM) path model.

Discussion

For ease of discussion, Figure 2 is a modified schematic of Figure 1 (which is in a SEM path diagram) to reflect the unidirectional relationships between PLF and PBH. Collectively, our results showed that having PLF (as indicated by a diagnosis of COPD) is in fact a strong predictor of PBH (as indicated by diagnosis of OP) as previously cited by other literature. The nature of SEM analysis does not allow proof of causation, however, our path model was deemed to be a good fit with an index of 0.88 (a value of >0.85 indicates good fit) , endorsing validity of our conclusions. That said, there is on-going debate regarding the contributory factor for PLF (or COPD) to PBH (or OP). One hypothesis is vitamin D deficiency. Interestingly, some studies have shown COPD patients were prone to be vitamin D deficient [20-22]. In one study using a vitamin D serum threshold of <80 nmol/L, 86% of COPD subjects were found to be deficient [11], and in another study using a cutoff of <50 nmol/L in age- matched smoking controls, 43%,53%, and 76%, mild-, moderate- and severe COPD patients were vitamin D deficient respectively [23]. In reverse, vitamin D deficiency may contribute to poor lung function although the mechanism is still a bit unclear [23], and some authors simply see vitamin D deficiency and COPD as in a vicious cycle [22] (Table 2).

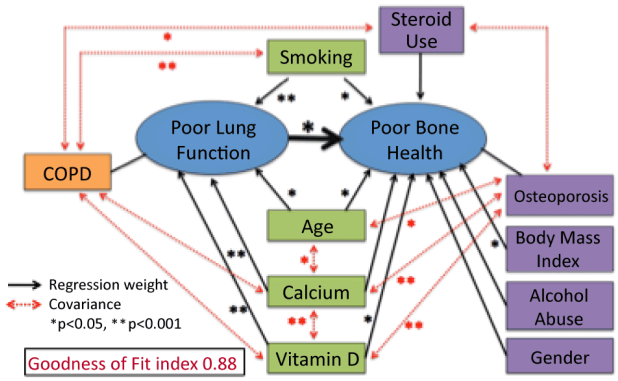

Figure 2: Modified SEM path model with statistical results.

Limitations of our study

Despite our patient population base of nearly 17,000, only 4.2% had a confirmed diagnosis of osteoporosis, which is well below the national prevalence of 12.5% (male) and 25% (female). This can be due to lack of documentation from the electronic record system. Unfortunately, we could not include vitamin D levels in our study as they were not routinely measured as part of clinical management in COPD or OP populations. As a surrogate measure, we looked at vitamin D and calcium intake to seek possible correlations. Our covariance analysis indeed showed that with a diagnosis of OP patients were more likely to take vitamin D and calcium supplementation. Our latent variable PBH also showed a correlative relationship with vitamin D, yet not with calcium. The discrepancy for this is unclear. Possible explanations include poor compliance to guidelines or intrinsic error from charting.

Our retrieved data showed a skewed male: female ratio of 108: 600 and thus may contribute to statistical insignificance when correlating gender to bone health. Yet, it is likely that men are often under screened for PBH [24]. In a way, our data with respect to gender therefore may well be an under-estimate for all patients with PBH and OP. About one third of all OP patients in our study were documented smokers. However, a negative regression correlation was seen between smoking and PBH. This remained to be interpreted, notwithstanding the obvious correlation between smoking and PLF which was shown to be strongly positive and statistically significant in our data. Other correlations such as age, BMI, alcohol abuse, prednisone were not robust enough statistically for sake of discussions.

	Poor Bone Health		**Poor Lung Function**	
	Regression	P- value	Regression	P- value
Poor Lung Function	5.753	0.017*		
COPD			1.00 (set value)	
Osteoporosis	1.00 (set value)			
Smoking	-0.061	0.018*	0.889	<0.001**

Age	14.831	0.015*	12.637	0.016*
Body Mass index	-0.255	0.010*		
Vitamin D intake	0.344	0.002*	-0.342	<0.001**
Calcium intake	-0.140	0.474	-0.776	<0.001**
Gender	0.004	0.482		
Steroid use	0.002	0.837	0.003	0.801
Alcohol abuse	-0.001	0.767	-0.002	0.212

Table 2: Regression weights as per the proposed SEM model.

Summary

In the last decade or so, studies have suggested a correlation between COPD and osteoporosis and yet, the underlying mechanism is still unknown and debated. Using regression and covariance analysis with structural equation modeling, we presented a path model demonstrating a relational correlation between poor lung function upon poor bone health amongst other measured variables. Thus said, more research into this area is needed before mandating BMD screening and vitamin D supplementation for patients with poor lung function and COPD.

Funding

None.

Conflict of Interest

None.

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