IMPAIRED LUNG FUNCTION IN A HISPANIC DIABETES POPULATION: THE RELATIONSHIP BETWEEN METABOLIC RISK FACTORS AND PULMONARY FUNCTION

By

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To my mother

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LIST OF ABBREVIATIONS

BMI	Body mass index
DM	Diabetes mellitus
HbA1c	Glycated Hemoglobin
HDL-c	High density lipoprotein cholesterol
FEV1	Forced expiratory volume in one second - the volume of air exhaled in the first second under force after a maximal inhalation
FEV1/FVC ratio	Percentage of the FVC expired in one second
FVC	Forced vital capacity - the total volume of air that can be exhaled during a maximal forced expiration effort
LDL-c	Low density lipoprotein cholesterol
PFT	Pulmonary function tests
TC	Total cholesterol

Abstract of Thesis Presented to the Graduate School
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Type 2 diabetes mellitus is a chronic disease whose prevalence increases with age. Inflammatory changes in lungs and glycosylation of connective tissues are observed in patients suffering type 2 diabetes mellitus. Additionally, these patients have higher risk than non-diabetic of developing infectious and non-infectious pulmonary diseases as well as intrinsic cardiovascular and neuropathic diabetic complications.

Lung function tests are painless, low-cost, and effective tools that produce important information to help with prognosis and reduce future complications; hence, lung function tests should be performed in this high-risk population. This study aims to measure the prevalence of abnormal lung function in a cohort of Hispanic patients with diabetes mellitus and investigate associations between metabolic risk factors and impaired lung function measured by spirometry showing either obstructive or restrictive pattern.

A cross-sectional study was performed including 386 type 2 diabetes mellitus (DM2) patients from a Public Health care unit in Quito, Ecuador. Prevalence of lung

disease characteristics of sample population were described. Wilcoxon test and t-test were used for mean differences calculations; univariate and multivariate logistic regression models were used to identify the correlates of pulmonary function and metabolic variables including glycated hemoglobin (HbA1c), total cholesterol, high and low density lipid cholesterol, triglycerides, body mass index and time of disease. Analyses were adjusted by sex, age and smoking status.

A total of 63 subjects had some kind of pulmonary functional impairment (17.8%). Among of them 40 (63.5%) had only restrictive pattern, 2 (3.2%) had only obstructive pattern and 21 (33.3%) subjects had a mixed spirometry pattern. In overall, 61 (15.8%) of the whole population exhibited restrictive type pulmonary changes. Glycated hemoglobin did not work as predictive biomarker for lung restrictive impairment.

Potential impairment of lung function should be assessed in DM2 patients, pulmonary function should be considered as important as renal or cardiac function evaluation in diabetic patients assessing pulmonary function tests reference values for this specific population regarding ethnicity and long-time high altitude residency.

CHAPTER 1
INTRODUCTION

Diabetes Mellitus and Lung Impairment

Type 2 Diabetes mellitus (DM) is one of the most prevalent chronic diseases worldwide. In Ecuador (INEC, 2011) and in the rest of the world (Alwan, Armstrong, Cowan, & Riley, 2011), DM is among the top five direct causes of death. The trend in adult diabetes prevalence worldwide has increased, or --at best-- remained unchanged since 1980 (NCD-RisC, 2016). In fact, the number of individuals with diabetes mellitus around the world is projected to rise from 135 million in 1995 to 300 million in 2025 (IDF, 2013; King, Hilary. Aubert, Ronald. Herman, 1998).

Pulmonary impairment in DM patients has not been investigated as much as cardiovascular, renal, and cerebrovascular complications. However, the prevalence of restrictive lung impairment related to metabolic diseases varies from 5% to 12% among Americans (Guerra et al., 2010; Kurth & Hnizdo, 2015). Reduced lung volumes and airflow limitation are likely to be chronic complications of DM, the severity of which relates to glycemic exposure (Davis, Knuiman, Kendall, Grange, & Davis, 2004; Mannino et al., 2012). While some studies have found that DM patients tend to have poorer lung function than non-diabetics (Walter, Beiser, Givelber, O'Connor, & Gottlieb, 2003), others have found that poor lung function can be treated as a predictive marker of developing diabetes (Yamane et al., 2013).

The proposed mechanisms of pulmonary impairment in DM patients include microangiopathy of lung capillaries and chronic low-grade systemic inflammation due to hyperglycemia, both of which are related to alterations of lung matrix proteins and basal lamina thickening (Weynand, B. et al 1999; Rodolfo, D. et al, 2010). Additionally, insulin

resistance, with or without hyperglycemia, is also associated to lung function impairment in the elderly (Fimognari et al., 2007). Fibrosis of lung parenchyma and respiratory muscle impairment due to myopathy or autonomic neuropathy are also proposed mechanisms to explain the relationship between DM and lung function impairment (Scarlata, Costanzo, Giua, Pedone, & Incalzi, 2012).

An increase in mean glycated hemoglobin (HbA1c) was associated with a decrease in the pulmonary function tests: forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) in diabetic (McKeever, Weston, Hubbard, & Fogarty, 2005) more than non-diabetic populations (Oh, Park, Lee, & Park, 2015), and may be a reliable predictor of poor lung function, especially the restrictive pattern (Godfrey & Jankowich, 2016). There is a predominant reduction in all the pulmonary function tests of diabetic patients toward the restrictive pattern (I., Hamdy, Amin, & Rashad, 2013); with significantly lower FEV1 and FVC values in DM patients than in non-diabetics, even after adjusting for age, sex, BMI, smoking status, diabetes duration, and HbA1c levels (Yeh et al., 2008). Moreover, in the first National Health and Nutrition Examination Survey (NHANES I), restrictive and obstructive pulmonary impairment have been shown as significant predictive factors for early mortality (Mannino, Buist, Petty, Enright, & Redd, 2003), independently of smoking, body mass index and adiposity (Hickson et al., 2011; Leone et al., 2009).

Lung Function

Spirometry is a basic-low cost tool for the exploration of lung function, and could be performed both in the specialist and primary care consultation. Understanding its principles, limitations, indications, and results is essential to assess the degree and type of respiratory dysfunction, monitor pulmonary diseases, and optimize treatments. The

American Thoracic Society (ATS) published recommendations for an adequate use of spirometry equipment and procedures in 1987 (Miller, Hankinson, et al., 2005). Those recommendations have been followed in many studies for a quality assessment during test performance.

Spirometry is a test designed to quantify functional pulmonary volumes, where a patient needs to expire as hard and fast in the spirometer as possible (Miller, Crapo, et al., 2005). The results of the test are compared to the predicted values that are calculated from their age, height, gender, and ethnic group (Pellegrino et al., 2005). The output are flow volumes curves and pulmonary function test (PFT) as: forced vital capacity (FVC, the total volume of air that can be exhaled during a maximal forced expiration effort), forced expiratory volume in one second (FEV1, the volume of air exhaled in the first second under force after a maximal inhalation), FEV1/FVC ratio, and the percentage of the FVC expired in one second. Then, on the basis of these PFT, percent predictive values are calculated to discriminate a normal or abnormal spirometry pattern (Barreiro & Perillo, 2004).

Pulmonary ventilatory function impairment is defined as the presence of restrictive, obstructive, or mixed abnormalities (Pellegrino et al., 2005). People with an obstructive spirometry pattern have difficulty exhaling all the air from the lungs, whereas, people with restrictive pattern have difficulty fully inhaling air (Pollard et al., 1997). The most common causes of an obstructive pattern are chronic obstructive pulmonary disease (COPD), which includes emphysema and chronic bronchitis; asthma, and cystic fibrosis (Athanazio, 2012). Other diseases as interstitial lung disease, autoimmune diseases, obesity and neuromuscular disease are the most

common causes of restrictive pattern. These diseases could be established independently of diabetes diagnosis. However diabetes is a commonly comorbidity of these pulmonary diseases (Cavailles et al., 2013) and depending on the population there is a 2% to 16% prevalence of diabetes in people with COPD (Chatila, Thomashow, Minai, Criner, & Make, 2008). Additionally, there is some evidence of a relationship between airway inflammation and insensitivity to insulin in patients with asthma (Gulcan, Bulut, Toker, & Gulcan, 2009; Mansi, Joshi, Pandloskar, & Dhar, 2007). In a retrospective longitudinal study, diabetic subjects were at increased risk of developing asthma, COPD, pulmonary fibrosis and pneumonia, but not lung cancer and that might be a consequence of diminished pulmonary function in diabetic patients (Ehrlich, Quesenberry, Eeden, Shan, & Ferrara, 2010).

The association between DM and reduced pulmonary function has been described for many years (I. et al., 2013; Litonjua, Lazarus, Sparrow, DeMolles, & Weiss, 2005), but the clinical significance of this association is unknown. Nevertheless, it is remarkable to understand how lungs might be affected by hyperglycemia and factors related to DM. The relationship between impaired lung function and risk factors related to DM is important to further understanding of pulmonary function in diabetic population and might imply strategies to impact the burden of significant conditions related to both poor lung function and diabetes. However, to the best of my knowledge, there are no published studies measuring pulmonary function in DM patients in Ecuador. The aim of this study is to determine prevalence of lung impairment and the relationship among metabolic risk factors and pulmonary function in Ecuadorian DM patients.

CHAPTER 2
METHODS

Study Population

The study population were DM patients who visited the Chimbacalle Non-Communicable Diseases Club located in Quito, Ecuador for periodic health examination. This is a public health care unit which provides basic and specialized ambulatory care for patients with chronic diseases. The dataset has been collected as part of a trend-descriptive observational study started in 2009 from medical records for measuring mortality and cardiovascular risk factors over time. We were granted access to an un-identified dataset containing medical records and baseline spirometry data from patients in 2012.

The sample population of this study was composed of Hispanic adults (Ecuadorians), who live in Quito at 2820 meters above sea level (masl), exercise for an hour at least 3 times per week, and attend either two or one one-hour lectures about type 2 diabetes or how to improve their health and nutrition per week. Additionally, all subjects had been taking daily doses of aspirin (100 mg) and cholesterol lowering drug (simvastatin 20 mg) as cardioprotection, as well as their diabetes medication.

Study Design

A cross-sectional study design was conducted. This study measured the prevalence of lung function in a cohort of Hispanic DM patients and investigated associations between metabolic risk factors and the outcome of interest. The sample included 386 patients. Inclusion criteria were patients previously diagnosed with type 2 diabetes under American Diabetes Association criteria of either sex, who had at least one spirometry in 2012. Patients with previous diagnosis of acute or chronic respiratory

disease, pregnancy, history of occupational exposure, collagen, neurological or neuromuscular diseases, deformities, or physical disability that might affect lung function or do not allow a reliable spirometry procedure were excluded.

Spirometry tests were performed with a SpiroPerfect™ PC-Based spirometer (Welch Allyn CardioPerfect, v1.6, NY, USA) using the acceptance and repeatability criteria set forth by the American Thoracic Society (Miller, Crapo, et al., 2005), adjusted for age, sex and height based on NHANES III reference values. Pulmonary function tests included: FVC, FEV1, and the ratio FEV1/FVC. Blood tests were performed by the Chimbacalle Non-Communicable Diseases Club and recorded in the medical histories. Blood samples were obtained after 12 hours overnight fast for the estimation of HbA1c, total cholesterol (TC), high density lipid (HDL), triglycerides (TG) and creatinine; LDL was calculated based on a mathematical formula using other lipid profile variables (LDL = TC - HDL - TG/5.0 (mg/dL))(Friedewald, W. 1972). Anthropometric measurements as height and weight were recorded and body mass index (BMI) were calculated by the formula of weight/height^2. Additionally, previous diagnosis of hypertension, age and duration of disease in years were recorded. Laboratory and spirometry variables were numerical. Glycated hemoglobin was used as a biomarker of optimal metabolic control in diabetes patients.

Case definition. Restrictive pulmonary pattern was defined as cases in which FVC values were lower than 80%, and FEV1/ FVC values were equal to or higher than 70%. Obstructive pulmonary pattern was defined as cases in which FEV1 values were lower than 80%, and FEV1/ FVC ratios were lower than 70%. Mixed pattern was

defined as cases in which both restrictive and obstructive definitions were satisfied (Barreiro & Perillo, 2004).

Statistical Analysis

Statistical analysis were performed using SAS 9.4 software package (SAS Institute Inc., Cary, NC, USA) in data corresponding to 386 patients. Metabolic variables were analyzed with descriptive statistics (mean and standard deviation) of the sample as a whole, as well as according to pulmonary function status. To compare differences in means between pulmonary function for the most relevant demographic and clinical characteristics, student's *t*-test (for parametric variables) and Wilcoxon test (for non-parametric variables) were used. Age was categorized based on NHANES III references values (CDC, 2015) and associated with pulmonary function stratified by gender using Cochran Mantel-Haenszel-Statistics (CMH). Univariate and multivariate logistic regression were used adjusted by sex and smoking status. Receiver operating characteristic (ROC) curve were graphically calculated to illustrate the accuracy of glycated hemoglobin to predict restrictive spirometry pattern; where AUC values of 0.5 corresponds to random chance and 1.0 for perfect accuracy to identify a disease and no-disease subjects.

Ethical Statement

The data of Chimbacalle Non-Communicable Diseases Club (CENCT -Spanish acronym-) in Quito, Ecuador has been gathered as part of an ongoing trend-descriptive observational study since 2009. This study has been authorized by the Ecuadorian Ministry of Public Health, with an aim to describe the overall health trends within this institution. The un-identified data from 2012 as long as with the spirometry results were

provided to this author by the authorities of Chimbacalle Non-Communicable Diseases Clinic for research purposes.

This secondary analysis study, along with the waiver of informed consent, were approved by the Institutional Review Board of University of Florida. Additionally, a letter of data use permission was provided by the Chimbacalle Non-Communicable Diseases Clinic (CECNT). (See Appendix A)

CHAPTER 3
RESULTS

As shown in Table 3-1, 311 (80.57%) subjects were females. The average age of the subjects was 60.41 years. The median age of the population was 60, and 64.51% of the participants were younger than 65 years old. Age was normally distributed. The majority (301, 77.98%) of subjects had high blood pressure as a comorbidity. Most (357, 92.49%) subjects were non-smokers at the time of the study.

Table 3-1. Baseline characteristic of Hispanic study population as a whole and by gender

	All subjects N=386 Mean/n (SD/%)	Women N=311 Mean/n (SD/%)	Men N= 75 Mean/n (SD/%)
Age (years)[b]	60.41 (11.70)	59.82(11.50)	62.84 (12.26)
Duration of Disease (years)	7.54 (7.06)	7.58(7.08)	7.37(7.03)
Smoking Status[a]			
Current	29(7.51%)	9(2.89%)	20(26.67%)
Former	53(13.73%)	24(7.72%)	29(38.67%)
Never	304(78.76%)	278(89.39%)	26(26.67%)
Hypertension[a]	301(77.98%)	245(78.78%)	56(74.67%)
HbA1c (%)	7.70(1.80)	7.72(1.79)	7.61 (1.81)
Body Mass Index (kg/m^2)[b]	29.84(4.79)	30.14(4.99)	28.5 (3.77)
Height (cm)	151.6(7.74)	149.32(5.92)	161.12(7.14)
Total Cholesterol (mg/dl)[b]	180.19(39.17)	182.41(39.14)	171.04(38.22)
HDL-c (mg/dl)[b]	78.51(17.10)	79.9(16.94)	72.58(16.56)
LDL-c (mg/dl)	66.73(30.32)	66.81(31.28)	66.36(25.98)
Triglycerides (mg/dl)	181.13(102.54)	181.58(93.75)	179.24(133.69)
Creatinine (mg/dl)[b]	1.09(0.40)	1.05(0.33)	1.23(0.59)

[a] Categorical Variables: Number and Percentage.
[b] Statistical significant differences in means ($p<0.05$) by gender
SD, standard deviation, HbA1c, glycated hemoglobin

The number of years since diagnosis with type 2 DM was positively skewed with a median of 5 and a range of 0 – 37 years. HbA1c and HDL-c showed positive skewness with a median of 7.30 (3.3-14.0) and 76 mg/dl (range of 45-166), respectively. Other covariates showed a positive skewness distribution, as well (data not shown). The difference in age, BMI, total cholesterol, HDL-c and creatinine between women and men was significant ($P < 0.05$).

Out of the 63 subjects with impaired spirometry pattern, 40 (63.5%) had only a restrictive pattern, 2 (3.2%) had only an obstructive pattern and 21 (33.3%) subjects had a mixed spirometry pattern. (Table 3-2) Mild restrictive and mild obstructive pattern were found in 88.52% and 91.30% of the lung impairment group. Therefore, a total of 61 subjects had some kind of restrictive spirometry pattern (15.8%). Restricted spirometry was found among 8 (10.7%) men and 53 (17.0%) women.

Table 3-2. Pulmonary Function Tests of study population and by gender.

	All subjects n=386		Women n=311	Men n= 75
	Mean/n (SD/%)	Median (Range)	Mean/n (SD/%)	Mean/n (SD/%)
FVC total volume (L)	2.66 (0.73)	2.60 (0.80 – 6.70)	2.46 (0.57)	3.51 (0.70)
FVC percent predicted (%)	96.47 (17.97)	95.00 (46 -208)	95.55 (17.97)	100.31 (17.59)
FEV1 total volume (L)	2.29 (0.65)	2.20 (0.80 - 6.00)	2.12 (0.51)	2.99 (0.67)
FEV1 percent predicted (%)	107.4 (22.10)	105.00 (49 – 252)	105.96 (21.58)	113.3 (23.39)
Absolute FEV1/ FVC ratio (%)	86.0 (7.29)	85.7 (56.4 -100)	86.18 (7.18)	85.25 (7.75)
Restrictive Spirometry Pattern[ab]	40 (63.5%)		36 (90.0%)	4 (10.00%)
Obstructive Spirometry Pattern	2 (3.2%)		1 (50.0%)	1 (50.0%)
Mixed Spirometry Pattern[ab]	21 (33.3%)		17 (80.9%)	4 (19.1%)

Subjects with restrictive pattern were found to have significantly higher mean HDL-c value and lower mean age than those with normal spirometry pattern ($P < 0.05$). Other risk factors, either unadjusted or adjusted, did not show association with pulmonary function (Table 3-3).

Table 3-3. Difference in Means and Odds Ratio of metabolic risk factors by Pulmonary Function Status (n=61)

	Pulmonary Function Status				
	Restrictive (n=61)	Normal (n=325)	p-value[a]	Crude OR (95%CI)	Adjusted OR (95%CI)[b]
	Mean (SD)				
Age (years)	57.46 (12.51)	60.96(11.48)	**0.046**	**0.97 (0.95-0.99)**	**0.98 (0.95-1.00)**
Duration of Disease (years)	7.23(6.35)	7.60(7.20)	0.584	0.99 (0.95-1.03)	0.99 (0.95-1.03)
HbA1c (%)	7.92(1.59)	7.66(1.83)	0.079	1.08 (0.93-1.25)	1.08(0.93-1.25)
Body Mass Index	29.66(6.15)	29.90(4.50)	0.247	0.98 (0.93-1.05)	0.98 (0.93-1.04)
Total Cholesterol (mg/dl)	188.10(43.76)	178.71(38.14)	0.177	1.01 (0.99-1.02)	1.01(0.99-1.02)
HDL-c (mg/dl)	84.64(30.38)	77.37(16.20)	**0.023**	**1.02 (1.01-1.04)**	**1.02(1.01-1.04)**
Triglycerides (mg/dl)	180.93(117.38)	181.17(99.72)	0.518	1.00 (0.99-1.01)	1.00(0.99-1.01)
Creatinine (mg/dl)	1.07(0.28)	1.09(0.42)	0.624	1.00 (0.99-1.01)	1.00(0.99-1.01)

[a]Wilcoxon test, age t-student
[b]Adjusted by gender and smoking status

The association between age and pulmonary function was significant but weak for females (p = 0.0430). In contrast, the results for males show a non-significant association (p < 0.05). The overall tests of association controlling for gender showed non-significance based on CMH statistics (p = 0.4190) (Table 3-4).\

Table 3-4. Categorized age by Pulmonary Function stratified by Gender

	Female[a] n (%)		Male n (%)	
Age (years)	Restrictive	Normal	Restrictive	Normal
20 – 40	1(9.09)	10(90.91)	1(33.33)	2(66.67)
41 – 60	34(22.08)	120(77.92)	3(11.54)	23(88.46)
61- up	17(88.36)	129(88.36)	5(10.87)	41(89.13)

[a]Female: p-value=0.0430

The test of homogeneity of age and pulmonary function across gender was non-significant (p-value=0.3506). Thus, the association can be considered to be the same for men and women.

To evaluate the accuracy of glycated hemoglobin as biomarker which might predict the developing of pulmonary restrictive pattern, we used ROC analysis expecting values of the area under the curve (AUC) close to 1.00 (Kelly Zhou). However, AUC was 0.57 showing that glycated hemoglobin, as a metabolic biomarker, has a weak predictive ability to discriminate patients with restrictive spirometry pattern from normal subjects (Fig. 3-1).

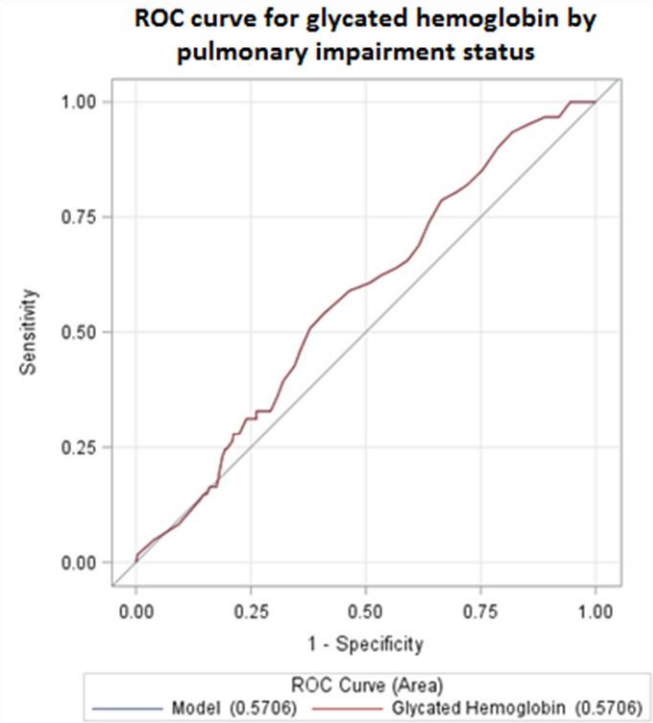


Figure 3-1. ROC curve for glycated hemoglobin by pulmonary impairment status.

CHAPTER 4
DISCUSSION

This study investigated the prevalence of pulmonary function impairment among adult Hispanic type 2 DM patients living at high altitudes and determined metabolic risk factors for pulmonary impairment. The key findings of the present study are that 1) high age is a protective factor among diabetes, 2) high HDL-c values were related with restrictive lung impairment, and 3) metabolic risk factors were not associated with pulmonary restrictive pattern.

Nevertheless, the prevalence of pulmonary impairment in present study was 17.80% of the screened patients and the prevalence of a restrictive pulmonary impairment was 15.8% which is higher as other populations where the prevalence of pulmonary restrictive impairment varies from 6.5 to 12.3% (NHANES III 2007-2010; Guerra et al., 2010, Kurth & Hnizdo, 2015, 0tata 1999). However, this comparison is not possible since our study population is Hispanic diabetics living at high altitude (9,000FASL), whereas, other studies have used healthy participants, living at sea level or not more than 2,000 FASL and Hispanics are not completely represented. Out of 63 patients with pulmonary impairment, 33.33% showed a mixed pattern; combined obstruction and restriction rarely occurs and is more common caused by a combination of pulmonary parenchymal and non-pulmonary disorders (Diaz-Guzman, McCarthy, Siu, & Stoller, 2010). Nevertheless, pulmonary impairment severity was measured as one of the principal clinical significance of spirometry, mild restrictive pattern was found in 88.5% and severe restrictive pattern just in less than 2% of the impaired subjects. Finally, in the present population and in others (Mannino et al., 2012) the prevalence of

restrictive pattern was higher in women than in men; it might due to the low prevalence of men in this sample population (19.43%).

FVC values for pulmonary restrictive impairment diagnosis has a positive predictive value of 43%, sensitivity of 60-86% and specificity of 83-90%(Shawn, Dales, & Cardinal, 1999) and patients with this diagnosis need further analysis to confirm the restrictive impairment. Although, this study found some evidence of high values of FVC and FEV1 in highland Ecuadorian population might be due to long-term residence at high altitudes is known to affect pulmonary capacity and oxygen intake (Pollard et al., 1997). However, the evidence of increased values of FVC among highlands populations is mixed. Increases in FVC and FEV1 were observed at increasing altitudes in Hispanic Peruvian (4,105 masl (Valenzuela & Ramos, 2004), Tibetan and Indian (3300 masl, (Wood, Norboo, Lilly, Yoneda, & Eldridge, 2003) populations. In contrast Hispanic Colombian population did not show differences in PFT altitudes over 2,600 masl (Szeinuk, 2016) and in Nepalese Himalaya population showed a decreasing FVC and FEV1 unchanged values with increasing altitude (Mason et al., 2000). Therefore, since PFT are influenced by body height, gender, and ethnicity (Nepal, Das, & Bhaila, 2014), a prediction equation for PFT spirometry parameters should be established for the Ecuadorian population. Hence, future studies about the clinical significance of PFT in DM patients living at high altitudes should be performed.

Metabolic risk factors did not show a significant association with pulmonary restrictive impairment, probably because diabetes is not the only cause of developing pulmonary restrictive pattern. Increased BMI values are clearly associated with increased prevalence of DM (Bays, Chapman, & Grandy, 2007). Persons with a higher

BMI are thus expected to have restrictive pulmonary pattern (McClean, Kee, Young, & Elborn, 2008; Wannamethee, Shaper, & Whincup, 2005) due to a thicker and less flexible body wall (Zammit, Liddicoat, Moonsie, & Makker, 2010). In light of these findings, was expected that diabetics with a higher BMI would have a restrictive pulmonary pattern. Nevertheless, our results do not support that theory. Differences in chest dimensions due to ethnicity in pulmonary function (Whittaker, Sutton, & Beardsmore, 2005), intrauterine factors (Lawlor, Ebrahim, & Davey Smith, 2005), or other body-weight components (Mohamed et al., 2002; Rossi et al., 2008) may be the causes for the observed no-relationship between BMI and restrictive pulmonary pattern in the present study.

In this study, glycated hemoglobin used as a biomarker of optimal glucose control showed a low predictive capacity to distinguish patients with lung impairment from normal subjects. Previous studies have shown that higher values of HbA1c are associated with a restrictive pattern in type 2 DM patients (Lange et al., 1989; Pitocco et al., 2012).This result may be explained by the fact that the high blood glucose in diabetes patients is not the only cause of developing a pulmonary restrictive pattern. Additionally, metabolic risk factors such as total cholesterol, triglycerides, serum creatinine or duration of disease, unadjusted and adjusted by gender and smoking status, did not show a significant association with lung restrictive impairment. The low percentage of subjects who smoke might be attributable to cultural factors (women generally do not smoke) and economic factors (very low disposable income, tobacco cost). These factors also explain the low prevalence of the obstructive pattern due to the intrinsic relationship between the major causes of obstructive ventilatory diseases and

smoking (Laniado-Laborin, 2009; Tamimi, Serdarevic, & Hanania, 2012). Furthermore, younger patients showed a reduced risk of having restrictive pulmonary impairment, and those patients with higher values of HDL-c showed increased risk. These results are opposite to the cited literature, which lung impairment risk increased with age (Mirabelli et al., 2016; Pitocco et al., 2012) and higher values of HDL-c were considered a protective factor for cardio-metabolic diseases (Assmann & Gotto, 2004; Goldbourt, Yaari, & Medalie, 1997; Verdier et al., 2013). These findings might be explained by risk factors for chronic respiratory diseases (smoking, indoor and outdoor pollutants, allergens or occupational agents) are more likely to be related to developing pulmonary restrictive impairment than metabolic risk factors.

Considering that this study was carried out at one time point and it is unknown whether lung impairment occurred before, after, or during the onset of diabetes, causality cannot be inferred. Additionally, the dataset included only hypertension data, without other major comorbidities because patients with acute or chronic lung diseases were excluded from the study and LDL was calculated using a mathematical formula. Higher HDL-c values and triglycerides outlier values could have made the LDL-c values unreliable to associate with pulmonary restrictive pattern.

Even though this fixed population has its own ethnic particularities, their exercise habits at high altitude and daily medication intake (aspirin and cholesterol lowering drug) cannot completely explain the higher values of HDL-c and the higher values of HDL-c among those with the pulmonary restrictive pattern found in this cohort of patients. In this study population, we found high mean HDL-c value and several patients exhibited HDL-c values over 80 mg/dl. It is challenging to compare HDL-c values

between this and other populations because most of the available literature reports HDL-c values above 40 mg/dl for men and 50 mg/dl for women as “normal” since these are the standard HDL-c cut-offs for diagnoses of dyslipidemia and cardiovascular risk factors (Rodriguez et al., 2014). Nevertheless, HDL-c genetic mutations have been associated with elevated HDL-c levels.(Bromley et al., 2005; Yamashita et al., 2000). Thus, it is possible that the extreme values of HDL-c can be genetically inherited in this population of Hispanic type 2 DM patients. Additionally, patients who reside at high altitudes have been found to have high HDL-c values in some cases (Riyami et al., 2014; Vats et al., 2013) but not in others (Gonzales & Tapia, 2013; Málaga, Zevallos-Palacios, De Los, Lazo, & Huayanay, 2010). Hence, future studies will be necessary to assess whether genetic, physiological, or a combination of factors are related to high HDL-c values.

While there were good reasons to support the use of NHANES III spirometry reference values, this decision may have an FVC and FEV1 been faulty. NHANES III spirometry data described normal pulmonary function for three major ethnic groups: Caucasians, African-Americans, and Mexican-Americans. Even though there were no longitudinal, large-sample studies in Hispanic non-Mexican populations, we thought the similar body types observed in Mexicans and Ecuadorians might allow us to use NHANES III as Hispanic references values for spirometry tests. However, the percent predicted values of PFT in this Ecuadorian population might be higher than the reference values due to geographical location or ethnic factors, further studies will be necessary to discern these differences.

While the results of this study cannot be completely generalized to other Hispanic populations because this population resides in a location found over 2,820 masl, comparison to other highland populations is warranted. Most important this study addressed an overall insight of the prevalence of pulmonary impairment and related characteristics which are important in public health for assessing the burden of disease in a diabetes highland population, as long as with a descriptive analyses for diabetic population pulmonary function tests characteristics.

Further studies need to be performed to ascertain the factors that contribute to pulmonary impairment amongst people in highlands. First, prediction equation for PFT spirometry parameters should be established for Ecuadorian population. Second, PFT spirometry parameters should be compared comparison between highland and sea level Ecuadorian populations. Finally, studies should be conducted to investigate differences in pulmonary function among healthy and diabetic patients.

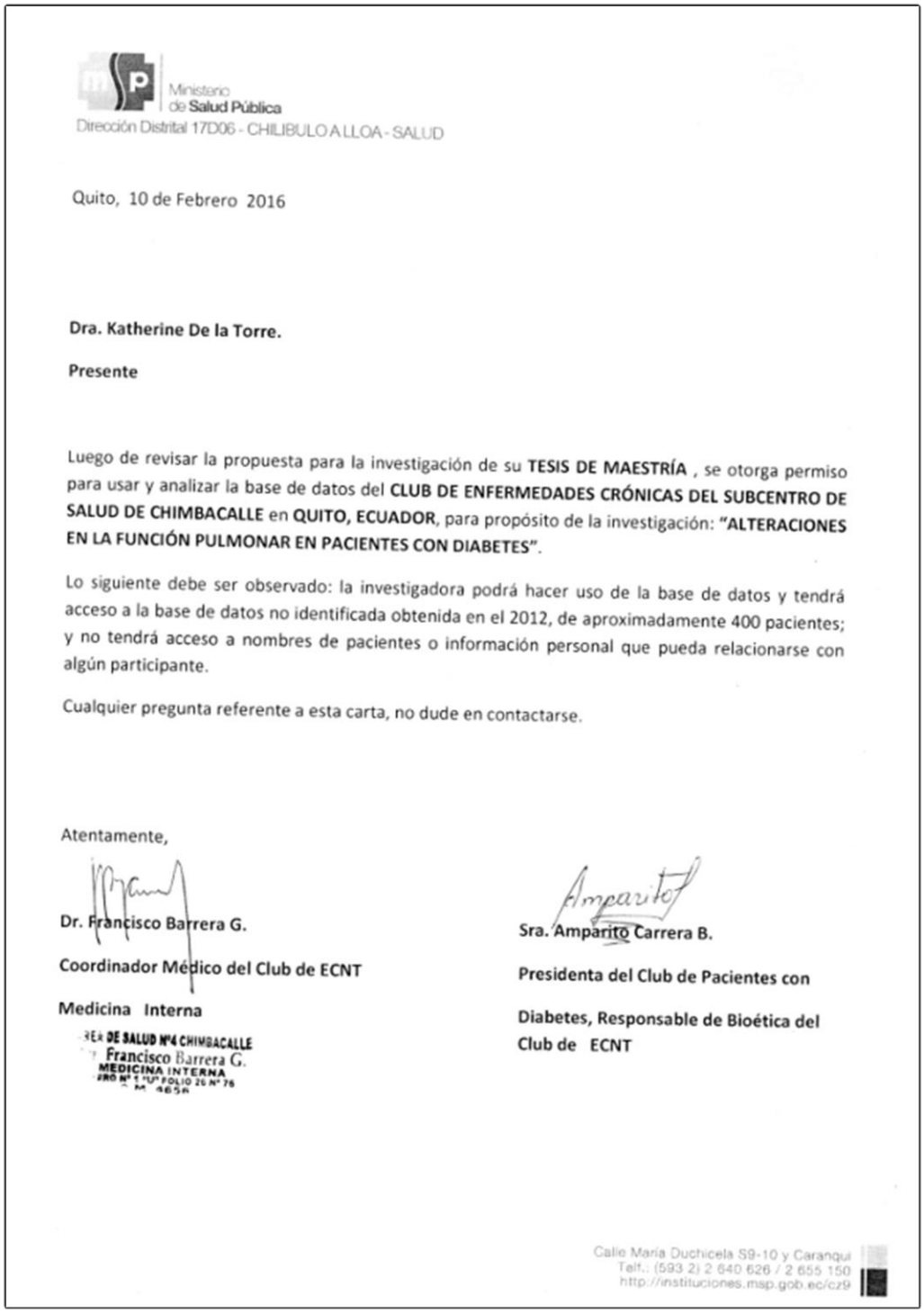
CHAPTER 5
CONCLUSIONS

Pulmonary function impairment should be considered as important as renal or cardiac function evaluation in diabetic patients. This study has shown a prevalence of 15.8% of pulmonary restrictive impairment among Hispanic diabetic population. Glycated hemoglobin was found to be a weak predict association with pulmonary impairment. Metabolic risk factors as lipid profile, BMI, and duration of disease were not statistical significant associated with lung restrictive impairment; however, subjects with restrictive lung impairment had lower mean age and higher mean HDL-c values than those with no lung impairment.

This study provided a basic information for further analysis of lung impairment in a diabetic highland Hispanic population and highlighted the importance of having spirometry reference values for this specific population regarding ethnicity and long-time high altitude residency.

APPENDIX
LETTER OF DATA USE PERMISSION

Letter of data use permission provided by the Chimbacalle Non-Communicable Diseases Club (CECNT Spanish acronyms). Spanish and English translated versions.



Ministerio de Salud Pública
Dirección Distrital 17D06 - CHILIBULO A LLOA - SALUD

Quito, 10 de Febrero 2016

Dra. Katherine De la Torre.

Presente

Luego de revisar la propuesta para la investigación de su **TESIS DE MAESTRÍA** , se otorga permiso para usar y analizar la base de datos del **CLUB DE ENFERMEDADES CRÓNICAS DEL SUBCENTRO DE SALUD DE CHIMBACALLE** en **QUITO, ECUADOR**, para propósito de la investigación: **"ALTERACIONES EN LA FUNCIÓN PULMONAR EN PACIENTES CON DIABETES"**.

Lo siguiente debe ser observado: la investigadora podrá hacer uso de la base de datos y tendrá acceso a la base de datos no identificada obtenida en el 2012, de aproximadamente 400 pacientes; y no tendrá acceso a nombres de pacientes o información personal que pueda relacionarse con algún participante.

Cualquier pregunta referente a esta carta, no dude en contactarse.

Atentamente,

Dr. Francisco Barrera G.

Coordinador Médico del Club de ECNT

Medicina Interna

DE SALUD Nº4 CHIMBACALLE
Francisco Barrera G.
MEDICINA INTERNA

Sra. Amparito Carrera B.

Presidenta del Club de Pacientes con

Diabetes, Responsable de Bioética del Club de ECNT

Calle María Duchicela S9-10 y Carangui
Telf.: (593 2) 2 640 626 / 2 655 150
http://instituciones.msp.gob.ec/cz9

February 10th, 2016

Dra. Katherine De la Torre.

Present.

I have reviewed your research thesis proposal and grant permission for you to use the dataset from **THE CHIMBACALLE NON-COMMUNICABLE DISEASES CLUB** located in **QUITO, ECUADOR** for the purpose of your research: **"SPIROMETRY IN TYPE 2 DIABETES MELLITUS: THE RELATIONSHIP BETWEEN PULMONARY FUNCTION AND METABOLIC RISK FACTORS"**

The following stipulations should be observed: the researcher only have access to a de-identified dataset gathered in 2012, and will not have access to the patient names or personal information that could link to any participant.

If you have any questions regarding this letter, do not hesitate to contact me.

Regards,

Francisco Barrera MD.
Medical Coordinator of
Chimbacalle Non-Communicable Diseases Club
Internal Medicine

Ms. Amparito Carrera
Director of
Chimbacalle Non-Communicable Diseases Club
Ethical Commision Board

LIST OF REFERENCES

Alwan, A., Armstrong, T., Cowan, M., & Riley, L. (2011). Noncommunicable Diseases Country Profiles 2011. *Who*, 1–207. http://doi.org/10.2471/BLT.07.045138

Assmann, G., & Gotto, A. (2004). HDL Cholesterol and Protective Factors in Atherosclerosis. *Journal of the American Heart Association*, *109*, 8–14. http://doi.org/10.1161/01.CIR.0000131512.50667.46

Athanazio, R. (2012). Airway disease: similarities and differences between asthma, COPD and bronchiectasis. *Clinics (São Paulo, Brazil)*, *67*(11), 1335–43. http://doi.org/10.6061/clinics/2012(11)19

Barreiro, T. J., & Perillo, I. (2004). An Approach to Interpreting Spirometry. *American Family Physician*, *69*(5), 1107–1114.

Bays, H. E., Chapman, R. H., & Grandy, S. (2007). The relationship of body mass index to diabetes mellitus, hypertension and dyslipidaemia: Comparison of data from two national surveys. *International Journal of Clinical Practice*, *61*(5), 737–747. http://doi.org/10.1111/j.1742-1241.2007.01336.x

Bromley, C., Moushumi, Chaudhury Craig, R., Deverill, C., Erens, B., Fuller, E., Gray, L., … Alison Prescott, 2 Kevin Pickering, 2 Paola Primatesta, 3 Shaun Scholes, 2 Nicola Shelton, 3 Svetlana Speight, 2 Emmanuel Stamatakis, 3 Heather Wardle, 2 Paola Zaninotto. (2005). The Scottish Health Survey 2003. In *The Scottish Health Survey 2003* (Vol. 1 Cardioav). Retrieved from http://www.scotland.gov.uk/Publications/2011/09/27084018/58

Cavailles, A., Brinchault-Rabin, G., Dixmier, A., Goupil, F., Gut-Gobert, C., Marchand-Adam, S., … Diot, P. (2013). Comorbidities of COPD. *European Respiratory Review*, *22*(130), 454–475. http://doi.org/10.1183/09059180.00008612

CDC. (2015). Spirometry Training Program. NHANES III references values. Retrieved from http://www.cdc.gov/niosh/topics/spirometry/nhanes.html

Chatila, W. M., Thomashow, B. M., Minai, O. a., Criner, G. J., & Make, B. J. (2008). Comorbidities in chronic obstructive pulmonary disease. *Proceedings of the American Thoracic Society*, *5*(4), 549–555. http://doi.org/10.1513/pats.200709-148ET

Davis, W., Knuiman, M., Kendall, P., Grange, V., & Davis, T. (2004). Glycemic Exposure Is Associated With Reduced Pulmonary Function in Type 2 Diabetes. The Fremante Diabetes Study. *Diabetes Care*, *27*, 752:757.

Diaz-Guzman, E., McCarthy, K., Siu, A., & Stoller, J. K. (2010). Frequency and causes of combined obstruction and restriction identified in pulmonary function tests in adults. *Respiratory Care*, *55*(3), 310–316. Retrieved from http://ezproxy.fiu.edu/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=rzh&AN=2010586535&site=ehost-live&scope=site

Ehrlich, S., Quesenberry, C., Eeden, S., Shan, J., & Ferrara, A. (2010). Patients diagnosed with diabetes are at increased risk for asthma, chronic obstructive pulmonary disease, pulmonary fibrosis, and pneumonia but not lung cancer. *Diabetes Care*, *33*(1), 55–60. http://doi.org/10.2337/dc09-0880.

Fimognari, F. L., Pasqualetti, P., Moro, L., Franco, A., Piccirillo, G., Pastorelli, R., … Incalzi, R. A. (2007). The association between metabolic syndrome and restrictive ventilatory dysfunction in older persons. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, *62*(7), 760–5. http://doi.org/10.1093/gerona/62.7.760

Godfrey, M. S., & Jankowich, M. D. (2016). The vital capacity is vital epidemiology and clinical significance of the restrictive spirometry pattern. *Chest*, *149*(1), 238–251. http://doi.org/10.1378/chest.15-1045

Goldbourt, U., Yaari, S., & Medalie, J. H. (1997). Isolated low HDL cholesterol as a risk factor for coronary heart disease mortality. A 21-year follow-up of 8000 men. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *17*(1), 107–113. http://doi.org/10.1161/01.ATV.17.1.107

Gonzales, G. F., & Tapia, V. (2013). Association of high altitude-induced hypoxemia to lipid profile and glycemia in men and women living at 4100m in the Peruvian Central Andes. *Endocrinología Y Nutrición (English Edition)*, *60*(2), 79–86. http://doi.org/10.1016/j.endoen.2012.06.010

Guerra, S., Sherrill, D. L., Venker, C., Ceccato, C. M., Halonen, M., & Martinez, F. D. (2010). Morbidity and mortality associated with the restrictive spirometric pattern: a longitudinal study. *Thorax*, *65*(6), 499–504. http://doi.org/10.1136/thx.2009.126052

Gulcan, E., Bulut, I., Toker, A., & Gulcan, A. (2009). Evaluation of glucose tolerance status in patients with asthma bronchiale. *The Journal of Asthma : Official Journal of the Association for the Care of Asthma*, *46*(2), 207–209. http://doi.org/10.1080/02770900802627302

Hickson, D., Burchfiel, C., Lui, J., Petrini, M., Harrison, K., White, W., & Sarpong, D. (2011). Diabetes, Impaired Glucose Tolerance, and Metabolic Biomarkers in Individuals with Normal Glucose Tolerance are Inversely Associated with Lung Function: The Jackson Heart Study. *Lung*, *189*(4), 520–529. http://doi.org/doi:10.1007/s00408-011-9296-1

I., A. A. E.-A., Hamdy, G., Amin, M., & Rashad, A. (2013). Pulmonary function changes in diabetic lung. *Egyptian Journal of Chest Diseases and Tuberculosis*, *62*(3), 513–517. http://doi.org/10.1016/j.ejcdt.2013.07.006

IDF. (2013). *Diabetes Atlas*. *International Diabetes Federation*.

King, Hilary. Aubert, Ronald. Herman, W. (1998). Global Burden of Diabetes, 1995–2025. *Diabetes Care*, *21*(9), 1414–1431. http://doi.org/10.2337/diacare.21.9.1414

Kurth, L., & Hnizdo, E. (2015). Change in prevalence of restrictive lung impairment in the U.S. population and associated risk factors: the National Health and Nutrition Examination Survey (NHANES) 1988-1994 and 2007-2010. *Multidisciplinary Respiratory Medicine*, *10*(1), 7. http://doi.org/10.1186/s40248-015-0003-6

Lange, P., Groth, S., Kastrup, J., Mortensen, J., Appleyard, M., Nyboe, J., … Schnorh, P. (1989). Diabetes mellitus, plasma glucose and lung function in a cross-sectional population study. *European Respiratory Journal*, *2*(1), 14–19.

Laniado-Laborin, R. (2009). Smoking and chronic obstructive pulmonary disease (COPD). Parallel epidemics of the 21st century. *International Journal of Environmental Research and Public Health*, *6*(1), 209–224. http://doi.org/10.3390/ijerph6010209

Lawlor, D. A., Ebrahim, S., & Davey Smith, G. (2005). Association of birth weight with adult lung function: findings from the British Women's Heart and Health Study and a meta-analysis. *Thorax*, *60*(10), 851–8. http://doi.org/10.1136/thx.2005.042408

Leone, N., Courbon, D., Thomas, F., Bean, K., Jégo, B., Leynaert, B., … Zureik, M. (2009). Lung function impairment and metabolic syndrome the critical role of abdominal obesity. *American Journal of Respiratory and Critical Care Medicine*, *179*(6), 509–516. http://doi.org/10.1164/rccm.200807-1195OC

Litonjua, A. A., Lazarus, R., Sparrow, D., DeMolles, D., & Weiss, S. T. (2005). Lung function in type 2 diabetes: The Normative Aging Study. *Respiratory Medicine*, *99*(12), 1583–1590. http://doi.org/10.1016/j.rmed.2005.03.023

Málaga, G., Zevallos-Palacios, C., De Los, M., Lazo, Á., & Huayanay, C. (2010). Elevada Frecuencia De Dislipidemia Y Glucemia Basal Alterada En Una Población Peruana De Altura* High Frequency of Dyslipidemia and Impaired Fasting Glycemia in a High Altitude Peruvian Population. *Rev Peru Med Exp Salud Publica*, *27*(4), 557–61.

Mannino, D., Buist, A., Petty, T., Enright, P., & Redd, S. (2003). Lung function and mortality in the United States: data from the First National Health and Nutrition Examination Survey follow up study. *Thorax*, *58*, 388–393.

Mannino, D., McBurnie, M., Tan, W., Kocabas, A., Anto, J., Vollmer, W., & Buist, A. (2012). Restricted spirometry in the burden of lung disease study. *International Journal of Tuberculosis and Lung Disease*, *16*(10), 1405–1411. http://doi.org/10.5588/ijtld.12.0054

Mansi, R., Joshi, S. V., Pandloskar, S. R., & Dhar, H. L. (2007). Correlation between blood sugar, cholesterol and asthma status. *Indian Journal of Allergy, Asthma and Immunology*, *21*(1), 31–34.

McClean, K. M., Kee, F., Young, I. S., & Elborn, J. S. (2008). Obesity and the lung: 1. Epidemiology 1. *Thorax*, *63*(1468-3296 (Electronic)), 649–654. http://doi.org/http://dx.doi.org/10.1136/thx.2007.086801

McKeever, T. M., Weston, P. J., Hubbard, R., & Fogarty, A. (2005). Lung function and glucose metabolism: An analysis of data from the Third National Health and Nutrition Examination Survey. *American Journal of Epidemiology*, *161*(6), 546–556. http://doi.org/10.1093/aje/kwi076

Miller, M. R., Crapo, R., Hankinson, J., Brusasco, V., Burgos, F., Casaburi, R., … ATS/ERS Task Force. (2005). General considerations for lung function testing. *The European Respiratory Journal : Official Journal of the European Society for Clinical Respiratory Physiology*, *26*(1), 153–161. http://doi.org/10.1183/09031936.05.00034505

Miller, M. R., Hankinson, J., Brusasco, V., Burgos, F., Casaburi, R., Coates, A., … Wagner, J. (2005). Standardisation of spirometry. *European Respiratory Journal*, *26*(2), 319–338. http://doi.org/10.1183/09031936.05.00034805

Mirabelli, M. C., Preisser, J. S., Loehr, L. R., Agarwal, S. K., Barr, R. G., Couper, D. J., … London, S. J. (2016). Lung function decline over 25 years of follow-up among black and white adults in the ARIC study cohort. *Respiratory Medicine*, *113*, 57–64. http://doi.org/10.1016/j.rmed.2016.02.003

Mohamed, E. I., Maiolo, C., Iacopino, L., Pepe, M., Di Daniele, N., & De Lorenzo, A. (2002). The impact of body-weight components on forced spirometry in healthy Italians. *Lung*, *180*(3), 149–159. http://doi.org/10.1007/s004080000089

NCD-RisC. (2016). Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4·4 million participants. *The Lancet*, *387*(10027), 1513–1530. http://doi.org/10.1016/S0140-6736(16)00618-8

Oh, H., Park, J. H., Lee, C. H., & Park, J. S. (2015). The association of normal range glycated hemoglobin with restrictive lung pattern in the general population. *PLoS ONE*, *10*(2), 1–10. http://doi.org/10.1371/journal.pone.0117725

Pellegrino, R., Viegi, G., Brusasco, V., Crapo, R. O., Burgos, F., Casaburi, R., … Wanger, J. (2005). Interpretative strategies for lung function tests. *European Respiratory Journal*, *26*(5), 948–968. http://doi.org/10.1183/09031936.05.00035205

Pitocco, D., Fuso, L., Conte, E. G., Zaccardi, F., Condoluci, C., Scavone, G., … Ghirlanda, G. (2012). R EVIEW The Diabetic Lung - A New Target Organ ?, 23–35. http://doi.org/10.1900/RDS.2011.9.23

Pollard, A. J., Barry, P. W., Mason, N. P., Collier, D. J., Pollard, R. C., Pollard, P. F., … Milledge, J. S. (1997). Hypoxia, hypocapnia and spirometry at altitude. *Clinical Science (London, England : 1979)*, *92*(6), 593–598.

Riyami, N. B. Al, Banerjee, Y., Al-Waili, K., Rizvi, S. G., Al-Yahyaee, S., Hassan, M. O., … Bayoumi, R. a. (2014). The Effect of Residing Altitude on Levels of High-Density Lipoprotein Cholesterol: A Pilot Study From the Omani Arab Population. *Angiology*, *66*(6), 568–73. http://doi.org/10.1177/0003319714544355

Rodriguez, C. J., Daviglus, M. L., Swett, K., Gonz??lez, H. M., Gallo, L. C., Wassertheil-Smoller, S., … Kaplan, R. C. (2014). Dyslipidemia patterns among Hispanics/Latinos of diverse background in the United States. *American Journal of Medicine*, *127*(12), 1186–1194.e1. http://doi.org/10.1016/j.amjmed.2014.07.026

Rossi, A., Fantin, F., Di Francesco, V., Guariento, S., Giuliano, K., Fontana, G., … Zamboni, M. (2008). Body composition and pulmonary function in the elderly: a 7-year longitudinal study. *International Journal of Obesity*, *32*(9), 1423–1430. http://doi.org/10.1038/ijo.2008.103

Scarlata, S., Costanzo, L., Giua, R., Pedone, C., & Incalzi, R. A. (2012). Diagnosis and prognostic value of restrictive ventilatory disorders in the elderly: A systematic review of the literature. *Experimental Gerontology*, *47*(4), 281–289. http://doi.org/10.1016/j.exger.2012.02.001

Shawn, A., Dales, R., & Cardinal, P. (1999). How accurate is spirometry at predicting restrictive pulmonary imapirment. *Chest*, *115*(i3), 869.

Tamimi, A., Serdarevic, D., & Hanania, N. A. (2012). The effects of cigarette smoke on airway inflammation in asthma and COPD: Therapeutic implications. *Respiratory Medicine*, *106*(3), 319–328. http://doi.org/10.1016/j.rmed.2011.11.003

Valenzuela, M., & Ramos, E. (2004). Medicion de la Capacidad Vital Forzada por Espirometria en habitantes adultos naturales de Junin. (4105m.s.n.m). *Revista de La Sociedad Peruana de Neumologia*, *48*(2).

Vats, P., Ray, K., Majumadar, D., Amitabh, Joseph, D. A., Bayen, S., … Singh, S. B. (2013). Changes in cardiovascular functions, lipid profile, and body composition at high altitude in two different ethnic groups. *High Altitude Medicine _ Biology*, *14*(1), 45–52. http://doi.org/10.1089/ham.2012.1071

Verdier, C., Martinez, L. O., Ferrières, J., Elbaz, M., Genoux, A., & Perret, B. (2013). Targeting high-density lipoproteins: Update on a promising therapy. *Archives of Cardiovascular Diseases*, *106*(11), 601–611. http://doi.org/10.1016/j.acvd.2013.06.052

Walter, R. E., Beiser, A., Givelber, R. J., O'Connor, G. T., & Gottlieb, D. J. (2003). Association between glycemic state and lung function: The Framingham Heart Study. *American Journal of Respiratory and Critical Care Medicine*, *167*(6), 911–916. http://doi.org/10.1164/rccm.2203022

Wannamethee, S., Shaper, A., & Whincup, P. (2005). Body fat distribution, body composition, and respiratory function in elderly men. *The American Journal of Clinical Nutrition*, *82*, 996–1003. Retrieved from http://discovery.ucl.ac.uk/162357/

Whittaker, a L., Sutton, a J., & Beardsmore, C. S. (2005). Are ethnic differences in lung function explained by chest size? *Archives of Disease in Childhood. Fetal and Neonatal Edition*, *90*(5), F423–8. http://doi.org/10.1136/adc.2004.062497

Wood, S., Norboo, T., Lilly, M., Yoneda, K., & Eldridge, M. (2003). Cardiopulmonary function in high altitude residents of Ladakh. *High Altitude Medicine and Biology*, *4*(4), 445–454. Retrieved from http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L38072352\nhttp://dx.doi.org/10.1089/152702903322616191\nhttp://sfx.umd.edu/hs?sid=EMBASE&issn=15270297&id=doi:10.1089/152702903322616191&atitle=Cardiopulmonary+function+in+high+alti

Yamane, T., Yokoyama, A., Kitahara, Y., Miyamoto, S., Haruta, Y., Hattori, N., … Kohno, N. (2013). Cross-sectional and prospective study of the association between lung function and prediabetes. *BMJ Open*, *3*(2), 1–7. http://doi.org/10.1136/bmjopen-2012-002179

Yamashita, S., Maruyama, T., Hirano, K. I., Sakai, N., Nakajima, N., & Matsuzawa, Y. (2000). Molecular mechanisms, lipoprotein abnormalities and atherogenicity of hyperalphalipoproteinemia. *Atherosclerosis*, *152*(2), 271–285. http://doi.org/10.1016/S0021-9150(00)00574-8

Yeh, H.-C., Punjabi, N. M., Wang, N.-Y., Pankow, J. S., Duncan, B. B., Cox, C. E., … Brancati, F. L. (2008). Cross-Sectional and Prospective Study of Lung Function in Adults With Type 2. *Diabetes Care*, *31*(4). http://doi.org/10.2337/dc07-1464.Abbreviations

Zammit, C., Liddicoat, H., Moonsie, I., & Makker, H. (2010). Obesity and respiratory diseases. *International Journal of General Medicine*, *3*, 335–343. http://doi.org/10.2147/IJGM.S11926

BIOGRAPHICAL SKETCH

Katherine A. De la Torre is a native of Quito, Ecuador. She received a Medical Degree from the Pontifical Catholic University of Ecuador in 2012. Additionally, she graduated from the University of Florida's Department of Epidemiology master's program in summer 2016. Her area of interested is in epidemiology of non-communicable and endocrinology diseases.