Factors Associated with FEV1 Decline in Alpha-1 Antitrypsin Deficient Patients

Radmila Choate, MPH [1], David M. Mannino, MD [1], Kristen E. Holm, PhD, MPH [2], Robert A. Sandhaus, MD, PhD [2]

[1] Department of Preventive Medicine and Environmental Health, University of Kentucky- Lexington, KY/US

[2] National Jewish Health, Denver, CO/US

Background

- Longitudinal decline in pulmonary function is common in patients with Alpha-1 Antitrypsin deficiency (AATD). It is known to be variable and usually is assessed as annual change in FEV1.
- The present study utilizes uniquely rich spirometry data of the **Step Forward Study** (SFS) to examine pulmonary function among AATD population and to identify factors associated with FEV1 decline.

Introduction

- SFS is a prospective (n=500) double-blind randomized 1:1 controlled trial evaluating a multi-component distance intervention (exercise aids such as Therabands, weights, peddlers, and nutritional guidance) versus standard of care (Alpha-1 Disease Management and Prevention program (ADMAP)) in improving health outcomes among individuals with AATD.

Inclusion Criteria:

- Males or females age ≥ 18 years at the time of entry
- Diagnosis of alpha-1 antitrypsin deficiency
- Evidence of pulmonary disease with one or more of the following:
  - FEV_1 < 80% predicted and FEV_1/FVC < 0.70
  - Emphysema on a previous CT scan of the chest
  - Receiving augmentation therapy for lung disease
- Accessible by telephone
- Ability and willingness to complete monthly and semi-annual questionnaires by telephone interview
- Ability and willingness to provide informed consent

Spirometry:

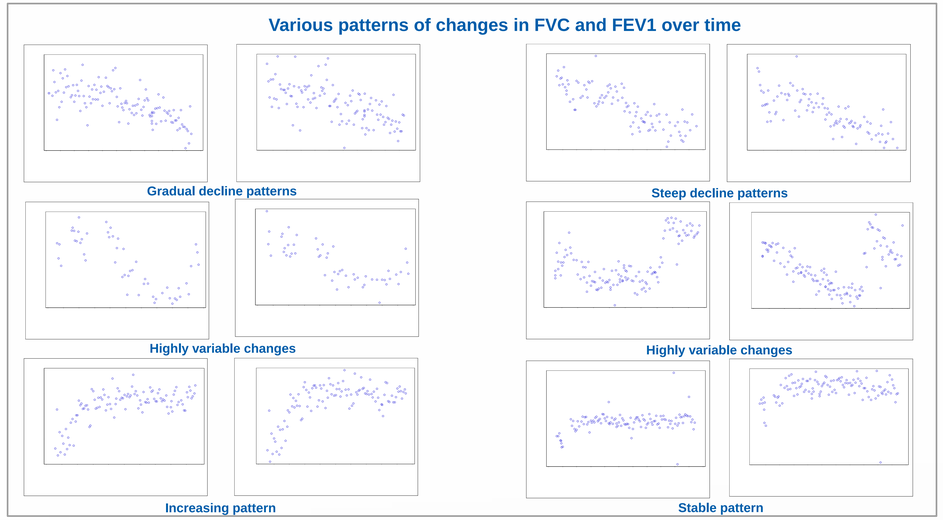
- Throughout the 5-year-long follow-up period, self-reported spirometry data was collected on a bi-weekly and daily (during exacerbations) basis with over twenty thousand valid pulmonary function data observations.
- Spirometry was assessed by providing each participant a high-end NDD EasyOne mass-flow sensing spirometer pre-programmed with the subject's height, birth date, sex, and race.
- Spirometry, including FEV1, FVC, FEF25-75, PEF, and flow-volume loop was obtained using strict ATS criteria as designed into the unit.
- Each participant received telephonic training by AlphaNet Coordinators in proper spirometer use and spirometer data download.
- Data was transferred to AlphaNet via mailing of flash memory cards from each spirometer every two-three months.

Materials and Methods

Data Analysis:

- The present analyses included 248 participants who provided at least four spirometry measurements/year for at least three years.
- Mean annual FEV1 were analyzed using repeated measures analysis stratified by the intervention group.
- Mean annual decline in FEV1 (ml/year) was calculated using baseline and last FEV1 values, and analyzed unadjusted and adjusted for age, gender, adherence to ADMAP, ever smoking and baseline FEV1.
- All statistical analyses were performed using SAS v9.4.

Scatter Plots of Select Measured Values for FVC, FEV1



SFS Study Events

Interventions

Intervention 1- Oct 2009	Exercise bands and exercise poster with instructions
Intervention 2- Jul 2010	SFS Diet and Nutrition small group teleconference live and audio recordings organized by BMI groups
Intervention 3- Feb 2011	SFS "Breathing Techniques in Alpha-1" instructional DVD
Intervention 4- Jul 2011	"Ask the Dr. Intervention"-a series of small group teleconferences presented by Dr. Sandhaus in which registered participants could ask questions regarding diet and exercise
Intervention 5- Feb 2012	Exercise Ball (tailored to each participant's height) with accompanying instructional poster
Intervention 6- Jul 2012	Exercise Peddler
Intervention 7- Apr-Nov 2013	AlphaNet's Virtual Pulmonary Rehabilitation (VPR) Program VPR teleconferences conducted in May, August and November 2013 VPR participants were asked to mail to AlphaNet a Pre and Post-Assessment /Fitness Card at the beginning and end of the VPR program

Mailings to Both Control and Intervention Groups

○ **Spirometers**	• NDD EasyOne mass-flow spirometers, pre-programmed with respondent's individual measurements of height, gender, race, DOB • Letter on proper procedure for spirometer data download • Eleven subsequent spirometer downloads and flash drive exchanges
○ University of San-Diego Self-Assessment tool	
○ Pedometers accompanied by a letter on its proper use	
○ Harmonica with instructional pamphlet	
○ "Physiology of exercise" audio recording by Dr. Sandhaus	
○ AlphaNet Family Cookbook	
○ Pulse Oximeter with a log for daily recordings	
○ iPads with AlphaNet app for personal data recording and instructional manual	

Results

- In the total cohort the average age was 59.3+8.8 years, mean FEV1% predicted at baseline was 37.6 (SD=16.4).
- In the intervention group (n=124, mean age: 58.6 years, 48.7% males), mean FEV1% predicted was 34.6 (SD=13.9).
- In the control group (n=124, mean age: 60.0 years, 46.2% males) mean FEV1% predicted was 40.5 (SD=18.1).

	Overall N=248	Intervention group N=124	Control group N=124
Age Mean (SD)	59.3 (8.8)	58.6 (7.7)	60.0 (9.4)
Gender Male, n (%)	117 (47.2)	60 (48.7)	57 (46.2)
FEV1 % predicted at baseline Mean (SD)	37.6 (16.4)	34.6 (13.9)	40.5 (18.1)

Repeated measures analysis:

- The results of the repeated measures analysis demonstrated a significant effect of time on change in FEV1 (F=6.51, p=0.002).
- There was no significant effect of intervention on change in FEV1 over time (F=0.63, p=0.53).
- Mean annual FEV1 decline of the total cohort was -15.2 ml/year (SD=64.9), (intervention group: -21.0 ml/ year (SD=48.0), control group: -9.37 ml/year (SD=78.2), p=0.16).
- Controlling for other variables in the model, mean annual FEV1 decline was positively associated with baseline FEV1 (p<0.001).

Conclusion

Annual decline in pulmonary function was associated with baseline FEV1, which supports previous research. Exposure to intervention had no significant impact on lung function. The relatively modest annual decline in lung function observed in this study may reflect the use of augmentation therapy by 97.4% of SFS participants.

Interesting longitudinal patterns were identified in individual lung function measurements over time.

These findings suggest the need for additional studies to better understand the variability of lung function change in patients with AATD.

References

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