Relation of Chronic Obstructive Pulmonary Disease to Atrial and Ventricular Arrhythmias

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Chronic obstructive pulmonary disease (COPD) is associated with increased cardiovascular morbidity and mortality, yet the exact pathophysiological links remain unclear. Whether the presence and severity of COPD are associated with atrial or ventricular arrhythmias recorded on continuous electrocardiographic monitoring is unknown. We identified consecutive adult patients who underwent clinically indicated pulmonary function testing as well as 24-hour Holter monitoring at the Mayo Clinic, Rochester, from 2000 to 2009. Demographic data and relevant co-morbidities were gathered from the electronic medical record; severity of COPD was classified according to the GOLD classification, and arrhythmias were classified in concordance with the current clinical guidelines. From 7,441 patients who were included (age 64 ± 16 years, 49% woman, 92% Caucasian), COPD was diagnosed in 3,121 (41.9%). Compared with those without COPD, the presence and severity of COPD were associated with increased likelihood of atrial fibrillation/atrial flutter (AF/AFL; 23.3% vs 11.0%, respectively, p <0.0001), nonsustained ventricular tachycardia (NSVT; 13.0% vs 5.9%, respectively, p <0.0001), and sustained ventricular tachycardia (0.9% vs 1.6%, respectively, p <0.0001). COPD remained a significant predictor of AF/AFL and NSVT (p <0.0001 and p <0.0001, respectively) after adjusting for age, gender, tobacco use, obesity, hypertension, coronary artery disease, heart failure, diabetes, anemia, cancer, chronic kidney disease, and rate/rhythm control medications. In conclusion, the independent association between the presence and severity of COPD and arrhythmias (AF/AFL and NSVT) provides further insight into the markedly increased cardiovascular mortality of patients with COPD. Further studies should explore which anti-arrhythmic strategies would best apply to the patients with COPD. **(Am J Cardiol 2014;114:272−277)**

In the United States, chronic obstructive pulmonary disease (COPD) ranks as the fourth leading cause of mortality, second leading cause of morbidity, and it remains the only common mortality etiology that continues to rise (COPD deaths increased by 58% from 1990 to 2010).[1] Large prospective and retrospective studies of patients with COPD showed that the most common causes of their demise were cardiovascular events,[2] and limited evidence suggests that some could be in part due to arrhythmias.[3,4] Previous studies using continuous electrocardiographic (ECG) monitoring in patients with COPD were limited in scope (largest n = 75)[5−7] and did not stratify COPD by its objectively documented severity. Knowing whether COPD is associated with arrhythmias could be crucial in appropriately directing our efforts aimed at reversing the alarming rise in COPD-related cardiovascular mortality in the United States and also around the World. We hypothesized that the most clinically significant arrhythmias (atrial fibrillation [AF], nonsustained ventricular tachycardia [NSVT], and sustained ventricular tachycardia [SustVT]) would be more commonly seen on 24-hour ECG Holter monitors of patients with COPD compared with patients without COPD, and that the severity of COPD would correlate with the prevalence of these arrhythmias.

Methods

This study protocol was approved by the Mayo Clinic Institutional Review Board. We retrospectively identified and searched the medical records at our institution for all unique adult patients who underwent clinically indicated 24-hour ECG Holter monitoring between the years 2000 and 2009. From this cohort, we identified those patients who performed pulmonary function testing (PFT) in our laboratory (spirometry variables necessary for inclusion: FEV1 and FVC). Relevant demographic variables, co-morbid

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Table 1
Patient characteristics

Variable	COPD				p
	No (n = 4,320)	Mild/Mod. (n = 2,239)	Severe (n = 698)	Very Severe (n = 184)	
Age (years)	59.8 ± 16.7	70.8 ± 11.6	71.6 ± 10.6	69.9 ± 11.9	
Women	2,533 (59%)	846 (38%)	239 (34%)	54 (29%)	<0.0001
Body mass index (kg/m^2)	29.0 ± 6.2	28.7 ± 5.7	28.9 ± 6.6	26.9 ± 6.5	0.0078
Forced expiratory volume in 1 second (percent predicted)	0.97 ± 0.11	0.72 ± 0.14	0.41 ± 0.06	0.24 ± 0.04	<0.0001
Forced vital capacity (percent predicted)	0.97 ± 0.11	0.88 ± 0.15	0.62 ± 0.13	0.49 ± 0.13	<0.0001
Forced expiratory volume in 1 second/forced vital capacity	0.79 ± 0.05	0.63 ± 0.06	0.53 ± 0.10	0.40 ± 0.11	<0.0001
Smoker	406 (9%)	311 (14%)	130 (19%)	36 (20%)	<0.0001
Coronary artery disease	1,877 (43%)	1,424 (64%)	452 (65%)	117 (64%)	<0.0001
Heart failure	894 (21%)	826 (37%)	343 (49%)	108 (59%)	<0.0001
Diagnosed hypertension	2,799 (65%)	1,741 (78%)	529 (76%)	136 (74%)	<0.0001
Anemia*	1,628 (38%)	1,024 (46%)	338 (48%)	94 (51%)	<0.0001
Diabetes mellitus	891 (21%)	578 (26%)	228 (33%)	55 (30%)	<0.0001
Chronic kidney disease	512 (12%)	434 (19%)	164 (23%)	45 (24%)	<0.0001
Diagnosed cancer	821 (19%)	688 (31%)	201 (29%)	53 (29%)	<0.0001
β-blocker use	887 (21%)	623 (28%)	187 (27%)	33 (18%)	<0.0001
Calcium channel antagonist use	240 (6%)	168 (8%)	66 (9%)	23 (13%)	<0.0001
Amiodarone use	91 (2%)	56 (3%)	15 (2%)	7 (4%)	0.2703
Other antiarrhythmic medication use	305 (7%)	240 (11%)	103 (15%)	31 (17%)	<0.0001

Data are presented as mean ± standard deviation or number (%). The p-value pertains to the difference between all patients in the "No COPD" group versus all patients in the "COPD" group.

* Anemia was defined as present if noted in the electronic medical record or International Classification of Diseases − 9th Revision coding system.

Table 2
Holter monitoring results stratified by the presence and severity of chronic obstructive pulmonary disease (COPD)

Variable	COPD				p
	No (n = 4,320)	Mild/Mod. (n = 2,239)	Severe (n = 698)	Very Severe (n = 184)	
Average heart rate (bpm)	74.6 ± 12.1	73.1 ± 12.6	75.8 ± 14.5	79.8 ± 15.2	0.0618
Minimum heart rate (bpm)	66.7 ± 11.3	65.8 ± 11.7	69.0 ± 13.8	72.6 ± 14.5	0.5150
Maximum heart rate (bpm)	89.6 ± 14.1	86.6 ± 14.5	88.1 ± 15.8	92.6 ± 16.5	<0.0001
Mean ventricular premature complexes	59.0 ± 203.8	94.0 ± 262.2	112.7 ± 261.5	134.8 ± 276.2	<0.0001
Number of ventricular premature complexes ≥ 30/hr	880 (20.4%)	641 (28.6%)	276 (39.5%)	80 (43.5%)	<0.0001
Mean atrial premature complex beats	36.0 ± 145.9	67.7 ± 234.9	73.8 ± 215.7	85.5 ± 355.1	<0.0001
Number of atrial premature complex ≥30/hr	592 (13.7%)	537 (24.0%)	185 (26.5%)	48 (26.1%)	<0.0001
Number of sinus pauses	0.5 ± 7.5	1.3 ± 10.2	1.2 ± 9.2	0.4 ± 4.7	0.0007
Atrial fibrillation/flutter	340 (11.0%)	357 (21.8%)	134 (26.0%)	40 (31.8%)	<0.0001
Nonsustained ventricular tachycardia	255 (5.9%)	256 (11.4%)	112 (16.1%)	39 (21.2%)	<0.0001
Sustained ventricular tachycardia	39 (0.9%)	30 (1.3%)	13 (1.9%)	6 (3.3%)	0.012

Data are presented as mean ± standard deviation or number (%). The p value pertains to the difference between all patients in the "No COPD" group versus all patients in the "COPD" group.

conditions, and medication use at the time of Holter monitoring were identified from the electronic medical record, Holter monitor patient log book, and the international classification of diseases codes. Exclusion criteria were (1) incomplete medical record, (2) restrictive or nonspecific pulmonary disease identified on PFT, and (3) patient's preference not to participate in research studies.

PFT was performed in the Mayo Clinic PFT Laboratory by a certified technician and the report then was read and confirmed by a board-certified pulmonary physician according to the current guidelines.[8] The CareFusion MS Body-Diffusion system using whole-body plethysmography was utilized for the lung volume estimation. Severity of COPD was classified in accordance with the current guidelines[8] in the following manner: (1) mild-to-moderate COPD defined as FEV1/FVC <0.7 and FEV1 percent predicted ≥0.5; (2) severe COPD defined as FEV1/FVC <0.7 and FEV1 percent predicted between 0.3 and 0.5 (0.3 ≤ FEV1 p < 0.5); and (3) very severe COPD defined as FEV1/FVC <0.7 and FEV1 percent predicted <0.3. Absence of COPD was defined as FEV1/FVC ≥0.7 and FEV1 percent predicted ≥0.8. Patients with restrictive or nonspecific pulmonary function test results were excluded.

Portable 3-channel Holter monitoring systems (Spacelabs Healthcare, Issaquah, Washington) were used for the 24 hours ECG recording, and the analysis was performed at