Potential Augmentation of the Risk of Ischemic Cerebrovascular Accident by Chronic Obstructive Pulmonary Disease in Patients with Atrial Fibrillation

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Background: Atrial fibrillation (AF) is a potent risk factor for ischemic cerebrovascular accident (ICVA). Inflammation is a potential pathogenic factor for atherosclerosis and ICVA. Chronic obstructive pulmonary disease (COPD) is associated with increased inflammatory markers. Subjects who frequently experience COPD and AF together may have higher risk of ICVA. The objective of the study is to compare the prevalence of ICVA in patients with atrial fibrillation and COPD together versus atrial fibrillation alone. *Methods:* Subjects diagnosed with COPD, AF, and ICVA were categorized into 3 groups: COPD, AF, and COPD plus AF. Prevalence of ICVA was compared. Confounding factors affecting ICVA risk were recorded: age, diabetes, hypertension, peripheral vascular disease, dyslipidemia, and congestive cardiac failure. *Results:* Total charts reviewed were 500: COPD alone 244, AF alone 188, and both together 68. ICVA was documented in 132 (26.4%) subjects. Prevalence of ICVA was 11.8% (COPD alone), 29.8% (AF alone), and 39.7% (AF plus COPD). COPD plus AF group had ICVA 2.05 (95% confidence interval [CI], 1.203-3.94; $P = .007$) times compared with others. ICVA was also higher in patients with AF only versus COPD only ($P < .001$). Logistic regression showed AF plus COPD was a stronger predictor of ICVA ($P = .001$) than AF only ($P = .07$) or COPD only ($P = .8$). Odds ratio for ICVA was 2.85 (CI, 1.57-5.16; $P = .001$) for AF plus COPD versus 1.81 (CI, .94-3.47; $P = .71$) for AF only and 1.08 (CI, .58-2.10; $P = .8$) for COPD only. *Conclusions:* COPD may increase the risk of ischemic stroke in subjects with AF. Presence of COPD may increase the risk of ischemic stroke in subjects with AF. **Key Words:** COPD—stroke—arrhythmia—inflammation—atherosclerosis.

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Annually, 15 million people worldwide experience a stroke; of these, 5 million die and another 5 million are left permanently disabled, placing immense burden on family and community. The World Health Organization estimates that a stroke occurs every 5 seconds.[1] Atrial fibrillation (AF) is the most common sustained arrhythmia[2] and confers an independent risk of stroke and death.[3] The role of inflammation in atherosclerosis and stroke has been well established.[4] Chronic obstructive pulmonary disease (COPD) with reduced lung function is associated with increased levels of systemic inflammatory markers which may have important pathophysiological and therapeutic implications.[5] COPD is also associated with higher rates of myocardial infarction (MI)[6] and an increased risk of developing cerebral microbleeds in deep or infratentorial locations.[7] About 14% of COPD subjects experience AF.[8] We identify COPD as a factor and inflammation as the mechanism of COPD as risk factor for ischemic stroke.

Methods

Hospital electronic medical records were screened to collect subjects who were diagnosed with either COPD or AF, over a period of 5 years from January 01, 2008, to December 31, 2012. All subjects were classified into 3 subgroups: only COPD, only AF, and COPD plus AF together. Charts were manually reviewed by more than 8 researchers and the following data were collected: age, presence of risk factors for ischemic cerebrovascular accident (ICVA), diabetes mellitus, hypertension, peripheral vascular disease (PVD), dyslipidemia, and congestive cardiac failure (CCF). Another list was generated by cross-screening with the diagnosis of ICVA and 2 groups were created: one with ICVA and the other without ICVA. Prevalence rates for ICVA were compared among the 3 groups: only COPD, only AF, and COPD plus AF together. The study was approved by the institutional review board at James A. Lovell Federal Health Care Center.

Statistical Methodology

Chi-square tests were performed to calculate odds ratios for ICVA for 3 groups. Logistic regression analysis was performed to evaluate whether COPD plus AF was found to be a significant predictor of ICVA while adjusting for all other independent predictors for ICVA.

Results

Total charts reviewed were 500: COPD alone 244, AF alone 188, and both together 68. ICVA was documented in 132 (26.4%) subjects. Prevalence of ICVA was 11.8% in patients with COPD alone, 29.8% in patients with AF alone, and 39.7% in AF plus COPD (Table 1).

Table 1. *Prevalence of ICVA in 3 groups*

Groups	CVA +	CVA −	Total
AF + COPD	27 (39.7%)	41 (60.3%)	68
AF	56 (29.8%)	132 (70.2%)	188
COPD	49 (20.1%)	195 (79.9%)	244
Total	132	368	500

Abbreviations: AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; ICVA, ischemic cerebrovascular accident.

In logistic regression model while adjusting for all significantly different confounding factors, AF plus COPD was found to be a strong predictor of ICVA ($P = .001$), much stronger than AF only ($P = .07$) or COPD only ($P = .8$). Odds ratio for ICVA was 2.85 (95% confidence interval [CI], 1.57-5.16; $P = .001$) for AF plus COPD versus 1.81 (CI, .94-3.47; $P = .71$) for AF only and 1.08 (CI, .58-2.10; $P = .8$) for COPD only.

Comparison of AF plus COPD Group with Only AF Group

Our sample comprised predominantly male subjects (98%), and gender difference across groups was not significant. AF plus COPD and only AF groups have a similar proportion of elderly subjects (>75 years; 62.4 versus 58.2%; $P = .06$), and subjects with CCF (44.1% versus 32.4%; $P = .1$), hypertension (76.5% versus 67.6%; $P = .21$), diabetes (27.9% versus 31.4%; $P = .64$), PVD (11.8% versus 9%; $P = .48$), and dyslipidemia (50% versus 52.1%; $P = .77$; Table 2).

Comparison of AF plus COPD Group with Only COPD Group

Our sample was comprised predominantly male subjects (98%), and gender difference across groups was not significant. AF plus COPD and only COPD groups have a similar proportion of subjects with diabetes (27.9% versus 27.9%; $P = 1$), PVD (11.8% versus 11.9%; $P = .1$), and dyslipidemia (50% versus 43.2%; $P = .33$).

AF plus COPD group has a higher proportion of elderly subjects (>75 years; 64.7% versus 32%; $P = .01$), hypertensive subjects (76.5 versus 61.5%; $P = .02$), and subjects with CCF (44.1% versus 16 %; $P = .001$).

Comparison of Only AF Group with Only COPD Group

Only AF group has a higher proportion of elderly subjects (>75 years; 51.6% versus 32%; $P < .001$) and subjects with CCF (32.4% versus 16%; $P = .001$) than only COPD group. Both groups have a similar proportion of subjects with hypertension (67.6% versus 61.5%; $P = .22$), diabetes (31.4% versus 27.9%; $P = .45$), PVD (9% versus 11.5%; $P = .43$), and dyslipidemia (52.1% versus 43.2%; $P < .08$).