Published in final edited form as:

Am Heart J. 2010 July ; 160(1): 95–101. doi:10.1016/j.ahj.2010.05.004.

Chronic Obstructive Pulmonary Disease after Myocardial Infarction in the Community

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Abstract

Background—Myocardial infarction (MI) and chronic obstructive pulmonary disease (COPD) are frequent and share common risk factors. Yet, studies on MI patients reported limited and conflicting results on the prevalence of COPD, its impact on outcome, and how these may have changed over time. We examined, in a geographically defined community, the prevalence of COPD in patients with MI, its impact on mortality, and how these associations changed over time.

Methods—Residents of Olmsted County, Minnesota who experienced an MI meeting standardized criteria from 1979 to 2007 were included (3438, 42% women, mean age 68±15 years). COPD was ascertained from the medical records.

Results—Of 3438 patients, 415 (12%) had COPD. During the study, COPD prevalence increased from 7% in 1979–1985 to 15% in 2000–2007, $p < 0.001$. Survival was worse among patients with COPD (5 years survival rate 46% {95%CI 41% to 52%} versus 68% {95%CI 66% to 70%} in those without COPD ($p < 0.01$). The association between COPD and death was independent of age and risk factors (adjusted HR 1.30, 95%CI 1.10 to 1.54; $p < 0.01$) and did not change over time.

Conclusions—In a large community of patients with MI, the prevalence of COPD increased over time and was associated with a marked increased risk of death after MI independently of age, risk factors, and comorbidity. This underscores the importance of this condition and the need to optimize care for these high-risk patients.

Myocardial infarction (MI) and chronic obstructive pulmonary disease (COPD) are both prevalent in the population,[1–3] thus it is not uncommon to encounter patients affected by both diseases.[4] In addition, these entities share common pathophysiological determinants such as smoking[5,6] and inflammation,[4,7] which play a role in the pathogenesis and outcomes of both diseases.

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Conflict of Interest: The authors state that they have no conflict of interest regarding the content of the article.

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Despite the links between these two diseases, there is limited data among patients with MI on the prevalence of COPD and on its impact on survival with few studies reporting discrepant results.[8–10] These studies consist chiefly of voluntary registries (SPRINT, PREMIER)[8, 10] or secondary analyses of clinical trials (VALIANT),[9,11] thus potentially affected by selection bias.[12] Population studies reported an increased risk of cardiovascular death among all subjects with COPD independently of smoking,[13] but did not examine this association after MI. Thus, it is still unclear whether COPD has an independent impact on the outcome of MI or whether it merely reflects the effect of smoking. Furthermore, although cardiovascular disease is the leading cause of death in patients with COPD,[14,15] evidence suggests that after MI, patients with COPD are less likely to receive optimal medical care than those without COPD,[10,16,17] with implications for survival.

Finally, epidemiologic studies suggest an increasing prevalence of COPD, but the magnitude of the problem and the importance of COPD among patients with MI remain unknown as the studies to date have not examined how the prevalence of COPD and its impact on post-MI survival may have changed over time.

Therefore, the goals of the present study were to address these gaps in knowledge by examining, in a geographically defined community, the prevalence of clinically diagnosed COPD among patients with a first MI, the characteristics and treatment of MI according to COPD status, the impact of COPD on mortality, and how these associations may have changed over time.

Methods

Study population-the Rochester Epidemiology Project

Rochester and Olmsted County, Minnesota, are relatively isolated from other urban centers, and nearly all medical care is delivered to local residents by a few providers. The characteristics of the population of Olmsted County are similar to those of US Whites.[18] Olmsted Medical Center, Mayo Clinic, and their affiliated hospitals provide comprehensive care in every specialty. Each provider uses a unified medical record system whereby all information is accumulated in a single file. The Rochester Epidemiology Project[18] has developed a indexing system resulting in the linkage of medical records from all sources of care used by the population and provides a rich infrastructure for outcomes research. This centralized system encompasses the records of a population of 124,277 at the 2000 census, which represent an estimated 3,600,000 person-years of health care.

All aspects of the study were approved by appropriate institutional review boards.

Ascertainment of myocardial infarction

MI was ascertained using standardized methods.[3,19] The medical record of patients discharged from Rochester hospitals in the period 1979–2007 with diagnoses compatible with an MI by the International Classification of Diseases, Ninth or Tenth Revision, was reviewed to validate the diagnosis using standardized criteria relying on cardiac pain, biomarkers, and Minnesota coding of the electrocardiogram.[20] The cohort consisted of patients with incident MI; thus, all patients with prior MI were excluded. Because of the change over time in normal values, peak creatine kinase (CK) ratio was defined as the ratio of the maximum CK value to the upper limit of normal. Time to presentation was defined as the interval (in hours) from the self-reported onset of acute symptoms to the first recorded ECG. Comorbidity was measured by the Charlson index, excluding COPD.[21] Clinical diagnoses were used to ascertain cardiovascular risk factors (hypertension, diabetes mellitus, hyperlipidemia, and familial coronary disease).

Definition of COPD

Information on COPD status was obtained by review of the entire medical record. Patients with documented chronic obstructive lung disease were included in the study but not patients with asthma. Pulmonary function tests were not performed in all patients, a limitation shared by other studies.[22,23] Hence, we could not use pulmonary function test results to further characterize COPD with post-bronchodilator reversibility assessment[2,24] due to selection bias and confounding by indication.

Follow-Up

Follow-up for death was provided through the community (inpatient and outpatient) medical records. The ascertainment of death incorporates death certificates filed in Olmsted County, autopsy reports, obituary notices, and electronic files of death certificates obtained from the State of Minnesota Department of Vital and Health Statistics.

Statistical Analysis

The data are presented as frequency or mean $\pm$ standard deviation. Characteristics were compared between patients with and without COPD with χ^2 tests for categorical variables and t-test for continuous variables. For highly skewed variables, presented as median and 25th–75th percentiles, the Kruskal-Wallis nonparametric test of rank scores was used. Logistic regression analysis was used to identify the baseline variables independently associated with COPD. Survival was determined by the Kaplan-Meier method. Patients were censored at the time of last follow-up. Univariate and multivariable Cox proportional hazards regression models were constructed to evaluate the risk of death according to the presence of COPD. Results were summarized as hazard ratios (HR) and 95% CI. Proportional hazards regression modeling was used to examine the independent effect of year on survival univariately and after adjusting for age and sex. Differences in time trends between COPD groups were examined by including interaction terms between year and COPD. The proportional hazards assumption was tested using Schoenfeld residuals and found to be valid. A P value less than 0.05 was considered statistically significant, except when testing for interactions when a P value up to 0.10 was considered significant.

Funding sources used to support the research and writing of this paper are grants from the Public Health Service, the National Institutes of Health (R01 HL59205, R01 HL72435), and by an American Heart Association Postdoctoral Greater Midwest Fellowship Award to Dr Bursi. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents.

Results

Between 1979 and 2007, 3454 incident MIs occurred in Olmsted County. Sixteen patients diagnosed with pulmonary fibrosis or restrictive lung disease were excluded, resulting in 3438 patients included in the analysis. Mean age at index was 68 $\pm$ 15 years, 42% were women. A clinical diagnosis of COPD was noted among 415 patients, corresponding to a 12% prevalence of COPD among patients with MI in the community. During the 29 years of the study, the prevalence of COPD increased more than 2-fold from 7% in the period 1979–1985, to 10% in 1986–1992, to 13% in 1993–1999, up to 15% in 2000–2007, $p<0.001$. (Figure 1) After adjustment for age, sex, and smoking and compared to the referent period 1979–1985, the odds ratio (OR) for COPD increased from 1.46 (95%CI, 0.98 to 2.18) in the period 1986–1992, to 1.87 (95%CI, 1.28 to 2.73) in 1993–1999, to 2.30 (95%CI, 1.60 to 3.30) in 2000–2007 ($p<0.001$).

Characteristics of patients with clinically defined COPD

Compared to patients without COPD, those with COPD were older, more likely to be smokers, to have hypertension, cancer diagnosis, and more comorbidities. They were less likely to have familial coronary disease and had lower body mass index. Patients with COPD more often presented with non-ST segment elevation MI (NSTEMI) and smaller biomarker increase, but they had a worse Killip class despite presenting earlier to the hospital. COPD patients were less likely to undergo reperfusion or revascularization during hospitalization and to receive beta-blockers at discharge, while they were more likely to be treated with angiotensin converting enzyme (ACE) inhibitors and diuretics. The length of hospital stay was similar in the two groups. (Table I)

Mortality

After a follow-up of 4.7 ± 4.6 years, 1462 patients died. Unadjusted survival was markedly reduced among patients with COPD compared to those without COPD ($p < 0.01$). The survival curves diverged early and this difference increased throughout the follow-up (Figure 2). At 5 years, survival was 46% (95%CI 41% to 52%) among patients with COPD versus 68% (95%CI 66% to 70%) in those without COPD, ($p < 0.01$). This equated to patients with COPD having an almost two-fold increased risk of death compared to those without COPD (unadjusted HR 1.88, 95%CI 1.63 to 2.15; $p < 0.01$). This association remained significant after adjustment for age, sex, smoking, hypertension, other comorbidities, NSTEMI, biomarker levels, Killip class, and treatment of MI (adjusted HR 1.30, 95% CI 1.10 to 1.54; $p < 0.01$) (Table II). Interactions between COPD and each of the confounding variables were tested and none were found to be significant.

The adverse association between COPD and death became stronger in more recent years ($p = 0.005$ for COPD by year interaction). Compared to patients without COPD, those with COPD had a 16% excess risk of death for MIs occurring in 1979–1985 (HR 1.16 95%CI, 0.82 to 1.64) which increased to more than two-fold for MIs occurring in 2000–2007 (HR 2.37, 95%CI, 1.85 to 3.04). However after adjustment for age and sex, and further adjustment for smoking, hypertension, other comorbidities, NSTEMI, biomarker levels, Killip class, and treatment of MI, the interactions between COPD and year of MI did not reach statistical significance (Table III).

Discussion

Among a large geographically-defined incident MI cohort, COPD was relatively frequent and carried an increased risk of death. The strong association between COPD and death following MI was independent of sex, and other major risk factors and was greater in younger patients. Over time, COPD has become more frequent and the association between COPD and increased risk of death, after adjustment for age and sex, remained stable over time.

COPD prevalence in the MI community

Studies on prevalence of COPD among patients with MI reported discrepant results. The PREMIER registry[10] reported a prevalence of COPD which was more than double (15.6%) that reported in the SPRINT registry (7%).[8] Herein, the prevalence of COPD among patients with MI was 12%. The SPRINT study enrolled patients who survived the acute phase of MI leading to a bias whereby COPD patients dying early were not enrolled leading to the lower prevalence of COPD among survivors. Conversely, the PREMIER registry, which also included MI survivors, used a “less strict” definition of COPD by including asthma. By including all individuals with a first MI and not including patients with asthma, we provide a more accurate estimate of the prevalence of COPD in the community.

Patient Characteristics

Patients with COPD were older, had more cardiovascular risk factors and comorbidities. They tended to have smaller infarcts but worse hemodynamic status (higher Killip class). Patients with COPD were treated more often with ACE inhibitors and diuretics, probably owing to the high prevalence of hypertension in this group and to concerns on the use of other drugs such as beta-blockers.[16] Indeed, they were less likely to receive beta-blockers, a drug that reduces mortality after MI and to undergo diagnostic tests and revascularization procedures (angioplasty or coronary bypass surgery). Our findings study resonates with previous observational data that patients with COPD are often denied the benefits of beta-blockers owing to concern about side effects.[16,25] Similarly, the reported higher perioperative mortality in patients with COPD[17] has resulted in a reluctance to refer these patients to more aggressive management.[10]

Mortality

Previous studies described an increased risk of cardiovascular events among patients with COPD free from cardiac disease.[26] However, few studies, most not current, have investigated the role of COPD on prognosis after MI, and reported controversial results as recently underscored.[27] The PREMIER study reported greater post-discharge mortality 1 year after MI among patients with COPD. This registry included MI survivors enrolled in 19 US centers, [10] therefore potentially reflecting survivor bias thereby underestimating the prognostic impact of COPD by excluding early deaths. Further, this study included patients with previous MI or coronary disease, and the distribution was unbalanced with COPD patients more often having previous coronary disease, possibly confounding the results. In the SPRINT registry, [8] COPD was not independently associated with increased risk of death among MI survivors. This study pertained only to patients requiring admission to coronary care units between 1981 and 1983 and used logistic regression to assess the independent risk of death at 1 and 5 years rather than Cox proportional hazards regression, thereby not taking into account the duration of survival.

Our study included all patients in the county who experienced an incident MI, therefore this design represents the comprehensive experience of a community. Herein, we observed that COPD was frequent and becoming more frequent over time and significantly increased the risk of death after MI, which manifested starting from the early post-MI phase, and persisted during follow-up.

Our study was not designed to explain the mechanism whereby COPD increases mortality in patients with MI, so we can only speculate that unfavorable conditions associated with COPD may mediate its effect on post-MI survival. Smoking is a risk factor for both MI and COPD, and is known to worsen prognosis after MI; thus it is a potential confounder. By demonstrating that the association between COPD and death was independent of smoking, we eliminated the effect of this important confounder. Similarly, the association between COPD and death was not explained by other risk factors like comorbidities, MI severity, and treatment.

Another hypothesis relates to inflammation. COPD is characterized by chronic inflammation of the airways.[4] Similarly, low levels of systemic inflammation are known to be associated with increased risk of atherosclerosis[28,29] and worse outcomes in patients with MI[30,31] The evidence that drugs such as statins and ACE inhibitors used in coronary disease reduce mortality of patients with COPD supports this hypothesis.[32] Finally, patients with COPD can experience hypoxia, which may trigger ischemia and MI.[33]

Temporal trends

Over time, the prevalence of COPD increased, which may reflect increased awareness to diagnose and report COPD. However, COPD was defined by in clinical notes and did not rely on tests possibly affected by time trends in its use. Further, as the impact of COPD on outcome did not diminish over time, it is unlikely that temporal trends reflect increased detection of milder cases. This trend likely thus reflects mostly a true increase in COPD prevalence underscoring that COPD is a major and growing comorbidity among patients with MI.

Consistent with previous studies from our group, we observed a decline over time in post-MI mortality[3] in the overall population. The unadjusted risk of death in patients with COPD versus patients without COPD increased over time, mostly due to the effect of age and underscoring that due to the aging of the population, the burden of COPD after MI will likely increase. The present study shows that after MI, community patients with a clinical diagnosis of COPD have an increased risk of death that did not diminish over time despite improvement in therapy.

Limitations and strengths

Potential limitations should be mentioned to aid in data interpretation. This study was retrospective, which is the only possible design to analyze prevalence and time trends. We relied on clinical diagnosis of COPD in the medical records to reduce biases due to use of tests. Indeed only 126 patients with clinically diagnosed COPD underwent pulmonary function tests with post-bronchodilator reversibility assessment within 5 years before the MI or within 90 days after the MI. These were too few to perform any further analysis.

We examined several potential confounders that could have accounted for the associations between COPD and death observed in this study. However, we cannot rule out that our results are due to an unknown confounder, as we cannot rule out the possibility that people with COPD had other unmeasured characteristics that confound the association between COPD and death.

Although the population of Olmsted County is becoming more diverse, during the study period, it consisted primarily of Caucasians.

The strengths of the study include its population-based approach, which reflects the entire experience of a community, the large sample size and person-years examined. This allows evaluating, for the first time, the trends in time of both prevalence and survival over three decades. Further strengths include the standardized definition of MI and the completeness of follow-up possible via the records linkage system of the Rochester Epidemiology Project.

Conclusions

In a large geographically defined community of patients with MI, COPD occurred relatively frequently and its prevalence increased over time. COPD markedly increased the risk of death after MI independently of age, risk factors and comorbidity. This excess risk, together with the increasing prevalence of COPD in the community and the aging of the population, underscores the importance of COPD for public health and clinical practice and the need to optimize the management of these high risk patients.

Acknowledgments

We thank Kay A. Traverse, RN, Susan Stotz, RN, and Kristie K. Shorter for their support with the study.

Abbreviation list

ACE	angiotensin converting enzyme
COPD	chronic obstructive pulmonary disease
CK	creatinine kinase
HR	hazard ratio
MI	myocardial infarction
NSTEMI	non-ST segment elevation MI
OR	odds ratio

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Figure 1.
Time trends in prevalence of COPD in patients with MI in the community

Figure 2.
Kaplan-Meier survival after MI in patients with COPD and without COPD.

Table I**Patient Characteristics According To COPD Status**

	No COPD (N=3023)	COPD (N=415)	P Value
Age (years), mean $\pm$ SD	67 $\pm$ 15	73 $\pm$ 11	<0.01
Women, %	43	41	0.53
Risk factors & comorbidities			
Smoking status			
Never, %	43	11	<0.01
Current, %	26	35	
Former, %	32	54	
Diabetes mellitus, %	21	23	0.54
Hyperlipidemia, %	39	43	0.12
Hypertension, %	57	68	<0.01
Family history of CAD, %	22	16	0.01
BMI, mean $\pm$ SD	27.8 $\pm$ 5.7	26.5 $\pm$ 7.1	<0.01
Modified Charlson comorbidity index (excluding COPD)			
0, %	45	24	<0.01
1–2, %	34	38	
3+, %	21	39	
Prior diagnosis of cancer, %	13	27	<0.01
Presentation			
Q wave, %	53	57	0.25
Anterior MI, %	37	36	0.83
Non-ST elevation MI, %	65	74	<0.01
Peak CK ratio			
Lowest tertile, %	30	40	<0.01
Middle tertile, %	34	36	
Highest tertile, %	36	24	
Killip class			
I, %	68	59	<0.01
II, %	6	6	
III, %	22	29	
IV, %	4	7	
Hours from onset of symptoms to 1 st ECG, median (25 th –75 th percentile)	1.9 (0.9–4.7)	1.5 (0.6–4.0)	<0.01
Therapy			
Reperfusion/revascularization during hospitalization, %	52	41	<0.01
Beta blocker *, %	61	47	<0.01
ACE inhibitor *, %	29	37	<0.01
Statin *, %	30	29	0.61
Diuretic *, %	23	34	<0.01
Use of tests during hospitalization			
Coronary angiography, %	59	51	<0.01

	No COPD (N=3023)	COPD (N=415)	P Value
Echocardiogram, % [†]	59	59	0.88
Length of hospital stay (days), median (25 th –75 th percentile)	6 (4–11)	7 (4–12)	0.19

* Prescribed at hospital dismissal; among those who did not die during hospitalization

[†] Among patients enrolled between 1987 and 2007

Table II

Unadjusted and Adjusted HR for Death Among Patients with COPD vs. Those without COPD.

	Unadjusted HR (95%CI) <i>P</i> Value	Adjusted HR (95%CI) [*] <i>P</i> Value	Adjusted HR (95%CI) [†] <i>P</i> Value	Adjusted HR (95%CI) [‡] <i>P</i> Value
No COPD (reference)	1	1	1	1
COPD	1.88 (1.63, 2.15) <0.01	1.54 (1.34, 1.77) <0.01	1.46 (1.26, 1.69) <0.01	1.30 (1.10, 1.54) <0.01

* Adjustment for age and sex

† Adjustment for age, sex, and smoking

‡ Adjustment for age, sex, smoking, hypertension, comorbidity, NSTEMI, CK ratio tertiles, Killip class, beta-blockers prescribed at hospital dismissal, ACE inhibitors prescribed at hospital dismissal, diuretics prescribed at hospital dismissal, and reperfusion/revascularization during the hospitalization.

Table III
Temporal Trends in Unadjusted and Adjusted HR for Death in Patients with COPD vs. Patients without COPD

	1979–1985	1986–1992	1993–1999	2000–2007	P-value for COPD* year interaction
Unadjusted HR (95% CI)					
No COPD (reference)	1	1	1	1	0.005
COPD	1.16 (0.82, 1.64)	1.83 (1.39, 2.42)	2.21 (1.68, 2.91)	2.37 (1.85, 3.04)	
HR (95% CI) adjusted for age and sex					
No COPD (reference)	1	1	1	1	0.33
COPD	1.21 (0.86, 1.71)	1.63 (1.23, 2.15)	1.78 (1.35, 2.35)	1.68 (1.31, 2.15)	
HR (95% CI) adjusted for age, sex and smoking					
No COPD (reference)	1	1	1	1	0.44
COPD	1.18 (0.83, 1.68)	1.55 (1.17, 2.06)	1.65 (1.25, 2.19)	1.60 (1.25, 2.06)	
Fully adjusted HR (95% CI)*					
No COPD (reference)	1	1	1	1	0.23
COPD	0.79 (0.45, 1.36)	1.43 (1.07, 1.91)	1.36 (1.01, 1.82)	1.22 (0.89, 1.67)	

* Adjustment for age, sex, smoking, hypertension, comorbidity, NSTEMI, CK ratio tertiles, Killip class, beta-blockers prescribed at hospital dismissal, ACE inhibitors prescribed at hospital dismissal, diuretics prescribed at hospital dismissal, and reperfusion/revascularization during the hospitalization.