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Full Length Research paper

The influence of chronic obstructive pulmonary disease in patients undergoing coronary artery bypass graft surgery

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The objective of this study was to assess if there are any differences between patients undergoing coronary artery bypass graft surgery with COPD compared to patients without COPD. We conducted a prospective hospitalization cohort study. The study population was patients undergoing CABG by the Cardiovascular Thoracic Surgery Group. Inclusion criteria included CABG surgery between 10/1/93 and 1/1/8 and age greater than eighteen. Exclusion criteria included any other surgery performed simultaneously with the CABG surgery, repeat procedures, and any patient with incomplete data for the COPD variable. Data were collected on 225 variables concurrently with admission. We controlled for seven variables. The primary outcome was thirty-day mortality. There were eight secondary outcomes. Ten thousand, four hundred and fourteen patients meet the criteria to be included in the cohort, (1,739 with COPD and a positive smoking history, 8,675 patients without COPD). Univariate analysis comparing the patients with and without COPD for the seven potential confounders found no significant difference between the two populations. The patients undergoing CABG surgery with COPD did experience significantly longer length of stay (6.7 ± 6.0 days vs. 5.9 ± 6.1 days, $p < 0.05$), more likely to significantly elevate their creatinine after surgery (OR 1.46, 95% CI 1.15 to 1.85), more prolonged ventilation (OR 1.99, 95% CI 1.60 to 2.49), more likely to get pneumonia (OR 2.99, 95% CI 2.25 to 3.96) and significantly more mortality (OR 1.78, (95% CI 1.32 to 2.40). Patients with COPD undergoing CABG surgery experience significantly more mortality and more morbidity compared to patients without COPD.

Key words: COPD, CABG.

INTRODUCTION

In the United States, approximately 12 million people are diagnosed with Chronic Obstructive Pulmonary Disease (COPD) and another 12 million have the disease without the diagnosis (www.cdc.gov/copd/, 2010). COPD is the fourth leading cause of death in the US (www.cdc.gov/copd/ Last updated February 3, 2010). This is the fifth consecutive year in which more woman than men have died attributed to COPD (Centers for Disease Control and Prevention, 2004). The annual cost to the nation from the added mortality and morbidity of COPD is estimated currently to be $43 billion (U.S. Department of health and Human Services, 2007). Chronic obstructive pulmonary disease is a common co-morbid condition in patients who present for coronary artery bypass surgery (CABG).

Previous research has suggested that patients with COPD undergoing CABG experience some increased morbidity and mortality risk following surgery (Leavitt et al., 2006; Samuels et al., 1998; Vavlukis et al., 2006; Fuster et al., 2006; Medalion et al., 2004; Manganas et al., 2007; Legare et al., 2001; Jensen and Yang, 2007; Loponen et al., 2003; Islamoglu et al., 2003; Tugtekin et al., 2007; Rosenfeld et al., 2006). Research into the

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mortality risk has gathered the greatest interest. Investigating 33,137 CABG patients over nine years, Leavitt et al. reported the long-term mortality was increased in patients with COPD (HR 1.8, 1.6 to 2.1) compared to controls (Leavitt et al., 2006). The long-term mortality risk was even higher in patients with COPD and other co-morbidities (HR 3.6, 3.3 to 3.9). Samuels et al. with a smaller cohort (N = 191), found the mortality rate was only increased for patients with severe COPD and advanced age (>75 years). They found patients with mild or moderate COPD to possess a similar mortality rate of those without COPD (Samuels et al., 1998). In contrast to these results, Manganas et al. (2007) divided 411 patients into three strata based on the measured FEV1/FVC. They found increased morbidity in the severe COPD patients but found the mortality rates to be comparable among all three strata.

They concluded that the degree of airflow obstruction in patients with COPD did not influence the mortality risk with CABG surgery (Manganas et al., 2007). The data on morbidity risk in patients with COPD is somewhat limited. Researchers have found COPD patients to have a longer ICU length of stay, increased risk of prolonged ventilation, post-operative congestive heart failure, and stroke (Legare et al., 2001; Jensen and Yang, 2007; Loponen et al., 2003; Islamoglu et al., 2003; Tugtekin et al., 2007). However, it is important to remember that researchers have also found patients with COPD who undergo CABG surgery experience improved quality of life following the procedure.[6] Unfortunately most studies investigating these outcomes are limited by size and retrospective data collection. It is our objective to prospectively assess a large population, to see if there is any mortality or morbidity differences between patients undergoing coronary artery bypass grafting with COPD compared to patients that do not have the co-morbidity COPD.

METHODS

We conducted a prospective hospitalization cohort study. Patients entered the cohort on admission to the hospital, and exited the cohort thirty days after surgery. The study population was patients undergoing CABG by the Cardiovascular Thoracic Surgery Group, located in Cincinnati, Ohio. Inclusion criteria included CABG surgery between 10/1/93 and 1/1/08 and age greater than eighteen. Exclusion criteria included any other surgery performed simultaneously with the CABG surgery, (that is CABG and valve surgery), repeat procedures, and any patient with incomplete data for the COPD variable. Patients in the cohort with both a positive history of COPD and a positive smoking history were compared to the remainder of the cohort. Institutional review board approval was obtained prior to conducting this study. Informed consent for data collection is obtained from all patients.

Data collection

Data were collected on 225 variables concurrently with admission by physicians, nurses, and perfusionists for all patients undergoing cardiac surgery (partial listing, Table 1). The data were grouped into demographic, medical history, post-op, perfusion, and procedure sections. All data forms were audited for completeness and consistency with a series of cross-checking questions answered by two different individuals. A random 10% of patient forms were additionally audited by a physician for accuracy and consistency. Data were stored in an interactive multi- institutional database (Patient Analysis and Tracking System, Axis Clinical Systems, Portland, OR).

Control variables

To minimize confounding, we controlled for seven variables. These included the demographic variables of age, gender, and race. We also controlled for the co-morbidities of body surface area (BSA), character of the operation, percentage performed off pump, and total number of arterial grafts.

Outcomes

The primary outcome was thirty-day mortality. The other eight outcomes that were analyzed included: total length of stay, time in the intensive care unit (ICU), intra-operative complications, pulmonary complications, neurologic complications, renal complications, re-operation for bleeding, and wound complications.

Analysis

Univariate analysis using chi-square and t-tests were performed analyzing the patients with COPD to the patients without COPD for each control variable. Then nominal regression analysis for dichotomous variables and linear regression for continuous variables investigated the adjusted risk between COPD patients and those patients without COPD for the nine outcomes of interest, while controlling for any significant confounding variables (significant confounder set at $p < 0.05$). Data analysis was conducted using SPSS software (SPSS Inc., Chicago, IL) statistical software. Utilizing a two-tailed alpha of 0.05 and a beta of 0.10, it was estimated that approximately 10,000 patients would be required for this study to have 90% power to find a significant difference between the two populations for any outcome if they differ by 2%.

RESULTS

Ten thousand, four hundred and fourteen patients (10,414) meet the criteria to be included in the cohort, (1,739 with COPD and a positive smoking history, 8,675 patients without COPD). Four hundred and twenty two patients (N = 422) were eliminated due to incomplete data for the COPD variable. Univariate analysis comparing the patients with and without COPD for the seven potential confounders found no significant difference between the two populations (Table 2). Nominal and linear regression comparing the patients with and without COPD for the nine outcomes found no difference between the two groups for wound infections, re-operation for bleeding, neurologic complications (TIA, CVA, coma), ICU LOS and intra-operative complications (Table 3). The patients undergoing CABG surgery with a

Table 1. Explanation of co-morbidities and risk factors.

Age	Age in years at time of surgery
Creatinine level	Pre-operative creatinine level
Pump time	Operative time patient was on mechanical perfusion in minutes
Body surface area	Body surface area in m^2
Number of vessels bypassed	Number of coronary arteries surgically bypassed with venous or arterial graft
Categorical variables	
Reported history of prior MI	Patient's self report of prior myocardial infarction in preoperative history and physical
Diabetes	Includes patients with dietary as well a medical control
Hypertension	Diastolic BP >90
History of tobacco use	The pack years of tobacco use in 10 year strata
Cerebrovascular Dx history	Reported History of TIA, CVA, carotid bruit, or abnormal carotid pulse.
Hypercholesterolemia	Yes, if total cholesterol was greater than 200 or on medical therapy.
Medicaid patient	Primary insurance carrier listed on inpatient chart
Left Ventricular hypertrophy	Mild, moderate or severe (measured by echocardiogram)
NYHA functional class	Class I, Class II, Class III, Class IV
Character of operation	
Elective	Yes or no
Urgent	Next available operating room within 24 h
Emergent	Operating room within 1 - 2 h
Desperate	On CPR or mechanical support
Race	White, black, hispanic, oriental, middle-eastern, other
Bleeding history	Bleeding complications at prior surgery or coagulation disorder (Hemophilia, ITP, Von wilenbrand's)
COPD	Mild (no medications), moderate (symptoms on exertion), severe (symptoms at rest)
IMA used in graft	Use of any part of IMA in any part of grafting process
Previous intervention < 30 days	Cardiac catherization, PTCA, atherectomy, stent placement
Re-operation for bleeding	Yes or No
Arrhythmia requiring treatment	Any arrhythmia requiring medical therapy or pacemaker
Positive culture (postoperative)	Including blood, urine (>10K), arterial or venous lines (>15)
Renal complications	Mild (double preoperative creatinine), moderate (creatinine > 4.0), severe (dialysis)
Neurologic complications	Any neurologic complication except mild mental status changes (Severe mental status change, CVA, peripheral nerve, seizure, TIA)
Pulmonary complications	Any pulmonary complication with the exception of mild atalectasis.
Gastrointestinal complications	Any including: (severe GI bleeding, perforated ulcer, cholecystitis, hepatitis, pancreatitis, bowel obstruction, ileus, ischemic bowel)
Low cardiac output	Mild (Dopamine <=2mcg/kg/min), Mod (press x 1), Severe (Press x2), IABP, IABP + pressor, IABP + 2 pressors
Return to ICU	Yes or No
Mortality	Patient expired within 30 days of hospitalization
Intra-operative complications	Included dissection, hemorrhage, arrhythmia, cardiac laceration, cardiac dilation, air embolism, MI, aortic tear, cardiac arrest, valve trauma, unsatisfactory graft harvest,
Hours in ICU	Time in hours
Hospitalization	Duration in days from operation to discharge

Table 2. Univariate analysis comparing the patients with and without COPD for seven potential confounders.

	COPD = 1739	Without COPD N = 8675	p value
Age	64.6 ± 9.9 years	64.3 ± 10.8 Years	0.27
Gender			0.34
Males	1217 (69.9%)	6170 (71.1%)	
Females	522 (30.1%)	2505 (28.9%)	
BSA	2.98	3	0.64
Character of operation			0.95
Elective	1086 (63.8%)	5389 (63.9%)	
Urgent/emergent	615 (36.2%)	3042 (36.1%)	
# of arterial grafts	1.12 ± 0.5	1.17 ± 0.56	0.12
Cardiac pump			
Off pump	49 (14.2%)	157 (11.1%)	0.11
Ethnicity			0.19
White	1635 (94.0%)	8078 (93.1%)	
African American	104 (6.0%)	597 (6.9%)	

diagnosis of COPD and a positive smoking history did experience significantly longer LOS (6.7 ± 6.0 days vs. 5.9 ± 6.1 days, $p < 0.05$), more likely to significantly elevate their creatinine after surgery (OR 1.46, 95%CI 1.15 - 1.85), more prolonged ventilation (OR 1.99, 95% CI 1.60 - 2.49), more likely to get pneumonia (OR 2.99, 95% CI 2.25 - 3.96) and significantly more mortality (OR 1.78, 95% CI 1.32 - 2.40).

DISCUSSION

In our experience, it is unusual to examine seven confounding variables without finding any significant differences between two surgical populations. We were expecting some differences; typically patients with COPD requiring CABG surgery are frequently a little younger with a higher percentage of males. The outcomes from this investigation were more predictable. Despite similar baseline characteristics in the two groups, patients with COPD possessed increased odds ratios for virtually every bad outcome. Several of the outcomes were statistically significantly when the prevalence of the outcome was moderate or higher.

Our finding of increased mortality in COPD patients undergoing CABG surgery is consistent with the majority of the literature in this area (Leavitt et al., 2006; Samuels et al., 1998; Vavlukis et al., 2006; Fuster et al., 2006; Medalion et al., 2004). Most investigations have found at least a doubling mortality risk due to COPD. Our mortality rates for COPD patients and controls were lower than those reported by other investigators (Leavitt et al., 2006; Samuels et al., 1998; Vavlukis et al., 2006; Fuster et al., 2006; Medalion et al., 2004). However, since our patients did not have spirometry to document their extent of obstructive lung disease, it is hard to compare patient populations. Our population of COPD patients may have had fewer co-morbidities and less obstructive disease compared to COPD patients in other investigations.

The literature contains less information about morbidity outcomes in patients with COPD undergoing CABG surgery. We expected to find increased pulmonary complications in this population. We found a two-fold increase in prolonged ventilation risk and a three –fold increase in pneumonia risk for our COPD patients. Legare et al. (2001) found a similar two-fold increase in prolonged ventilation risk in their patients with COPD. Jensen and Yang (2007) found COPD diagnosis to be a risk factor for both pneumothorax and post-operative congestive heart failure. However, neither author found an increased risk of pneumonia for COPD patients. We are surprised that no investigation into pulmonary complications after CABG surgery has ever demonstrated an increased risk of pulmonary embolism for COPD patients. It may be possible that some of the increased short-term mortality seen in COPD patients may be due to undiagnosed pulmonary clots.

It was encouraging to see that the majority of the remaining morbidity outcomes were similar for our two surgical groups. Loponen et al. (2003) found COPD

Table 3. Comparing outcomes for patients with and without COPD.

Outcomes	COPD N=1739	Without COPD N=8675	OR	P value
LOS	6.7 days ± 6.0	5.9 days ± 6.1		<0.05
ICU LOS	53.4 h + 109.7	49.1 h +263.0		0.51
Mortality	59 (3.4%)	168 (1.9%)	1.78 (1.32 - 2.40)	<0.05
Intra-operative complications	65 (3.9%)	300 (3.6%)	1.07 (0.81 - 1.40)	0.62
Renal complications				
crt > 2.0/2xPre-op	93 (5.4%)	323 (3.7%)	1.46 (1.15 - 1.85	<0.05
New dialysis	22 (1.3%)	68 (0.8%)	1.63 (1.00 - 2.64	0.06
Neurologic complications				
CVA	5 (1.4%)	11 (0.8%)	1.86 (0.64 - 5.39)	0.34
TIA/RIND	1 (0.1%)	15 (0.2%)	2.91 (0.39 - 22.0)	0.49
Coma > 24 h	0 (0.0%)	6 (0.4%)		0.61
Wound Infections				
Sternum	7 (0.40%)	18 (0.20%)	1.94 (0.81 - 4.66)	0.17
Harvest site	6 (0.30%)	17 (0.20%)	1.76 (0.69 - 4.47)	0.25
Re-operation for bleeding			1.07 (0.69 - 1.64)	0.74
yes	25 (1.4%)	117(1.4%)		
no	1711 (98.6%)	8541(98.6%)		
Pulmonary complications				
prolonged ventilation	117 (8.2%)	304 (4.3%)	1.99 (1.60 - 2.49)	<0.05
pulmonary embolism	2 (0.10%)	5 (0.1%)	2.03 (0.39 - 10.47)	0.32
pneumonia	80 (5.6%)	137 (2.0%)	2.99 (2.25 - 3.96)	<0.05

patients to possess an increased risk of peri-operative stroke. In our population, COPD had a non-significant, nearly two-fold higher risk ratio compared to controls. However, our rate of stroke was significantly lower than the reported rate by Loponen (2003) (1.0% vs. 2.6%). This low prevalence of the outcome experienced with our population limited our power to find statistical significance. Other investigators of morbidity risk in CABG patients have also found little significant added risk for COPD patients (Islamoglu et al., 2003; Tugtekin et al., 2007). Even though there are increased mortality and pulmonary risks for these patients, investigators generally agree that CABG surgery is generally safe in this population, and lower risk than the natural progression of vascular disease without a surgical conduit. To further emphasize this point, for patients with COPD who survive CABG surgery, they report a significantly higher quality of life years after surgery (Vavlukis et al., 2006).

When considering our results, it is also important to ponder the limitations of this investigation. The biggest limitation of our endeavor is the lack of spirometry documentation of COPD in the experimental group. Given the population size of this project, spirometry on every patient is virtually impossible. Requiring a forced expiratory volume in one second (FEV1) for each patient would have radically reduced our patient numbers and our ability to investigate several morbidity outcomes due to a lack of power. Similarly, there were likely control patients with undiagnosed COPD in our investigation. This potential mixing of the two study groups would make them more similar and make it harder to find a significant difference between the two groups for any outcome. This adds power to the outcomes that we did find a significant difference. In addition, although COPD was stratified into three strata in our data table (mild, moderate and severe), we choose to combine all three strata since they were completely subjective. This made the COPD variable dichotomous. Although there is legitimate concern about the study definition of COPD, this large study allows multiple outcomes to be explored in a single population that previously have not been able to evaluate.

Conclusion

Patients with COPD undergoing CABG surgery

experience significantly more mortality and more pulmonary complications compared to patients without COPD.

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