RESEARCH ARTICLE

Identifying High Comorbidity Index in COPD Hospital Re-Admission

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Abstract

Introduction: COPD affects 12 million Americans and is one of the leading causes of death worldwide. The national data on COPD readmission rate is about 20% in the U.S. Patients are usually admitted for acute exacerbation with acute or chronic respiratory failure, albeit many were admitted with other comorbidities rather than COPD acute exacerbation. The purpose of this study was to identify high index comorbidities that contribute to COPD hospital readmissions.

Method: Retrospective analysis of a large database on COPD patients who were admitted from 01/01/2013 to 12/31/2015 to a major university health care system in the Southeastern United States was used for this study. Information on patient demographics, medical problems, medications, COPD admissions and readmissions was collected. The Charlson Comorbidity Index (CCI) was used for identifying comorbidities.

Results: The common comorbidities identified in patients who were admitted and re-admitted included congestive heart failure (41.5%), diabetes without complications (33.6%), and renal disease (31.4%). Higher hemoglobin and albumin levels were inversely related to 30-day readmission.

Conclusion: Patients admitted with COPD exacerbation had co-morbidities which included heart failure, diabetes, renal disease, and other diseases sharing the pathophysiology of chronic inflammatory processes. Therefore, we recommend that COPD management should be comprehensive in monitoring chronic inflammatory processes and optimizing management of co-morbidities in addition to the improvement of pulmonary function and lung health.

Keywords: COPD or Chronic Obstructive Pulmonary Disease; Hospital Readmission, comorbidity, Chronic Inflammatory Response.

Introduction

Twelve million Americans have been diagnosed with chronic obstructive pulmonary disease or COPD in the United States.[1] The national data suggest that a 30-day readmission rate for COPD is about 20%[2,3], and COPD was ranked as the second most frequent diagnosis after CHF (Congestive Heart Failure) for hospital readmission.[4] COPD is a disease characterized by several subtypes or phenotypes including chronic bronchitis, asthma, and bronchiectasis associated with chronic airway obstruction. Most common symptoms in patients with COPD are pulmonary related, however, these patients often have non-pulmonary related symptoms such as anxiety, depression, and other symptoms associated with chronic medical conditions.[5] COPD is a chronic inflammatory disease; however, other comorbidities that often co-exist in these patients reflect systemic inflammation and immunocompromised states. [6,7] The combination of these comorbidities could potentially make the management of COPD difficult, thus, subsequently increasing the hospital admission and re-admission rates. [8]

Most of COPD readmissions are associated with acute exacerbation. The cause of the exacerbation is included but not limited to acute infection/inflammatory response, fluid overload, and CHF. The common infections associated are viral and bacterial. Among bacterial infection *Haemophilus influenzae* has been particularly associated with lower Forced Expiratory Volume in one second (FEV_1), a longer length of hospital stay, and greater rates of readmission. In addition to being a chronic inflammatory disease, COPD is a catabolic disease, therefore most patients with severe COPD tend to have a lower Body Mass Index (BMI) and poor nutrition as reflected by their serum albumin. Studies have shown that hypoalbuminemia and high Charlson comorbidity index score at admission can predict readmission risk. [9] Although a high BMI has also been associated with a higher morbidity and mortality, a low BMI has been shown to correlate with poorer pulmonary function. [10]

Cardiovascular diseases (CVD) and Peripheral vascular diseases (PVD) are associated with atherosclerosis, which results in decreased cardiac function, and is often associated with chronic hypoxia. Emerging data suggest that the pathogenesis of these conditions is associated with chronic inflammation. Epidemiologic data suggest that patients with COPD are at two to three times the risk of developing CVD—including hypertension, ischemic heart disease, stroke, atrial fibrillation, and heart failure—than individuals of the same age without COPD.[11] The presence of diabetes, a metabolic and endocrine disease, has been shown to accelerate progression of COPD, as hyperglycemia deleteriously affects lung physiology through chronic inflammation and increased risk for bacterial infection.[12,13] COPD and chronic kidney disease have been reciprocally related. The respiratory failure and tissue oxygen deprivation in COPD patients impacts glomerular function. Thus, in general, the comorbidity index is usually high in COPD patients with kidney disease because of the chronicity of the disease and its prolonged effect on lung function.

There are several factors that contribute to the increased morbidity and mortality in patients with COPD. In addition to the cost of treating patients with COPD, progression of disease and a high association with the hospital readmissions leads to rapid decline

in quality of life. Therefore, it is essential to identify a simplified tool to guide risk assessment for COPD readmissions. The purpose of this study was to examine the comorbidities of patients readmitted for COPD, and identify the relationship between the diseases associated with chronic inflammatory processes and COPD readmissions.

Methods

Statistical strategies: A retrospective database of COPD patients who were admitted from 01/01/2013 to 12/31/2015 from a large university health care system in the Southeastern United States was used for this study. COPD for this dataset includes International Classification of Diseases) ICD-9 codes of 490-492, 494, 496 ranges from chronic bronchitis, asthma, bronchiectasis, and chronic airway obstruction.[14] The sixteen comorbidities (besides COPD) were identified by processing ICD-9 diagnostic and procedure codes for: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, connective tissue disorder (rheumatologic disease), peptic ulcer disease, mild liver disease, diabetes, diabetes with complications (with end organ damage), hemiplegia, moderate or severe renal disease, malignancy (leukemia or lymphoma), moderate or severe liver disease, metastatic solid tumor, AIDS (Acquired Immune Deficiency Syndrome) following the coding guidelines described by Quan, et.al.[15]

Relevant and available variables that were included in the study are as follows: social-demographic (age, race, gender), physiological and biological factors [sixteen comorbidities, first and last Creatinine, Potassium, Hemoglobin, white blood counts (WBC), INR (International normalization ratio), albumin, AST (Aspartate Aminotransferase), ALT (Alanine Aminotransferase), Total bilirubin], medications (Coumadin, ACEI, beta-blockers, aspirin, statin, antibiotics, prednisone, nebulizer therapy, and use of non-invasive ventilation. The sixteen comorbidities (besides COPD) were identified by processing ICD-9 diagnostic and procedure codes for: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, connective tissue disorder (rheumatologic disease), peptic ulcer disease, mild liver disease, diabetes, diabetes with complications (with end organ damage), hemiplegia, moderate or severe renal disease, malignancy (leukemia or lymphoma), moderate or severe liver disease, metastatic solid tumor, AIDS (**Table 1**) following the coding guidelines described by Quan, et.al.[15] in addition to procedure codes available in our dataset. The initial dataset had 6468 encounters from admissions during the three year period. However, 105 of the admissions after 12/01/2015 were for patients who did not return within 30 days and were censored – these were excluded from analysis. The final dataset included 6363 encounters (count for each admission) for 4506 patients. Time to readmission was computed as the number of days between sequential admissions. A few of the encounters captured (<1%) were for patients kept under observation where the elapsed time between sequential encounters were 23 hours or less – these encounters were not marked as readmissions. An encounter was marked as a readmission within 30 days if the time elapsed between sequential readmission was between 1 and 30 days.

Table 1: Enhanced ICD-9-CM codes used for scoring comorbidities

Comorbidity	**Enhanced ICD-9-CM codes[1,2]**	**Additional codes included**
Myocardial Infarction	410.x, 412.x	
Congestive Heart Failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4-425.9, 428.x	429.3, 425.x
Peripheral Vascular Disease	093.0, 437.3, 440.x, 441.x, 443.1-443.9, 447.1, 557.1, 557.9, V43.4	442.x, 785.4, Procedure Codes 38.13-38.14, 38.16, 38.18, 38.33-38.34, 38.36, 38.38, 38.43-38.44, 38.46, 38.48*, 39.22-39.26, 39.29
Cerebrovascular Disease	362.34, 430.x-438.x	781.4, 784.3, 997.00, Procedure codes 38.12, 38.42
Dementia	290.x, 294.1, 331.2	331.0-331.1
Chronic Pulmonary Disease	416.8, 416.9, 490.x-505.x, 506.4, 508.1, 508.8	415.00
Rheumatic Disease	446.5, 710.0-710.4, 714.0-714.2, 714.8x, 725.x	
Peptic Ulcer Disease	531.x-534.x	
Mild Liver Disease	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 570.x, 571.x, 573.3, 573.4, 573.8, 573.9, V42.7	
Diabetes (w/o chronic complications)	250.0-250.3, 250.8, 250.9	
Diabetes (with chronic complications, e.g. organ damage)	250.4-250.7	
Hemiplegia or Paraplegia	334.1, 342.x, 343.x, 344.0-344.6, 344.9	344.7, 344.8
Renal Disease	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582.x, 583.0-583.7, 585.x, 586.x, 588.0, V42.0, V45.1, V56.x	Procedure codes 39.27, 39.4, 39.93-39.95, 54.98
Any malignancy (including lymphoma and leukemia, except malignant neoplasm of skin)	140.x-172.x, 174.x-195.8, 200.x-208.x, 238.6	273.0, 273.3, V10.46 Procedure codes 60.5, 62.40, 62.41
Moderate or Severe Liver Disease	456.0-456.2, 572.2-572.8	Procedure codes 39.1, 42.1
Metastatic Solid Tumor	196.x-199.x	
AIDS/HIV	042.x-044.x	

[1]Table 1, p.1133, Quan, et.al., 2005
[2]Additional information on ICD-9-CM codes may be obtained at www.findacode.com

Data analysis: All variables were reviewed for completeness. Descriptive statistics were run for all measures with means and standard deviations reported for normally distributed measures; medians and interquartile range (IQR) reported for non-normal skewed measures; and frequencies and percentages reported for categorical measures. Generalized linear multilevel models (GzMLM) were used to evaluate each risk factor individually and to build a risk model for 30-day readmission using a binomial response with a logit-link function (e.g. logistic regression). The multilevel model approach adjusted for varying numbers of encounters per patient. Initially, each of the variables was evaluated individually to screen potential variables considered for inclusion in the final GzMLM model – those with p-values < 0.1 were included. The demographics of age, gender and race were also included in the combined multivariable GzMLM model to control for these factors. Further refinement of the final multivariable GzMLM risk model was performed to further exclude non-significant variables (p>.1) to achieve a more parsimonious solution and meet multicollinearity assumptions (condition index < 30, variance inflation factors < 2 and tolerance > 0.8).

Results

The ages of the 4506 patients (determined at first admission) ranged from 17 to 106 years old with an average age of 67.5 ± 12.8 years (**Table 2**). Only 2.2% (97) of the participants were less than 40 years old. The gender of the patients was evenly split between males (50.8%) and females (49.2%). The majority was white (63.3%) with less than a third African American (29.9%). For the sixteen comorbidities reported during one or more encounters (in addition to COPD), the most frequently occurring were congestive heart failure (40.8%), diabetes (without complications) (34.5%), moderate to severe renal disease (31.2%), peripheral vascular disease (23.5%), and malignancy (leukemia or lymphoma) (21.9%) (**Table 2**). Of the 6363 encounters, 623 (9.5%) were readmissions that occurred within 30 days.

Table 2: Demographics and Comorbidities Across 4506 COPD Patients

	N	**Mean (SD)**
Age (years)	4506	67.4 (12.9)
	Category	**n (%)**
Gender	Female	2216 (49.2%)
	Male	2290 (50.8%)
Race	Caucasian	2852 (63.3%)
	African American	1345 (29.8%)
	Asian	27 (0.6%)
	American Indian / Alaskan Native	12 (0.3%)
	Pacific Islander / Native Hawaiian	6 (0.1%)
	Other	29 (0.6%)
	Unknown / Unreported	235 (5.2%)
Comorbidities* (reported during any encounter observed)		
	Myocardial Infarction	796 (17.7%)
	Congestive Heart Failure	1838 (40.8%)
	Peripheral Vascular Disease	1060 (23.5%)
	Cerebrovascular Disease	893 (19.8%)
	Dementia	187 (4.2%)
	Connective Tissue Disorder (Rheumatologic disease)	199 (4.4%)
	Peptic Ulcer Disease	87 (1.9%)
	Mild Liver Disease	465 (10.3%)
	Diabetes (without complications)	1552 (34.5%)
	Diabetes (with complications)	277 (6.1%)
	Hemiplegia	163 (3.6%)
	Moderate or Severe Renal Disease	1404 (31.2%)
	Malignancy (Leukemia or Lymphoma)	988 (21.9%)
	Moderate or Severe Liver Disease	144 (3.2%)
	Metastatic Solid Tumor	335 (7.4%)
	AIDS	37 (0.8%)

* One COPD subject was missing comorbidity data
SD (standard deviation)

The descriptive statistics of the biomarkers obtained across all of the 6363 encounters are provided in **Table 3**. The data had varying amounts of missing data due to various factors; however, this can be expected due to large number of clinicians who had managed the disease during the hospitalization. Evaluating each of these biomarkers individually, those patients who had a higher hemoglobin and albumin levels were found to be protected significantly from readmission to the hospital (odds ratios < 1, $p<.05$), whereas the first potassium level that was low was associated with a significant risk of readmission (odds ratio 1.136, $p=.030$, **Table 3**).

Table 3: Age at encounter and biomarkers by encounter for patients with and without a subsequential 30-day readmission

		All Encounters	**No 30d readmit**	**Yes 30d readmit**	**GzMLM***	**GzMLM**
	n	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**OR**	**p-value**
Age at Encounter	6363	67.9 (12.5) [17-106]	67.4 (12.9)	68.2 (11.8)		.313
First Hemoglobin	6251	11.82 (2.32)	11.87 (2.31)	11.40 (2.40)	**0.930**	**<.001**
Last Hemoglobin	6263	10.74 (2.07)	10.77 (2.07)	10.53 (1.97)	**0.955**	**.040**
First Albumin	5494	3.23 (0.60)	3.26 (0.61)	3.17 (0.57)	**0.838**	**.024**
Last Albumin	5497	3.00 (0.66)	3.02 (0.66)	2.90 (0.60)	**0.817**	**.006**
	n	**Median [IQR]**	**Median [IQR]**	**Median [IQR]**		
First creatinine	6276	1.07 [0.82, 1.51]	1.06 [0.81, 1.50]	1.13 [0.86, 1.67]		.180
Last creatinine	6278	0.99 [0.76, 1.40]	0.99 [0.76, 1.40]	1.03 [0.77, 1.46]		.250
First Potassium	6277	4.00 [3.70, 4.40]	4.00 [3.70, 4.40]	4.10 [3.70, 4.50]	**1.136**	**.030**
Last Potassium	6279	4.00 [3.70, 4.30]	4.00 [3.70, 4.30]	4.00 [3.80, 4.40]		.348
First WBC	6249	8.20 [6.20, 10.80]	8.15 [6.20, 10.80]	8.20 [6.40, 11.10]		.498
Last WBC	6261	7.90 [6.00, 10.20]	7.90 [6.00, 10.20]	8.00 [6.20, 10.40]		.783
First AST	5440	25.00 [19.00, 35.00]	25.00 [19.00, 35.00]	26.00 [20.00, 39.00]		.258
Last AST	5444	24.00 [18.00, 34.00]	24.00 [18.00, 33.00]	25.00 [19.00, 35.00]		.226
First ALT	5440	20.00 [14.00, 29.00]	19.00 [14.00, 29.00]	21.00 [14.00, 34.00]		.317
Last ALT	5444	19.00 [14.00, 30.00]	19.00 [14.00, 30.00]	21.00 [14.00, 33.00]		.454
First T Billi	5442	.70 [0.50, 1.00]	0.70 [0.50, 1.00]	0.70 [0.50, 1.00]		.842
Last T Billi	5446	.70 [0.50, 1.00]	0.70 [0.50, 1.00]	0.70 [0.50, 0.90]		.808
First INR	4224	1.13 [1.04, 1.36]	1.13 [1.04, 1.35]	1.15 [1.05, 1.38]		.472
Last INR	4229	1.15 [1.06, 1.38]	1.15 [1.05, 1.38]	1.16 [1.06, 1.37]		.717

OR = odds ratio

*odds ratios reported for significant (p<.05) variables

In addition to COPD, the patients were reported most often to have congestive heart failure (41.5%), diabetes without complications (33.6%), and renal disease (31.4%, **Table 4**). Evaluating each of these comorbidities individually for each encounter, patients who were reported to have a MI, CHF and renal disease were at significantly higher risk for a 30-day readmission (odds ratios > 1.23, p<.03) (**Table 5**).

Table 4: Comorbidities reported by encounter for patients with and without a subsequential 30-day readmission

	All Encounters	**No 30d readmit**	**Yes 30d readmit**	**GzMLM***	**GzMLM**
	N=6361	**N=5739**	**N=622**	**OR**	**p-value**
MI	1061 (16.7%)	930 (16.2%)	131 (21.2%)	**1.321**	**.015**
CHF	2637 (41.5%)	2341 (40.8%)	296 (47.6%)	**1.229**	**.025**
PVD	1350 (21.2%)	1210 (21.1%)	140 (22.5%)		.254
CVD	1082 (17.0%)	1008 (17.6%)	74 (11.9%)	**0.655**	**.002**
Dementia	222 (3.5%)	209 (3.6%)	13 (2.1%)		.074
COPD	6361 (100%)	5739 (100%)	622 (100%)		---
Rheumatologic/ Connective tissue disorder	255 (4.0%)	238 (4.1%)	17 (2.7%)		.170
PUD	96 (1.5%)	85 (1.5%)	11 (1.8%)		.654
MLD	597 (9.4%)	534 (9.3%)	63 (10.1%)		.713
Diabetes (no comp)	2135 (33.6%)	1934 (33.7%)	201 (32.3%)		.606
Diabetes (w/comp)	360 (5.7%)	323 (5.6%)	37 (5.9%)		.599
Hemiplegia	188 (3.0%)	175 (3.0%)	13 (2.1%)		.338
Renal disease	1997 (31.4%)	1769 (30.8%)	228 (36.7%)	**1.286**	**.009**
Any malignancy	1302 (20.5%)	1169 (20.4%)	133 (21.4%)		.292
SLD	178 (2.8%)	157 (2.7%)	21 (3.4%)		.285
Metastatic tumor	409 (6.4%)	375 (6.5%)	34 (5.5%)		.559
AIDS	59 (0.9%)	55 (1.0%)	4 (0.6%)		.423
	Median [IQR]	**Median [IQR]**	**Median [IQR]**		
Number of Comorbidities	3 [2,4] Range 1-9	3 [2,4] Range 1-9	3 [2,4] Range 1-8		.141
CCI (weighted comorbidity index scores)	4 [2,5] Range 1-20	4 [2,5] Range 1-18	4 [2, 6] Range 1-20		.253

OR = odds ratio

*odds ratios reported for significant (p<.05) variables

Table 5: Generalized Linear Multilevel Model for 30-day Readmission

						95% CI for Odds Ratio	
Model Term	**B**	**SE_B**	**t**	**p-value**	**Odds Ratio**	**Lower**	**Upper**
Intercept	-1.665	.4000	-4.163	**.000**	.189	.086	.414
Age at Encounter	.002	.0041	.513	.608	1.002	.994	1.010
Gender (male)	.124	.1006	1.235	.217	1.132	.930	1.379
Race (white)	.159	.1050	1.516	.130	1.173	.954	1.441
First Hemoglobin	-.061	.0224	-2.699	**.007**	**.941**	.901	.984
Last Albumin	-.127	.0801	-1.581	.114	.881	.753	1.031
MI	.251	.1218	2.059	**.040**	**1.285**	1.012	1.632

Discussion

In our study cohort, the readmission rate was 9.5%, which is relatively less than the national readmission rates which have been as high as 20%. Being one of the large university health care systems and a regional referral center, patients may be referred from remote areas for the initial management and admission but not seek subsequent hospitalizations. Our data also show that higher hemoglobin and albumin levels are inversely related to 30-day readmission. The common comorbidities identified in patients who were re-admitted included congestive heart failure (41.5%), diabetes without complications (33.6%), and renal disease (31.4%). These findings suggest that morbidity and worsening of COPD is associated with conditions that are linked to chronic inflammation that may predispose patients to exacerbations.

Several conditions such as Obesity, Diabetes Mellitus (DM) and Chronic Kidney Disease (CKD) have been associated with chronic inflammation. In a study conducted by Blum et al., they suggested the "obesity paradox". This theory implies that there is an inverse relationship between obesity and good health (i.e. lung function and survival). [10] They studied patients with COPD along with the comorbidities of atherosclerosis and peripheral artery disease (PAD) and found that the patients with PAD were of older age with lower BMI and worse lung disease. Thus it is suggested that the "obesity paradox"—lower BMI—can be attributed to poor prognosis associated with atherosclerosis present in the COPD patients.[10] Type II Diabetes Mellitus results in macrovascular and microvascular disease which can be exacerbated by tissue hypoxia from the COPD disease progression.[12,16] Kinney et al showed that the thickened alveolar epithelial basal lamina and microvascular changes in pulmonary capillary beds eventually leads to reduced capillary blood volume and reduced diffusing capacity, causing reductions in FEV_1 and FVC. [17] Renal failure adversely influences lung function and could possibly lead to fluid overload, pulmonary edema, and pleural effusion.[18] In severe COPD, CKD may impair gas exchange as well as acid-base regulation. Comorbidity of CVD/PAD with macro and micro atherosclerotic vascular disease can also contribute to CKD. Patients with CKD have been found to have increased circulatory inflammatory proteins in response to infection, ischemia, or autoimmune injuries. [19]

In a recent study, Laribi et al. showed a correlation between a higher rate of mortality in patients with COPD who were

admitted with an exacerbation and elevated admission levels of cardiac high-sensitivity troponin, copeptin, and B-type natriuretic peptide (BNP).[20] These data suggest an increased risk for early mortality with predicted 30-day mortality in these patients who have underlying cardiac disease. In addition to cardiac conditions, the risk of venous thromboembolic disease is increased in patients with COPD. Kubota et al. showed that patients with COPD are at an increased risk for morbidity and mortality from pulmonary embolism.[21] Patients with COPD in general are at a heightened risk for Venous Thromboembolism (VTE) related to decreased exercise tolerance and macro and microvasculature pathophysiology. [22]

COPD is a chronic inflammatory disease associated with systemic characteristics. The power of using the CCI as a disease specific paradigm and isolating each disease to assess the risk for readmission can be limited in this population. COPD with acute exacerbation is positively associated with the concurrent comorbidity that shares the common pathway of chronic inflammatory processes. Our data suggest that perhaps conditions that are indicative of increased inflammatory response may provide clues for predisposition to exacerbations and readmissions in these patients. Decreased BMI, hemoglobin, and albumin are often associated with chronic inflammatory diseases. These changes are associated with alterations in liver function with a shift to producing other proteins, such as C-reactive protein (CRP), serum amyloid A (SAA), and fibrinogen rather than albumin in response to inflammation. [19 23] Freeman et al reported that Interleukin (IL)-10, IL – 15, and other pro inflammatory factors are elevated in the serum as well as C-Reactive Protein (CRP) is also increased in COPD patients.[24] Another study compared COPD patients who walked less than 350 meters to those who were able to walk more than 350 meters and found that those with decreased walk distances had elevated pro-inflammatory cytokines such as IL-8 levels and lower physical functional scores. [25-27]Moreover, those with higher walk distances had surfactant protein B levels that were associated with a higher physical functionality. [28]

The finding that low albumin is associated with increased readmissions is particularly interesting, as albumin is often depleted in conditions with inflammatory responses. [7] One of the major limitations of our study is that it was retrospective and therefore we had few patients with data on markers of inflammation such as CRP or fibrinogen. Thus we suggest that CRP, fibrinogen, hemoglobin, albumin, and BMI should also be evaluated as potential markers to stratify the risk for re-admission. However, further studies are needed before we can conclude factors indicating the chronic inflammatory processes and risk of readmission.

In conclusion, COPD is a chronic inflammatory disease that involves multi-organ inflammatory responses. The acute exacerbation may have been contributed by other comorbidities rather than just the COPD alone. [29] This may also explain that, thus far, not a single high readmission risk index tool can be used to predict COPD readmission. Health care management companies should view the COPD readmission as a systemic disease rather than a single disease that only involves pulmonary pathophysiology. A comprehensive management team should include management of COPD as well as any other

chronic inflammatory disease. In particular, attention should also be focused on functional improvement through cardio-pulmonary rehabilitation. The team should have a keen awareness that any chronic inflammatory diseases and / or immunocompromised disease such as chronic anemia, hypoalbuminemia, MI (Myocardial Infarction), CHF, diabetes mellitus, and chronic kidney disease can trigger acute exacerbation. The comprehensive pulmonary management team should develop protocols on providing integrated primary care incorporating collaboration with other specialties (specialty providers, respiratory therapists, nutritionists, psychologists, and care coordinators) to ensure the COPD management goes beyond the management of only pulmonary disease.

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