Association Between Blood Glucose Level and Outcomes in Patients Hospitalized for Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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ABSTRACT

Background: Increased blood glucose is associated with adverse clinical outcomes among patients with major illnesses. This study examined the association between blood glucose and adverse outcomes among hospitalized patients with acute exacerbation of chronic obstructive pulmonary disease, for which limited prior data were available.

Methods: We studied a cohort of 209 hospitalized patients with acute exacerbation of chronic obstructive pulmonary disease. Univariate analyses and multivariate logistic regression analyses with backward elimination method were performed to evaluate factors associated with in-hospital complications, length of hospitalization, 30-day hospital readmission, and 90-day all-cause mortality.

Results: Multivariate logistic regression analysis with backward elimination method revealed that lower blood glucose and age at hospital admission were the most significant risk factors for in-hospital complication. Received respiratory support and in-hospital complications were the most significant risk factors for the length of hospitalization. There were no significant risk factors associated with 30-day hospital readmission and 90-day all-cause mortality.

Conclusion: The analyses failed to reveal significant associations between higher blood glucose levels and adverse outcomes. We showed that lower glucose levels (hypoglycemia) results in higher risk for in-hospital complications. In-hospital complications results in longer length of hospitalization, which implies that lower glucose levels (hypoglycemia) indirectly may result in longer length of hospitalization. More studies are needed to better clarify the cause for these associations.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a condition affecting 24 million people and is the fourth leading cause of death in the United States,[1] with in-hospital mortality ranging from 2% to 30%.[2] Identification of prognostic factors may lead to improved treatment strategies and clinical outcomes for COPD. Among acute exacerbation of COPD (AECOPD) patients, adverse outcomes are associated with lower arterial pH, older age,[2-5] male gender, underlying comorbidities, higher income,[2,4,5] disease severity, and in-hospital complications.[5]

One readily available prognostic indicator is blood glucose. Data show that higher blood glucose is associated with adverse outcomes among patients with acute myocardial infarction,[6,7] brain injury,[8] community-acquired pneumonia,[9,10] severe trauma,[11] critical illness,[12-14] and those undergoing cardiothoracic surgery.[15-17] These results, along with the fact that nearly half of patients hospitalized with AECOPD suffer from hyperglycemia during hospitalization,[18,19] suggest that blood glucose could serve as an important tool for patient monitoring during AECOPD hospitalization. Studies have shown that hospitalized COPD patients with elevated blood glucose have longer hospital stays,[20] more frequent isolation of gram negative bacteria,[21] late non-invasive ventilatory failure,[22] and higher mortality risk.[23]

The association between hyperglycemia and AECOPD outcomes has not been fully described. Baker et al[18] reported a 15% increase in absolute risk of adverse outcomes for each 1 mol/l increase in blood glucose; however, the case definition used created the potential for inclusion of patients with conditions in

Table 1. Serum Glucose Measurements (Capillary and Serum) During Hospitalization

Number of Blood Glucose Measurements Taken in a 24-hour Period	N	Mean	Median	Standard Deviation	Minimum	Maximum
1	97	132	133	38	54	252
2	19	191	183	69	98	364
3	10	205	209	66	114	312
4	28	218	205	75	121	427
5	43	273	265	77	162	483
6	8	380	398	121	223	560
7	3	360	373	63	291	415
8	4	534	528	51	478	600
9 or more	3	283	292	45	234	322

addition to AECOPD, such as bronchial asthma and pneumonia. Also, the authors' limited analysis to the highest value occurring at any time during the hospitalization[18] allows inference to be drawn from the absolute peak blood glucose value, but not from a complete picture of blood glucose during hospitalization.

The purpose of this study was to explore the association between blood glucose levels and clinical outcomes among hospitalized AECOPD patients on a general medical floor. We hypothesized that abnormal blood glucose (hypoglycemia and hyperglycemia) would be associated with adverse clinical outcomes.

METHODS

Study Population

A retrospective cohort of 209 patients hospitalized with a diagnosis of AECOPD within the Marshfield Epidemiology Surveillance Area (MESA), a 24-ZIP code area in central and northwestern Wisconsin,[24,25] were identified. Following institutional review board approval (with waiver of informed consent), patients were validated manually as meeting the study's inclusion criteria. Details about MESA are published elsewhere,[24,25] but briefly, this cohort consists of about 85,000 residents who receive health care at Marshfield Clinic and its affiliates. Patients had been admitted to the largest 2 hospitals in the MESA catchment area with a diagnosis of AECOPD from January 1, 2004 to December 31, 2008. Each patient was identified using ICD-9 Code 491.21 and a prehospitalization diagnosis of COPD based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria,[26,27] which included (1) age 40–80 years; (2) history of smoking (>20 pack-years); (3) clinical history of COPD as measured at any time by an FEV_1/FVC (FEV_1 = forced expiratory volume in the first second of expiration/FVC = forced vital capacity) ratio <70% and FEV_1 <50% predicted. Inclusion criteria also included admission and discharge diagnosis of AECOPD and at least 2 blood glucose measurements during hospitalization. We excluded patients who were transferred from other facilities or those who were transferred to palliative or intensive care units within 24 hours of admission, newly diagnosed with lung cancer or pneumonia during the hospitalization, known to be HIV positive prior to admission, and those who left against medical advice. For patients with multiple admissions, the first admission was used. Data were obtained through electronic interrogation of the MESA database and manual chart abstraction.

Data Collection

Demographic and clinical data collected for all subjects included age, gender, spirometry results, arterial blood gas on admission, body mass index (BMI), smoking history, comorbid conditions (identified in the Charlson Comorbidity Index[28]), use of noninvasive ventilation, plasma and serum blood glucose levels throughout the hospitalization, corticosteroid use with total daily dose (intravenous or oral), management of hyperglycemia (eg, diet, oral agents, insulin), and hospital discharge for reasons other than AECOPD within 30 days after the index hospital admission date.

Medical complications were extracted manually by review of patients' discharge summaries, and were defined as health care-associated infections (bacteremia, pneumonia, systemic inflammatory response syndrome), neurological (delirium, cerebrovascular accidents, coma), cardiac (new onset atrial fibrillation, decompensated congestive heart failure, myocardial infarction), or renal (acute renal failure defined as a rise in serum creatinine of at least 0.5 mg/dL over 24 hours). Serum glucose measurements (capillary and serum) measured during hospitalization were obtained (Table 1). For each patient, a daily mean blood glucose value was calculated from all measurements (fasting and random) done during hospitalization. Random blood glucose measurements were taken using a portable glucometer; fasting blood glucose was measured by Siemens Chemistry analyzer (Dimesions Xpand and Dimension EXL200 models) using a spectrophotometric hexokinase method. Daily mean blood glucose was expressed in milligrams per deciliter (mg/dL).

Statistical Analysis

Univariate analyses and multivariate logistic regression analyses with backward elimination method were used to evaluate the effects of blood glucose on length of hospitalization (LOH),

Table 2. Association Between Length of Hospitalization and Characteristics in a Population of Adults Hospitalized for Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Category of Hospital Complication	n	Percent of Patients with an In-hospital Complication (n = 24)	Percent of Patients Included in Analysis (n = 209)
Acute renal failure	3	(13)	(1)
Cardiac	17	(71)	(8)
Pulmonary	0	(0)	(0)
Neurologic	4	(8)	(2)
Health care associated infection	0	(0)	(0)

complications, 30-day hospital readmission, and 90 days all-cause mortality. The other variables considered in multivariate logistic regression models were age, diabetes mellitus (DM) status, sex, steroid use 24 hours before hospitalization, current or past smoker, BMI, inhaled medications at time of presentation, history of chronic steroid use, number of blood glucose measurements taken per day, and respiratory support (invasive and noninvasive ventilation) received during hospitalization.

LOH was considered as a discrete outcome (ie, ≤3 days vs >3 days). In-hospital complication was considered as a categorical variable comparing those patients who had at least 1 complication during the index hospitalization to those who did not, while blood glucose was classified 2 ways: as a discrete variable (at least 1 daily mean <90 mg/dl vs others) and a discrete variable (at least 1 daily mean >140 vs others). All analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, North Carolina).

RESULTS

In-hospital Complications

Twenty-four patients had in-hospital complications (Table 2). Univariate analysis revealed that lower blood glucose (at least 1 daily mean <90 mg/dl vs others) was significantly associated with in-hospital complication by comparing 37.5% of at least 1 daily mean <90 mg/dl at complication group with 9.2% at noncomplication group, $P = 0.0003$, and OR (95% CI = 5.93 (2.26-15.57). Higher blood glucose (at least 1 daily mean >140 mg/dl vs others) was not significantly associated with in-hospital complication by comparing 75.0% of at least 1 daily mean >140 mg/dl at complication group with 82.2% at noncomplication group, $P = 0.40$, and OR (95%CI) = 0.65(0.24-1.77) (Table 3). Multivariate logistic regression analysis with backward elimination method revealed that the lower blood glucose and age at hospital admission were the most significant risk factors for in-hospital complications, where OR (95% CI) = 6.45(2.12-19.66) for the lower blood glucose, and 1.08 (1.01-1.15) for age.

Length of Hospitalization

Univariate analysis revealed that lower blood glucose was significantly associated with LOH by comparing 20.7% of at least 1 daily mean <90 mg/dl at hospitalization >3 days group with 9.3% at hospitalization ≤3 days group, $P = 0.03$, and OR (95% CI) = 2.55 (1.10-5.92). Higher blood glucose was not significantly associated with LOH by comparing 87.9% of at least 1 daily mean >140 mg/dl at hospitalization >3 days group with 78.8% at hospitalization ≤3 days group, $P = 0.13$, and OR (95%CI) = 1.95(0.81-4.73) (Table 4). Multivariate logistic regression analysis with backward elimination method revealed that respiratory support and in-hospital complication were the most significant risk factors for LOH, where OR (95% CI)) = 4.68 (1.88-11.67) for respiratory support, and 3.74 (1.45-9.67) for in-hospital complication.

Hospital Readmission Within 30 Days

Thirty-six people were readmitted within 30 days of discharge from index hospitalization. Univariate analysis did not identify any factor associated with 30-day readmission, where OR (95% CI)) = 1.96 (0.75-5.07) and P-value = 0.17 for the lower blood glucose, as well as 1.18 (0.45-3.06) and P-value = 0.74 for the higher blood glucose. Multivariate logistic regression analysis with backward elimination method failed to reveal any significant risk factor associated with 30-day hospital readmission. (Data not shown.)

Ninety Day All-cause Mortality

Eight people died due to any cause within 90 days of index hospitalization. Similarly, univariate analysis did not show any factor associated with 90-day all-cause mortality, where OR (95% CI)) = 1.01(0.12-8.52) and P-value = 0.996 for the lower blood glucose, as well as 0.36 (0.08-1.59) and P-value = 0.18 for the higher blood glucose. Multivariate logistic regression analysis with backward elimination method did not reveal any significant risk factor either associated with 90-day hospital readmission. (Data not shown.)

DISCUSSION

Our study among hospitalized AECOPD patients on the general medical floor failed to reveal significant relationship between higher blood glucose and adverse clinical outcomes.

Our study differs from the study by Baker et al,[18] which may explain the difference in results. First, our study population was defined based on prior spirometric measurements and World Health Organization (WHO) criteria for exacerbation, whereas the Baker study relied solely on ICD-10 codes. Second, the Baker study did not utilize any radiological data to rule out other pulmonary comorbidities, like pneumonia, which might confer a confounding effect on the data. Third, there were differences in methods for reporting blood glucose data. Studies utilized either a single admission blood glucose,[8-11] daily mean blood glucose,[14,15] or a single blood glucose obtained (fasting or nonfasting) during

Table 3. Association Between In-hospital Complications and Characteristics in a Population of Adults Hospitalized for Acute Exacerbation of Chronic Obstructive Pulmonary Disease

	Complications During Index Hospitalization	No. Complications During Index Hospitalization	Univariate Analysis		
Characteristic	**n = 24**	**n = 185**	**OR**	**95% CI**	***P*-value**
Blood glucose: at least 1 daily mean >140mg/dl – n (%)	18 (75.0)	152 (82.2)	0.65	0.24-1.77	0.40
Blood glucose: at least 1 daily mean <90mg/dl – n (%)	(37.5)	17 (9.2)	5.93	2.26-15.57	0.0003
Age (years) at hospital admission – mean (sd)	67.3 (9.5)	64.5 (8.1)	1.05	0.99-1.11	0.11
Diabetes Mellitus at hospital admission – n (%)	7 (29)	56 (30)	0.95	0..37-2.42	0.91
Male sex – n (%)	7 (29)	73 (39)	0.63	0.25-1.60	0.33
Corticosteroids given within 24 hours of hospitalization – n (%)	24 (100)	176 (96)	*		
Current smoker – n (%)	8 (33)	75 (41)	0.73	0.30-1.80	0.50
Body mass index in kg/m^2 – mean (sd)	32.6 (8.7)	31.1 (8.8)	1.02	0.97-1.07	0.45
Inhaled medications at the time of presentation – n (%)	20 (83)	165 (89)	0.61	0.19-1.95	0.40
History of chronic steroid use – n (%)	1 (4)	21 (11)	0.34	0.04-2.63	0.30
Received respiratory support during hospitalization – n (%)	5 (21)	23 (12)	0.54	0.18-1.59	0.26
Number of blood glucose measurements taken per day –mean (sd)	1.7 (1.9)	2.6 (1.8)	0.66	0.47-0.93	0.02

Table 4. Association Between Length of Hospitalization and Characteristics in a Population of Adults Hospitalized for Acute Exacerbation of Chronic Obstructive Pulmonary Disease

	Hospitalization > 3 Days	Hospitalization ≤ 3 Days	Univariate Analysis		
Characteristic	**n = 58**	**n= 151**	**OR**	**95% CI**	***P*-value**
Blood glucose: at least 1 daily mean>140mg/dl – n (%)	51 (87.9)	119 (78.8)	1.95	0.81-4.73	0.13
Blood glucose: at least 1 daily mean<90mg/dl – n (%)	12 (20.7)	14 (9.3)	2.55	1.10-5.92	0.03
Age (years) at hospital admission – mean (sd)	64.6 (8.5)	64.9 (8.3)	0.996	0.96-1.03	0.85
Diabetes Mellitus at hospital admission – n (%)	21 (36.2)	42 (27.8)	1.47	0.77-2.80	0.24
Received respiratory support during hospitalization – n (%)	17 (29.3)	11 (7.3)	5.28	2.29-12.16	<0.0001
Complications during hospitalization – n (%)	14 (24.1)	10 (6.6)	4.49	1.86-10.81	0.0004
Male sex – n (%)	21 (36.2)	59 (39.1)	0.89	0.47-1.66	0.70
Corticosteroids given within 24 hours of hospitalization – n (%)	56 (96.6)	144 (96.0)	1.17	0.23-5.95	1.000
Current smoker – n (%)	21 (36.2)	62 (41.1)	0.82	0.44-1.52	0.52
Body mass index in kg/m^2 – mean (sd)	32.4 (9.9)	30.9 (8.4)	1.02	0.98-1.06	0.29
Inhaled medications at the time of presentation – n (%)	55 (94.8)	130 (86.1)	2.96	0.85-10.34	0.08
History of chronic steroid use – n (%)	8 (13.8)	14 (9.3)	1.55	0.62-3.93	0.35
Number of blood glucose measurements taken per day – mean (sd)	2.6 (2.5)	2.9 (2.0)	0.94	0.81-1.09	0.43

hospitalization.[10,18,19,21-23] Our study utilized a daily mean blood glucose, since blood glucose levels among AECOPD patients on systemic corticosteroids tend to peak around afternoon and evening hours.[29] Therefore, blood glucose measurements taken throughout the day more accurately capture patients' glycemic status, although all of the approaches discussed are imperfect.

Our a priori expectation that adverse outcomes in hospitalized AECOPD patients would be associated with the higher blood glucose (as noted in recent observational data) was not validated. In fact, our study revealed that the lower blood glucose levels resulted in higher risk for in-hospital complication, and in-hospital complication resulted in longer duration of hospitalization. Therefore, lower blood glucose may indirectly result in longer duration of hospitalization. The occurrence of normal or lower blood glucose among AECOPD patients is not common, since COPD exacerbation is characterized by an inflammatory process involving prohyperglycemia agents like stress hormones and cytokines,[30-32] and patients routinely are treated with systemic corticosteroids that increase blood glucose.

Recent data show that the lower blood glucose is associated with adverse outcomes in other conditions including increased morbidity and mortality.[10,33-38] The presence of hypoglycemia itself may be a marker for severity of illness, may have direct consequences itself, or be a treatment related side-effect. The presence of hypoglycemia, independent of treatment-related effects, may reflect defects in glucose counter-regulation, an imbalance between reduction in circulating insulin and enhanced glucagon secretion in response to lower glucose levels, or aberrant physiologic response to falling glucose levels. Therefore, the patient's inability to mount a hyperglycemic response in the presence of these 2 biochemical processes might portend an adverse clinical outcome. Our study is the first to demonstrate that hypoglycemia as defined by a blood sugar less than 90 mg/dl in patients with AECOPD is associated with adverse clinical outcomes.

This study was performed in a rural, white population, which limits its generalizability to other populations. The role of ste-

roids in the treatment of COPD exacerbations has long been established,[21,22,32,39] but we were unable to collect data regarding corticosteroid dosage, which is highly variable in clinical practice. Corticosteroid dosage likely exerts great influence on blood glucose trends, but the clinical importance of these fluctuations remains unclear. Although we looked at patients with spirometry, baseline disease severity per WHO/GOLD criteria staging was not included in our analysis. Also, it is important to note that although our study is large compared to previous studies, it is possible that it was not large enough to have the power necessary to detect the significant relationship between higher blood sugars and adverse outcomes in this population. Therefore, further larger studies in this population to incorporate this data would help to elucidate the complex interactions between metabolic control of blood glucose, extraneous hyperglycemic agents, and clinical outcomes.

CONCLUSION

Our study differed from previous studies by the absence of a relationship between adverse outcomes and increased blood glucose levels. Interestingly, we found that blood sugars less than 90 mg/dl were associated with in-hospital complication and may indirectly result in longer LOH. Further studies examining dose and duration of steroid dose, as well as stratification based on spirometric data, may provide further insights of the many subtleties and complexities of this association on LOH and adverse medical complications.

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REFERENCES

1. National Heart, Lung, and Blood Institute. *Morbidity and mortality: Chart book on cardiovascular, lung, and blood diseases.* US Department of Health and Human Services, Public Health Service, National Institutes of Health; 2007. http://www.nhlbi.nih.gov/resources/docs/cht-book.htm. Accessed October 24, 2013.

2. Patil SP, Krishnan JA, Lechtzin N, Diette GB. In-hospital mortality following acute exacerbations of chronic obstructive pulmonary disease. *Arch Intern Med.* 2003;163(10):1180-1186.

3. Warren PM, Flenley DC, Millar JS, Avery A. Respiratory failure revisited: acute exacerbations of chronic bronchitis between 1961-68 and 1970-76. *Lancet.* 1980;1(8166):467-470.

4. Groenewegen KH, Schols AM, Wouters EF. Mortality and mortality-related factors after hospitalization for acute exacerbation of COPD. *Chest.* 2003;124(2):459-467.

5. Bustamante-Fermosel A, De Miguel-Yanes JM, Duffort-Falcó M, Muñoz J. Mortality-related factors after hospitalization for acute exacerbation of chronic obstructive pulmonary disease: the burden of clinical features. *Am J Emerg Med.* 2007;25(5):515-522.

6. Malmberg K, Ryden L, Wedel H, et al. Intense metabolic control by means of insulin in patients with diabetes mellitus and acute myocardial infarction (DIGAMI 2): effects on mortality and morbidity. *Eur Heart J.* 2005;26(7):650-661.

7. Norhammar AM, Ryden L, Malmberg K. Admission plasma glucose Independent risk factor for long-term prognosis after myocardial infarction even in nondiabetic patients. *Diabetes Care.* 1999;22(11):1827-1831.

8. Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. *Stroke.* 2001;32(10):2426-2432.

9. McAlister FA, Majumdar SR, Blitz S, Rowe BH, Romney J, Marrie TJ. The relation between hyperglycemic and outcomes in 2,471 patients admitted to the hospital with community-acquired pneumonia. *Diabetes Care.* 2005;28(4):810-815.

10. Godar DA, Kumar DR, Schmelzer KM, et al. The impact of serum glucose on clinical outcomes in patients hospitalized with community-acquired pneumonia. *WMJ.* 2011;110(1):14-20.

11. Laird AM, Miller PR, Kilgo PD, Meredith JW, Chang MC. Relationship of early hyperglycemia to mortality in trauma patients. *J Trauma.* 2004;56(5):1058-1062.

12. van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in the critically ill patients. *N Engl J Med.* 2001;345(19):1359-1367.

13. van den Berghe G, Wilmer A, Hermans G, Meersseman W, Wouters PJ, Milants I, Van Wijngaerden E, Bobbaers H, Bouillon R. Intensive insulin therapy in the medical ICU. *N Engl J Med.* 2006;354(5):449-461.

14. Krinsley JS. Association between hyperglycemia and increased hospital mortality in a heterogeneous population of critically ill patients. *Mayo Clin Proc.* 2003;78(12):1471-148.

15. Gandhi GY, Nuttall GA, Abel MD, et al. Intraoperative hyperglycemia and perioperative outcomes in cardiac surgery patients. *Mayo Clin Proc.* 2005;80(7):862-866.

16. Estrada CA, Young JA, Nifong W, Chitwood WR Jr. Outcomes and perioperative hyperglycemia in patients with or without diabetes mellitus undergoing coronary artery bypass grafting. *Ann Thorac Surg.* 2003;75(5):1392-1399.

17. Furnary AP, Gao G, Grunkemeier GL, et al. Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting. *J Thorac Cardiovasc Surg.* 2003;125(5):1007-1021.

18. Baker EH, Janaway CH, Philips BJ, Wu Y, Zerr KJ, Bookin SO, Floten HS, Starr A. Hyperglycaemia is associated with poor outcomes in patients admitted to hospital with acute exacerbations of chronic obstructive pulmonary disease. *Thorax.* 2006(4):284-289.

19. Chakrabarti B, Angus RM, Agarwal S, Lane S, Calverley PM. Hyperglycaemia as a predictor of outcome during non-invasive ventilation in decompensated COPD. *Thorax.* 2009; 64(10):857-862.

20. Parappil A, Depczynski B, Collett P, Marks GB. Effect of comorbid diabetes on length of stay and risk of death in patients admitted with acute exacerbations of COPD. *Respirology.* 2010;15(6):918-922.

21. Loukides S, Polyzogopoulos D. The effect of diabetes mellitus on the outcome of patients with chronic obstructive pulmonary disease exacerbated due to respiratory infections. *Respiration.* 1996;63(3):170-173.

22. Moretti M, Cilione C, Tampieri A, Fracchia C, Marchioni A, Nava S. Incidence and causes of non-invasive mechanical ventilation failure after initial success. *Thorax.* 2000;55(10):819-825.

23. Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Endocrinol Metab.* 2002;87(3):978–982.

24. Greenlee RT. Measuring disease frequency in the Marshfield Epidemiologic Study Area (MESA). *Clin Med Res.* 2003;1(4):273–280.

25. DeStefano F, Eaker ED, Broste SK, et al. Epidemiologic research in an integrated regional medical care system: the Marshfield Epidemiologic Study Area. *J Clin Epidemiol.* 1996;4949(6):643–652.

26. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS; GOLD Scientific Committee. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. *Am J Respir Crit Care Med.* 2001;163(5):1256–1276.

27. Rabe KF, Hurd S, Anzueto A, et al. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med.* 2007;176(6):532-555.

28. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40(5):373-383.

29. Burt MG, Roberts GW, Aguilar-Loza NR, Frith P, Stranks SN. Continuous monitoring of circadian glycemic patterns in patients receiving prednisolone for COPD. *J Clin Endocrinol Metab.* 2011;96(6):1789-1796.

30. Chung KF. Cytokines in chronic obstructive pulmonary disease. *Eur Respir J Suppl.* 2001;34:50s-59s.

31. Mannino DM, Ford ES, Redd SC. Obstructive and restrictive lung disease and markers of inflammation: data from the Third National Health and Nutrition Examination. *Am J Med.* 2003;114(9):758-762.

32. Wood-Baker RR, Gibson PG, Hannay M, Walters EH, Walters JA. Systemic corticosteroids for acute exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev.* 2005;(1):CD001288.

33. Foltran F, Gregori D, Caropreso A, Pagano E, Bruno A. Is blood glucose on admission a predictor of mortality in adult acute pneumonia? *Clin Respir J.* 2012;Sep 14. doi: 10.1111/crj.12003. [Epub ahead of print]

34. Mortensen EM, Garcia S, Leykum L, Nakashima B, Restrepo MI, Anzueto A. Association of hypoglycemia with mortality for subjects hospitalized with pneumonia. *Am J Med Sci.* 2010;339(3):239-43.

35. Gamble JM, Eurich DT, Marrie TJ, Majumdar SR. Admission hypoglycemia and increased mortality in patients hospitalized with pneumonia. *Am J Med.* 2010;123(6):556.e11-556.e16.

36. Duning T, van den Heuvel I, Dickmann A, et al. Hypoglycemia aggravates critical illness-induced neurocognitive dysfunction. *Diabetes Care.* 2010;33(3):639-644.

37. Egi M, Bellomo R, Stachowski E, et al. Hypoglycemia and outcome in critically ill patients. *Mayo Clin Proc.* 2010;85(3):217-224.

38. Arabi YM, Tamim HM, Rishu AH. Hypoglycemia with intensive insulin therapy in critically ill patients: predisposing factors and association with mortality. *Crit Care Med.* 2009;37(9):2536-2544.

39. Majori M, Corradi M, Caminati A, Cacciani G, Bertacco S, Pesci A. Predominant TH1 cytokine pattern in peripheral blood from subjects with chronic obstructive pulmonary disease. *J Allergy Clin Immunol.* 1999;103(3 Pt 1):458-462.

CME

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Quiz: Association Between Blood Glucose Level and Outcomes in Patients Hospitalized for Acute Exacerbation of Chronic Obstructive Pulmonary Disease

EDUCATIONAL OBJECTIVES

Upon completion of this activity, participants will be able to:

1. Appreciate the factors associated with adverse clinical outcomes in patients hospitalized with an acute exacerbation of chronic obstructive pulmonary disease (AECOPD).
2. Recognize the role that an altered blood glucose level may have on hospitalized patients with AECOPD and other acute illnesses.

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QUESTIONS

1. Chronic obstructive pulmonary disease is a chronic condition affecting 50 million people and is the sixth leading cause of death in the United States, with in-hospital mortality ranging from 2% to 30%.
   - ❑ True
   - ❑ False
2. Adverse outcomes of AECOPD are associated with:
   - ❑ Lower arterial pH, older age, female gender
   - ❑ Underlying comorbidities, disease severity, in-hospital complications
   - ❑ In-hospital complications, lower arterial pH, younger age, male gender
   - ❑ Underlying comorbidities, disease severity, in-hospital complications, higher arterial pH, older age, male gender
   - ❑ None of the above
3. Data from other studies have shown that higher blood glucose is associated with adverse outcomes among patients with acute myocardial infarction, brain injury, community-acquired pneumonia, severe trauma, critical illness, and those undergoing cardiothoracic surgery.
   - ❑ True
   - ❑ False
4. Hospitalized COPD patients with elevated blood glucose have been found in other studies to have longer hospital stays, more frequent isolation of gram negative bacteria, ventilatory failure, and a higher mortality risk.
   - ❑ True
   - ❑ False
5. The present study revealed a significant relationship between higher blood glucose levels and adverse clinical outcomes among patients hospitalized with AECOPD.
   - ❑ True
   - ❑ False
6. The present study revealed that among patients hospitalized with AECOPD, a lower blood glucose level was a significant risk factor associated with an in-hospital complication and increased hospital length of stay.
   - ❑ True
   - ❑ False
7. In the present study of patients with AECOPD, hospital readmission within 30 days and 90-day all cause mortality were significantly increased in patients with both increased and decreased blood sugar levels during hospitalization.
   - ❑ True
   - ❑ False

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