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Association between right heart failure and hospital mortality in exacerbation of COPD

Brenda Santellano-Juárez, Dulce González-Islas,* Edna Contreras-Ramírez,* Arturo Orea-Tejeda,* ✉ Juan Pineda-Juárez,* Viridiana Peláez-Hernández,* C. Keirns-Davies,‡ Raúl Herrera-Saucedo,* Marcela Elizondo-Montes,* Guillermo Pérez-Cortes**

*Heart Failure and Respiratory Distress Clinic, Cardiology Department at Instituto Nacional de Enfermedades Respiratorias Ismael Cosío Villegas, Mexico City, Mexico; ‡Massachusetts General Hospital Interpreter Services, Boston, MA 02114, U.S.A.
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ABTRACT. Background: Patients with chronic obstructive pulmonary disease (COPD) have a high prevalence of heart failure (HF). Patients with concurrent HF and COPD have worse prognosis. However, the impact of Right Heart Failure (RHF) on hospital mortality has not been explored. **Objective:** To evaluate the association between of right heart failure (RHF) and hospital mortality in COPD patients. **Methods:** An analytical cross-sectional study was performed in hospitalized COPD patients. The patients hospitalized between 2014 and 2015 were including in study. **Results:** Ninety-five patients diagnosed with COPD were analyzed: COPD alone (n = 25), COPD and HF with preserved ejection fraction (HFpEF) (n = 29), COPD and RHF (n = 41) and COPD and HF with reduced ejection fraction (HFrEF) (n = 0). The variables associated with risk of hospital mortality were RHF (OR: 10.91, 95% CI: 1.28 to 92.65, p = 0.029), stroke (OR: 14.4, 95% CI: 2.64 to 78.37, p 0.002), pulmonary thromboembolism (OR: 2.09, 95% CI: 1.47-2.98, <0.001) and chronic renal disease (OR: 4.08, 95% CI: 3.36 to 7.01, p < 0.001). Finally, RHF with COPD subjects has 9.42 times more risk of hospital mortality (OR: 9.42, 95% CI: 1.00 to 88.31, p = 0.049) than COPD without RHF adjusted by confusing variables. **Conclusion:** RHF is a independient risk factor for hospital mortality in COPD patients.

Key words: Right heart failure, prognosis, chronic obstructive pulmonary disease, hospital mortality, right ventricular disfunction.

RESUMEN. Antecedentes: Los pacientes con enfermedad pulmonar obstructiva crónica (EPOC) tienen alta prevalencia de insuficiencia cardíaca (IC). Los pacientes con concurrente IC y EPOC tienen peor pronóstico. Sin embargo, el impacto de la insuficiencia cardíaca derecha (ICD) sobre la mortalidad hospitalaria no ha sido explorada. **Objetivos:** Evaluar la asociación entre la ICD y la mortalidad hospitalaria en pacientes con EPOC. **Métodos:** Estudio transversal analítico llevado a cabo en pacientes con EPOC hospitalizados. Los pacientes hospitalizados entre el 2014 y 2015 fueron incluidos. **Resultados:** Noventa y cinco pacientes con diagnóstico de EPOC fueron analizados: EPOC solo (n = 25), EPOC con ICFEp (insuficiencia cardíaca con fracción de expulsión preservada) (n = 29), EPOC e IC (n = 41), y EPOC con ICFEc (insuficiencia cardíaca con fracción de expulsión reducida) (n = 0). Las variables asociadas con riesgo de mortalidad hospitalaria fueron ICD (OR: 10.91, 95% CI: 1.28 a 92.65, p = 0.029), evento cerebrovascular (OR: 14.4, 95% CI: 2.64 a 78.37, p 0.002), tromboembolia pulmonar (OR: 2.09, 95% CI: 2.09 1.47-2.98 < 0.001) y enfermedad renal crónica (OR: 4.08, 95% CI: 3.36 a 7.01, p < 0.001). **Conclusión:** La ICD es un factor de riesgo independiente para mortalidad hospitalaria en los pacientes con EPOC, que incrementa 9.42 veces.

Palabras clave: Insuficiencia cardíaca derecha, pronóstico, enfermedad pulmonar obstructiva crónica, mortalidad hospitalaria, disfunción del ventrículo derecho.

Abbreviations
COPD = Chronic obstructive pulmonary disease.
GOLD = Global initiative for chronic obstructive lung disease.
HF = Heart failure.
HFpEF = Heart failure with preserved ejection fraction.
HFrEF = Heart failure with reduced ejection fraction.
RHF = Right heart failure.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable condition characterized by persistently limited flow in the air ways of a progressive nature associated with an inflammatory response in the lungs to noxious particles or gases. It is estimated that by 2020 it will be the third most common cause of death worldwide.[1] The prevalence of COPD has been found to be from 7.6% to 34.1%,[2,3] depending on the criteria used for diagnosis and classification. The PLATINO study (Latin American Project for the Investigation of

Obstructive Lung Disease) showed higher prevalence in men and older adults with less formal education, lower body mass index and greater exposure to tobacco.[4]

Exacerbations and associated conditions contribute to the overall severity of COPD in affected patients. In the United States from 1979 to 2001 it was the first and second cause of hospital admission associated with higher mortality and co-morbidity compared with patients admitted without COPD.[5] Mortality at one year is relatively low around 3%[6] but increases to 25% after hospital admission.[7]

Some 79 co-morbidities have been reported with COPD, of which the 12 most prevalent are associated with an increase in risk of death. The most common associated conditions are diabetes, hyperlipidemia, arterial hypertension, cancer, peripheral arterial disease and cardiovascular disease. Cardiovascular disease accompanying COPD has been associated with a poor prognosis with increased risk of hospital admission and death. The risk of death in COPD patients in heart failure increases 33% (HR 1.33, 95% CI 1.06-1.68).[8-10]

Heart failure (HF) is a clinical syndrome resulting from any structural or functional alteration in ventricular filling or systolic function. The risk of developing HF is 20% in Americans ≥ 40 years of age.[11] In the ARIC study, the mortality rate at 30 days, 1 year and 5 years after hospitalization for HF was 10.4%, 22% and 42.3% respectively.[12]

HF and COPD are associated with high morbidity and mortality worldwide. Because they share risk factors and pathophysiological mechanisms they often co-exist. This implies that together they may represent an independent predictor of morbidity and mortality, functional deterioration and use of health services.[13] From 10% to 40% of patients with HF are estimated to have COPD as well.[14] The prevalence of HF in patients with exacerbated COPD is 20.9%, while it ranges from 17% to 20.5% in stable COPD.[14-16] Thus, COPD is an independent predictor of hospitalization and death in patients with HF.[17] In a 5 year follow-up of patients admitted to the hospital for HF a worse prognosis was observed in those with COPD (HR 1.53, 95% CI 1.21-1.94) adjusted for confounding factors.[8] However, the effect of the type of HF in hospital mortality in patients with COPD is unknown. The objective of this study was to evaluate the association between of right heart failure (RHF) and hospital mortality in COPD patients.

METHODS

Study design

An analytical cross-sectional study was performed in hospitalized COPD patients at Instituto Nacional de Enfermedades Respiratorias Ismael Cosío Villegas. The patients hospitalized between Janury 2014 and May 2015 were including in study. This study was approved by the Ethics and Research Committee of the Instituto Nacional de Enfermedades Respiratorias Ismael Cosío Villegas (Approval Number E04-15).

Participants

Inclusion criteria were patients who were > 40 years old, hospitalized for exacerbation, patients who had a primary or secondary diagnosis of COPD established according to the criteria proposed by the Global initiative for Chronic Obstructive Lung Disease (GOLD) with a FEV_1/FVC ratio after a bronchodilator ≤ 0.70%.[18] Patients with asthma and atrial fibrillation were excluded.

Data sources/measurement

The clinical data were collected from patient´s medical records. The indepented variables included were: age, sex, length of hospital stay and reason for discharge (improvement or death) and co-morbidities. These comorbilities includes: Diabetes mellitus, sistemic hypertension, obstructive sleep apnea syndrome, stroke, pulmonary thromboembolism, chronic kidney disease, gastro-esophageal reflux disease and heart failure. The heart failure type was established according to the European Cardiology guidelines (ESC).[19] The diagnosis was performed when the patients were stable and before hospital admission.

Once the types of HF were classified the population was divided into the following groups: COPD alone, COPD with HFpEF, COPD with HFrEF and COPD with RHF.

Statistical analysis

For Statistical analysis qualitative characteristics of patients were considered as frequencies and percentages. Continuous variables were evaluated using the Shapiro-Wilk statistical program in order to determine the type of distribution of each variable. Variables with normal distribution were presented as mean and standard deviation, while variables with abnormal distribution were reported with median values and percentiles [25-75]. The different study groups COPD alone, COPD with HFpEF, COPD with HFrEF and COPD with RHF were analyzed using χ^2 for categorical variables and ANOVA for continuous variables with normal distribution and Kruskal-Wallis test for variables with abnormal distribution. In order to identify the variables independently associated with risk of death univariate logistic regression was performed for

Table 1. Patient characteristics.

	Total (n = 95)	COPD (n = 25)	COPD + HFpEF (n = 29)	COPD + RHF (n = 41)	p-value
Age (years)	74.54 ± 11.35	73.12 ± 13.44	76.96 ± 7.47	73.70 ± 12.22	0.384
Men [n (%)]	29 (30.53)	6 (24)	15 (51.72)	8 (19.51)	0.011
Length of stay (days)	10 [7-15]	9 [5-11]	10 [7-12]	9 [6-14]	0.365
Comorbidities					
DM [n (%)]	4 (4.21)	0 (0)	4 (13.79)	0 (0)	0.009
Systemic hypertension	17 (17.89)	5 (20)	6 (20.69)	6 (14.63)	0.769
OSAS [n (%)]	2 (2.11)	1 (4)	1 (3.45)	0 (0)	0.456
Stroke [n (%)]	21 (22.11)	1 (4)	3 (10.34)	17 (41.46)	< 0.001
PTE [n (%)]	7 (7.37)	2 (8)	0 (0)	5 (12.2)	0.156
CKD [n (%)]	8 (8.42)	2 (8)	5 (17.24)	1 (2.44)	0.089
GERD [n (%)]	1 (1.05)	0 (0)	0 (0)	1 (2.44)	0.514

DM = Diabetes *mellitus*; OSAS = Obstructive sleep apnea syndrome; PTE = Pulmonary thromboembolism; CKD = Chronic kidney disease; GERD = Gastro-esophageal reflux disease.

which a confounding variable was considered to be one with a $p < 0.20$. Finally, multivariate logistic regression analysis adjusted for confounding variables was used to determine risk of hospital mortality in subjects with RHF. A finding with $p < 0.05$ was considered to be statistically significant. Stata software (version 12) was used for statistical analysis (Stata Corp., College Station, TX, USA).

RESULTS

Three hundred twenty-two cases were reviewed. Of these, 95 patients met the inclusion criteria with complete information: 25 with COPD alone, 29 with COPD and HFpEF and 41 with COPD and RHF. No patients had COPD and HFrEF. The mean age of the population was 74.54 ± 11.35 years, 30.53% of whom were men. The co-morbidities most frequently found were systemic hypertension (17.89%) and stroke (22.11%). In the study groups a higher proportion of men was found in the group with COPD and HFpEF (51.72%) compared to the groups with COPD alone and COPD with RHF (24% and 19.51% respectively = 0.011). Higher prevalence of diabetes mellitus and chronic renal disease was found in patients with COPD and HFpEF, while stroke was more common in patients with the COPD with RHF (41.46%) in comparison with the other two groups (COPD alone 4% and COPD with HFpEF 10.34%, $p < 0.001$; table 1).

Using univariate logistic regression, the variables associated with risk of hospital mortality in COPD patients were RHF (OR: 10.91, 95% CI: 1.28 to 92.65, p = 0.029), stroke (OR: 14.4, 95% CI: 2.64 to 78.37, p 0.002), pulmonary thromboembolism (OR: 2.09, 95% CI: 1.47 - 2.98, p <0.001) and chronic renal disease (OR: 4.08, 95% CI: 3.36 to 7.01, $p < 0.001$) (table 2).

Table 2. Univariate analysis of association between patient characteristics and risk of hospital mortality in chronic obstructive pulmonary disease.

	OR	CI 95%	p-value
Gender	1.4	0.31-6.32	0.656
Age	1.05	0.97-1.13	0.159
Length of stay (days)	1.01	0.97-1.06	0.415
RHF	10.91	1.28-92.65	0.029
HFpEF	1.95	0.44-8.70	0.377
Co-morbidity			
DM	1.11	0.78-1.58	0.535
Systemic hypertension	0.63	0.07-5.52	0.680
OSA	2.20	0.21-22.08	0.502
Stroke	14.4	2.64-78.37	0.002
PTE	2.09	1.47-2.98	< 0.001
CKD	4.08	3.36-7.01	< 0.001

RHF = Right Heart Failure; HFpEF = Heart Failure with preserved ejection fraction; DM = Diabetes *mellitus*; OSA = Obstructive sleep apnea syndrome; PTE = Pulmonary thromboembolism; CKD = Chronic kidney disease.

Finally, a multivariate logistic model showed that RHF with COPD subjects had 9.42 times more risk of hospital mortality (OR: 9.42, 95% CI: 1.00 to 88.31, p = 0.049) than COPD without RHF adjusted by age, stoke, pulmonary thromboembolism, chronic kidney disease and HFpEF.

DISCUSSION

The most outstanding result of our study was finding that when RHF was isolated from other types of HF it represented an independent risk factor for hospital

mortality in exacerbation of COPD patients. Moreover, when it occurred concurrently with COPD it significantly increased risk of death.

It is known that the effects of COPD are not limited to the lungs, and the inflammation associated with COPD produces stress, vasomotor changes and alteration in endothelial function.[20] These effects of inflammation in turn increase cardiovascular risk and mortality. In addition, the pulmonary vascular changes in COPD patients —predominantly pulmonary hypertension— lead to RHF.

Prior studies have shown that HF patients who also have COPD have a worse prognosis. Fisher *et al.*[21] reported that in patients hospitalized for decompensated HF those with a concurrent diagnosis of COPD had a higher risk of death at 1 year (RR: 1.10; 95% CI: 1.06-1.14) and 5 years (RR: 1.40; 95%CI: 1.28-1.52) after hospitalization compared to patients without COPD. Likewise, in a study of 378 patients hospitalized for HF, Yoshihisa *et al.*[22] found a prevalence of COPD of 28%. During follow-up there were 36 deaths from cardiovascular and 96 re-hospitalizations for decompensated HF. They concluded that once results were adjusted for confounding variables moderate COPD (GOLD II) was an independent predictor of mortality in patients with HF.

The outstanding achievement of our study was to show that RHF is an independent risk factor for hospital mortality in exacerbation COPD patients, and that when types of HF were examined separately there was a particularly significant effect on mortality in those patients with concomitant RHF and COPD.

It was also noteworthy that patients with COPD and HF had twice the mortality of those without heart failure over a follow-up period of 4.2 years (RR: 2.1; 95% CI 1.2 to 3.6).[23] In addition, when Beom-June Kwon *et al.*[24] determined the prognosis of patients with COPD according to type of left HF they found no difference in the prognosis of patients with COPD and HFrEF vs COPD and HFpEF. However, these 184 patients had an elevated incidence of cardiovascular events: 53% with HFpEF and 47% with HFrEF. During follow-up the 3 patients with HFpEF had an event that required hospitalization or died, in 19 from cardiovascular cause that did not involve HF and 13 with decompensated HR. In the HFrEF group 38 had cardiovascular events, 16 of which did not involve HF and 12 decompensated HF. There were 64 re-hospitalizations, 23 for decompensated HF and 7 deaths, 2 from HF. Nevertheless, no statistical difference in incidence was found between the two groups (p = 0.238).

In contrast to our approach, Fisher *et al.* examined patients who were hospitalized for decompensated HF,[21] while our patients were in a period of stability as regards HF, and the principle cause of hospitalization was COPD. This indicates the necessity of ruling out subclinical HF in COPD patients when they are hospitalized with particular attention to RHF. In spite of the fact that COPD and HF share a common pathophysiological process involving low level inflammation,[20,25-28] in our series left HF was not a significant cause of hospital mortality, even though diabetes mellitus and systemic hypertension were more prevalent than in RHF. Moreover, in our cases HFrEF did not even appear among the risk factors of death as would be expected. It is possible that this is because ischemic heart disease was the main cause of this type of HF and was not considered a co-morbidity.

It is also noteworthy that among the co-morbidities of patients with COPD and RHF the prevalence of stroke is very high. Indeed, in our experience RHF is a risk factor for stroke in COPD patients.[29] Inexplicably, heart disease has not received the attention it deserves in patients with obstructive pulmonary conditions, yet when we intentionally searched for right and left ventricular dysfunction in our patients, we found that the prevalence of both was extremely high and that risk of death was increased, especially with RHF.

The principal limitations of this study are the small sample size, the lack of data about the spirometry and BMI, Obstruction, Dyspnea, Exercise (BODE) index, that is widely validated how predictive survival, however these are the problem of the a cross-sectional study, However, one of its strong points is that unlike other studies, it evaluates the risk of hospital mortality in exacerbation of COPD patients according to the type of HF and includes right ventricular dysfunction. RHF has rarely been considered as an independent cause and warrants new prospective studies focused on the impact of RHF on the hospital mortality of COPD patients.

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REFERENCES

1. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet 1997;349(9064):1498-504.
2. Lindberg A, Jonsson AC, Rönmark E, Lundgren R, Larsson LG, Lundbäck B. Prevalence of chronic

obstructive pulmonary disease according to BTS, ERS, GOLD and ATS criteria in relation to doctor's diagnosis, symptoms, age, gender, and smoking habits. Respiration 2005;72(5):471-479.
3. Rosenberg SR, Kalhan R, Mannino DM. Epidemiology of Chronic Obstructive Pulmonary Disease: Prevalence, morbidity, mortality, and risk factors. Semin Respir Crit Care Med 2015;36(4):457-469. doi: 10.1055/s-0035-1555607.
4. Menezes AMB, Perez-Padilla R, Jardim JRB, et al. Chronic obstructive pulmonary disease in five Latin American cities (the PLATINO study): a prevalence study. Lancet 2005;366(9500):1875-1881.
5. Holguin F, Folch E, Redd SC, Mannino DM. Comorbidity and mortality in COPD-related hospitalizations in the United States, 1979 to 2001. Chest 2005;128(4):2005-2011.
6. Lange P, Marott JL, Vestbo J, et al. Prediction of the clinical course of chronic obstructive pulmonary disease, using the new GOLD classification: a study of the general population. Am J Respir Crit Care Med 2012;186(10):975-981. doi: 10.1164/rccm.201207-1299OC
7. Groenewegen KH, Schols AM, Wouters EF. Mortality and mortality-related factors after hospitalization for acute exacerbation of COPD. Chest 2003; 124(2):459-467.
8. Rusinaru D, Saaidi I, Godard S, Mahjoub H, Battle C, Tribouilloy C. Impact of chronic obstructive pulmonary disease on long-term outcome of patients hospitalized for heart failure. Am J Cardiol 2008;101(3):353-358. doi: 10.1016/j.amjcard.2007.08.046.
9. Divo M, Cote C, de Torres JP, et al.; BODE Collaborative Group. Comorbidities and risk of mortality in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2012;186(2):155-161. doi: 10.1164/rccm.201201-0034OC.
10. Divo MJ, Casanova C, Marin JM, et al.; BODE Collaborative Group. COPD comorbidities network. Eur Respir J 2015;46(3):640-650. doi: 10.1183/09031936.00171614.
11. Djoussé L, Driver JA, Gaziano JM. Relation between modifiable lifestyle factors and lifetime risk of heart failure. JAMA 2009;302(4):394-400. doi: 10.1001/jama.2009.1062.
12. Loehr LR, Rosamond WD, Chang PP, Folsom AR, Chambless LE. Heart failure incidence and survival (from the Atherosclerosis Risk in Communities study). Am J Cardiol 2008;101(7):1016-1022. doi: 10.1016/j.amjcard.2007.11.061.
13. Buist AS, McBurnie MA, Vollmer WM, et al.; BOLD Collaborative Research Group. International variation in the prevalence of COPD (the BOLD Study): a population-based prevalence study. Lancet 2007;370(9589):741-750.
14. Hawkins NM, Virani S, Ceconi C. Heart failure and chronic obstructive pulmonary disease: the challenges facing physicians and health services. Eur Heart J 2013;34(36):2795-2803. doi: 10.1093/eurheartj/eht192.
15. Macchia A, Rodriguez Moncalvo JJ, Kleinert M, et al. Unrecognised ventricular dysfunction in COPD. Eur Respir J 2012;39(1):51-58. doi: 10.1183/09031936.00044411.
16. Boschetto P, Fucili A, Stendardo M, et al. Occurrence and impact of chronic obstructive pulmonary disease in elderly patients with stable heart failure. Respirology 2013;18(1):125-130. doi: 10.1111/j.1440-1843.2012.02264.x.
17. Hawkins NM, Petrie MC, Jhund PS, Chalmers GW, Dunn FG, McMurray JJ. Heart failure and chronic obstructive pulmonary disease: diagnostic pitfalls and epidemiology. Eur J Heart Fail 2009;11(2):130-139. doi: 10.1093/eurjhf/hfn013.
18. Vestbo J, Hurd SS, Agustí AG, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2013;187(4):347-365. doi: 10.1164/rccm.201204-0596PP.
19. McMurray JJ, Adamopoulos S, Anker SD, et al.; ESC Committee for Practice Guidelines. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail 2012;14(8):803-869. doi: 10.1093/eurjhf/hfs105.
20. Fabbri LM, Rabe KF. From COPD to chronic systemic inflammatory syndrome? Lancet 2007;370(9589):797-799.
21. Fisher KA, Stefan MS, Darling C, Lessard D, Goldberg RJ. Impact of COPD on the mortality and treatment of patients hospitalized with acute decompensated heart failure: the Worcester Heart Failure Study. Chest 2015;147(3):637-645. doi: 10.1378/chest.14-0607.
22. Yoshihisa A, Takiguchi M, Shimizu T, et al. Cardiovascular function and prognosis of patients with heart failure coexistent with chronic obstructive pulmonary disease. J Cardiol 2014;64(4):256-264. doi: 10.1016/j.jjcc.2014.02.003.
23. Boudestein LCM, Rutten FH, Cramer MJ, Lammers JWJ, Hoes AW. The impact of concurrent heart failure on prognosis in patients with chronic obstructive pulmonary disease. Eur J Heart Fail 2009;11(12):1182-1188. doi: 10.1093/eurjhf/hfp148.
24. Kwon BJ, Kim DB, Jang SW, et al. Prognosis of heart failure patients with reduced and preserved ejection fraction and coexistent chronic obstructive pulmonary disease. Eur J Heart Fail 2010;12(12):1339-1344. doi: 10.1093/eurjhf/hfq157.
25. Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. Circulation 2002;105(9):1135-1143.
26. Perera WR, Hurst JR, Wilkinson TM, et al. Inflammatory changes, recovery and recurrence at COPD exacerbation. Eur Respir J 2007;29(3):527-534.
27. Patel AR, Kowlessar BS, Donaldson GC, et al. Cardiovascular risk, myocardial injury, and exacerbations of chronic obstructive pulmonary disease. Am J Respir

Crit Care Med 2013;188(9):1091-1099. doi: 10.1164/rccm.201306-1170OC.
28. Chang C, Yao W. Time course of inflammation resolution in patients with frequent exacerbations of chronic obstructive pulmonary disease. Med Sci Monit 2014;20:311-320. doi: 10.12659/MSM.889828.
29. Orea-Tejeda A, Bozada-Gutiérrez KE, González-Islas D, et al. Right heart failure as a risk factor for cerebrovascular event in patients with chronic obstructive pulmonary disease. Global Heart 2016;11(Suppl 2):e44.

✉ **Corresponding author:**
PhD. Arturo Orea-Tejeda. Cardiology Department Coordinator at Instituto Nacional de Enfermedades Respiratorias Ismael Cosío Villegas.
Address: Calzada de Tlalpan 4502, Col. Sec XVI, No. 14080, Del. Tlalpan, Ciudad de Mexico, Mexico
Tel: (52)555487 1700, ext. 5506
E-mail: oreatart@gmail.com

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