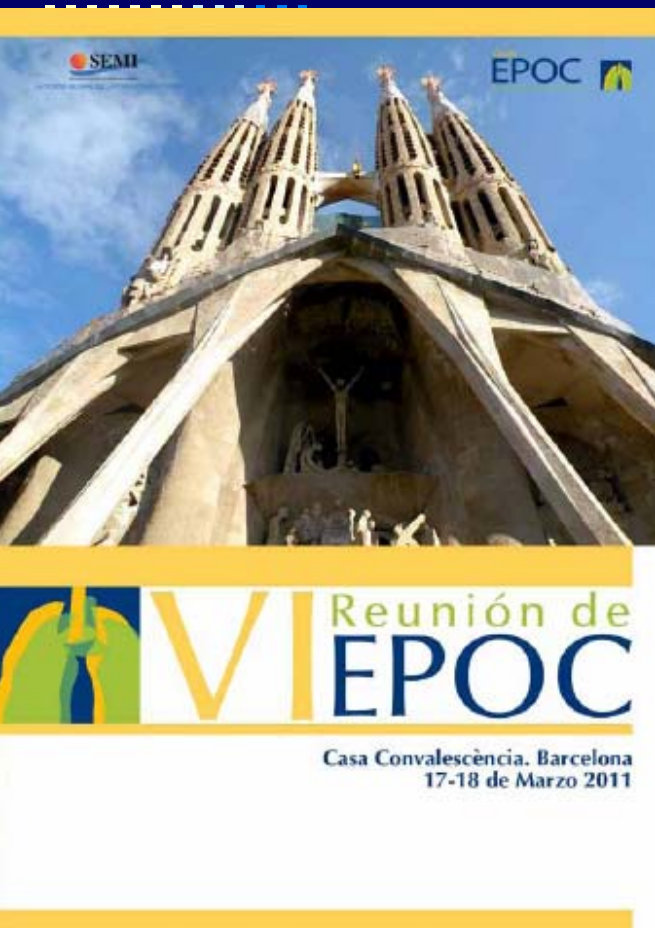




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CORRESPONDENCE

Susceptibility to Exacerbation in COPD
To the Editor: In their article on exacerbation in patients with chronic obstructive pulmonary disease (COPD), Hurst et al. (Sept. 16 issue) report that the rate of occurrence appears to reflect a susceptibility phenotype. I believe that stimulation of nonmyelinated bronchial or alveolar vagal C-fiber...
December 30, 2010 | N Engl J Med 2010; 363:2670 - 2671
[Free Full Text](#)

REVIEW ARTICLE

Medical Progress: Airway Mucus Function and Dysfunction
...by 30% or less during inflammation. However, hyperplasia may play a major role in augmented submucosal gland MUC5B production in chronic obstructive pulmonary disease (COPD) and cystic fibrosis, since gland volume increases

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SEARCH SUGGESTIONS

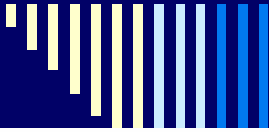
- copd exacerbation
- outpatient management of severe copd
- copd review
- chronic obstructive pulmonary disease
- copd management
- pneumonia
- severe copd
- review
- eclipse
- hurst

TRENDS: MOST VIEWED (Last Week)

Diuretic Strategies in Patients with Acute Decompensated Heart Failure
March 3, 2011

Deep-Vein Thrombosis of the Upper Extremities
March 3, 2011

Long-Term Effects of Intensive Glucose



Seleccionados

ORIGINAL ARTICLE

Percent Emphysema, Airflow Obstruction, and Impaired Left Ventricular Filling

R. Graham Barr, M.D., Dr.P.H., David A. Bluemke, M.D., Ph.D., Firas S. Ahmed, M.D., M.P.H., J. Jeffery Carr, M.D., Paul L. Enright, M.D., Eric A. Hoffman, Ph.D., Rui Jiang, M.D., Dr.P.H., Steven M. Kawut, M.D., Richard A. Kronmal, Ph.D., João A.C. Lima, M.D., Eyal Shahar, M.D., M.P.H., Lewis J. Smith, M.D., and Karol E. Watson, M.D., Ph.D.

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ORIGINAL ARTICLE

A Randomized Study of Endobronchial Valves for Advanced Emphysema

Frank C. Sciurba, M.D., Armin Ernst, M.D., Felix J.F. Herth, M.D., Charlie Strange, M.D., Gerard J. Criner, M.D., Charles H. Marquette, M.D., Ph.D., Kevin L. Kovitz, M.D., M.B.A., Richard P. Chiacchierini, Ph.D., Jonathan Goldin, M.D., Ph.D., and Geoffrey McLennan, M.D., Ph.D., for the VENT Study Research Group*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

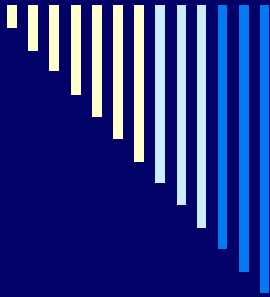
Susceptibility to Exacerbation in Chronic Obstructive Pulmonary Disease

John R. Hurst, M.B., Ch.B., Ph.D., Jørgen Vestbo, M.D., Antonio Anzueto, M.D., Nicholas Locantore, Ph.D., Hana Müllerova, Ph.D., Ruth Tal-Singer, Ph.D., Bruce Miller, Ph.D., David A. Lomas, Ph.D., Alvar Agustí, M.D., Ph.D., William MacNee, M.B., Ch.B., M.D., Peter Calverley, M.D., Stephen Rennard, M.D., Emiel F.M. Wouters, M.D., Ph.D., and Jadwiga A. Wedzicha, M.D., for the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) Investigators*

Aproximación diferente a la fisiopatología.

Aproximación diferente al tratamiento.

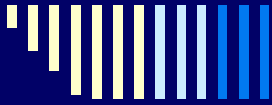
Aproximación al “caballo de batalla”.



ORIGINAL ARTICLE

Percent Emphysema, Airflow Obstruction, and Impaired Left Ventricular Filling

R. Graham Barr, M.D., Dr.P.H., David A. Bluemke, M.D., Ph.D.,
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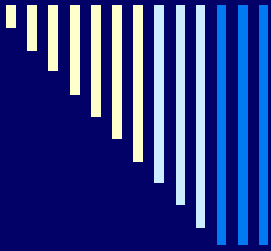


□ Situación del tema:

- En estadios muy avanzados la EPOC provoca una elevación de la resistencia vascular pulmonar. Esto secundariamente reduce el llenado ventricular izquierdo, el volumen sistólico y gasto cardiaco.

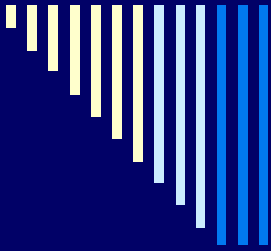
□ Hipótesis:

- El enfisema, definido por imagen TC, y la obstrucción bronquial (medida por espirometría) están inversamente relacionado con la función ventricular izquierda (medida por RMN)



□ Población:

- Estudio de base poblacional en USA para estudio de la Arteriosclerosis (MESA: Multi-Ethnic Study of Atherosclerosis).
 - 40-75 años.
 - SIN enfermedad pulmonar avanzada
- N: 2.816 pacientes

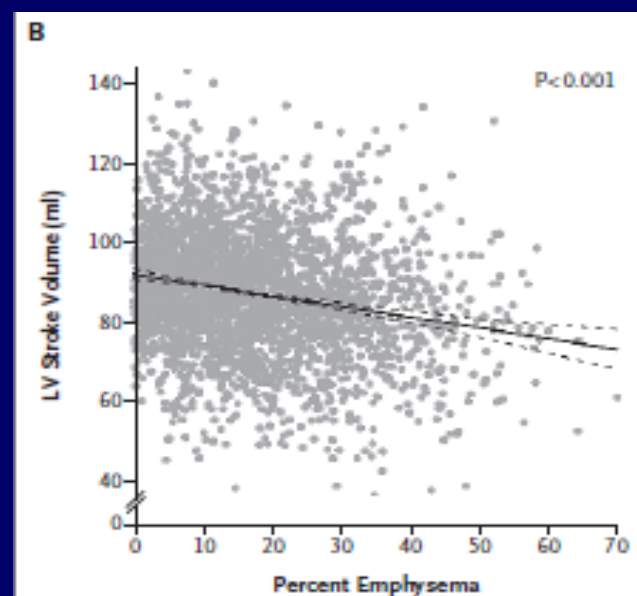
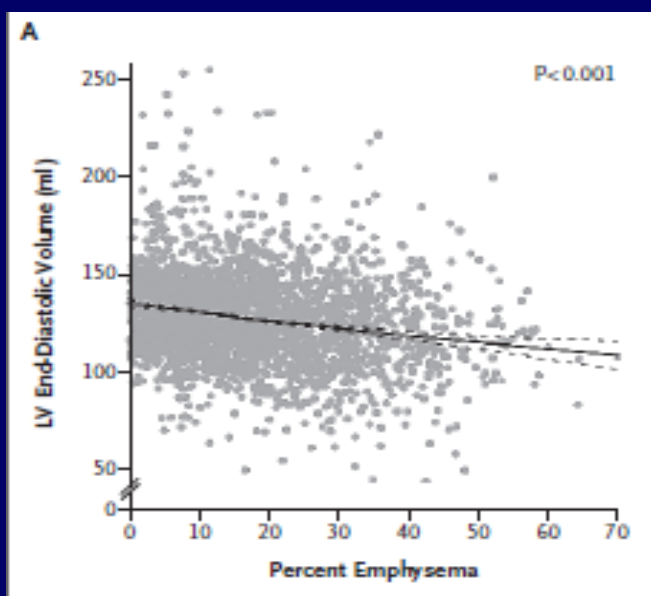


□ Métodos:

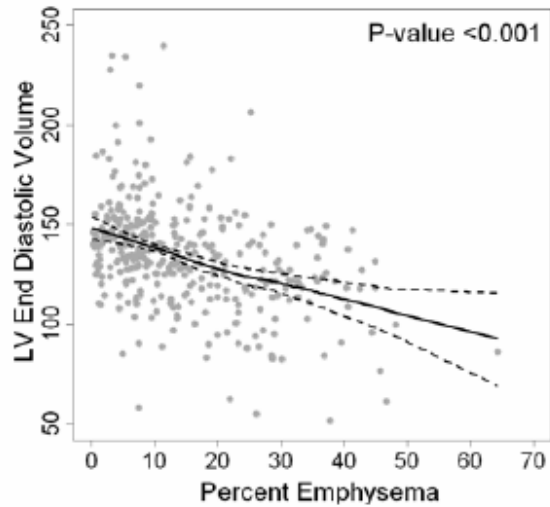
- MRI cardiaca para valoración Ventrículo izdo.
- TC y software para valoración áreas baja atenuación.
- Espirometría

Table 3. Predicted Values for and Mean Change in Left Ventricular Structure and Function According to Percent Emphysema on CT.*

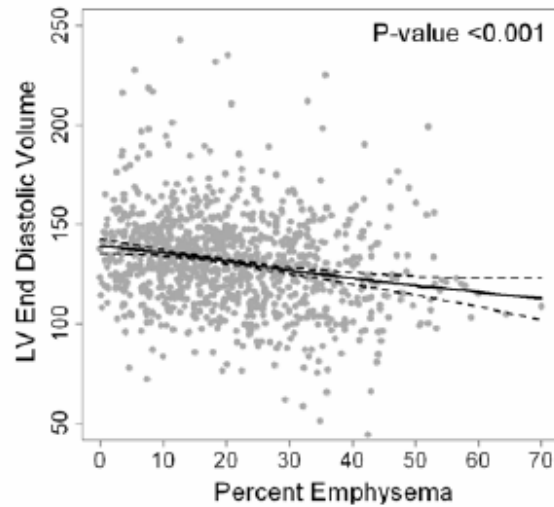
Variable	Percent Emphysema					Mean Change in LV Measure per 10-Percentage-Point Increase in Emphysema (95% CI)	P Value
	3.5% (N=563)	9.1% (N=563)	15.0% (N=564)	22.5% (N=564)	34.5% (N=562)		
LV end-diastolic volume — ml	124.9	121.8	118.8	115.8	111.2	-4.1 (-4.9 to -3.3)	<0.001
LV end-systolic volume — ml	37.8	36.7	35.4	34.3	32.9	-1.4 (-1.9 to -0.9)	<0.001
LV stroke volume — ml	87.1	85.1	83.4	81.5	78.3	-2.7 (-3.3 to -2.2)	<0.001
Cardiac output — liters/min	5.90	5.72	5.61	5.45	5.27	-0.19 (-0.23 to -0.14)	<0.001
LV ejection fraction — %	70.4	70.5	70.8	70.7	70.7	0.02 (-0.22 to 0.25)	0.89
LV mass — g	138.3	134.7	134.2	131.9	129.3	-2.5 (-3.4 to -1.6)	<0.001



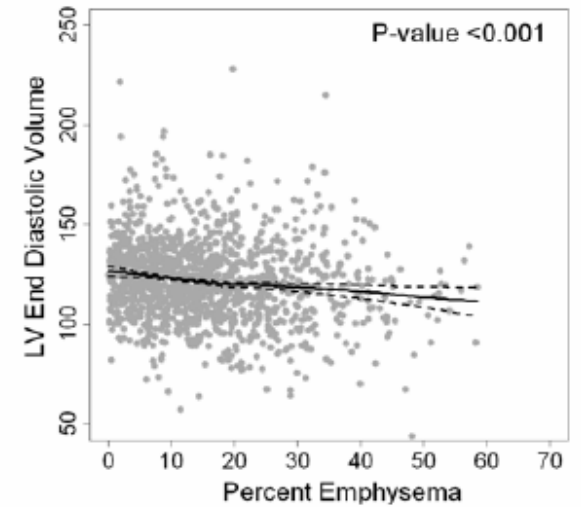
Current Smokers



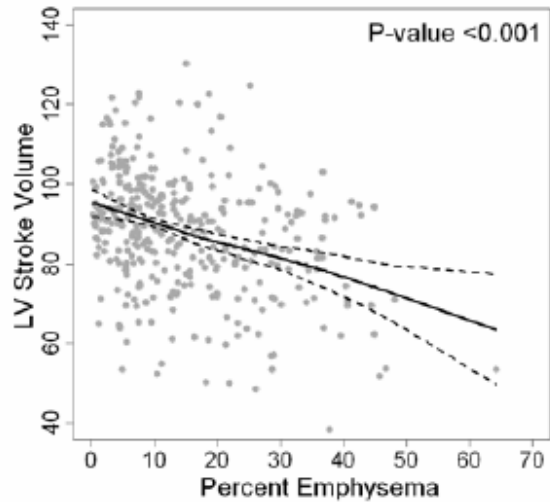
Former Smokers



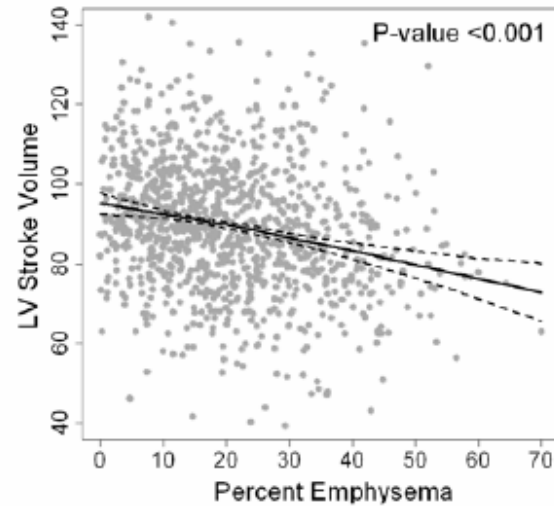
Never Smoked



Current Smokers



Former Smokers



Never Smoked

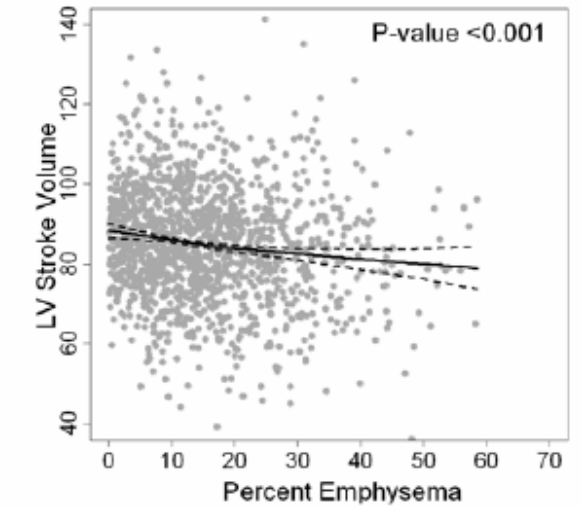
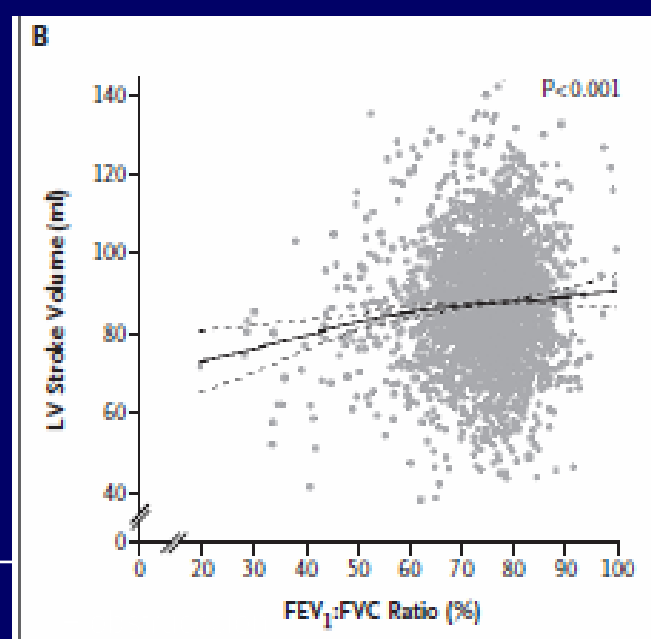
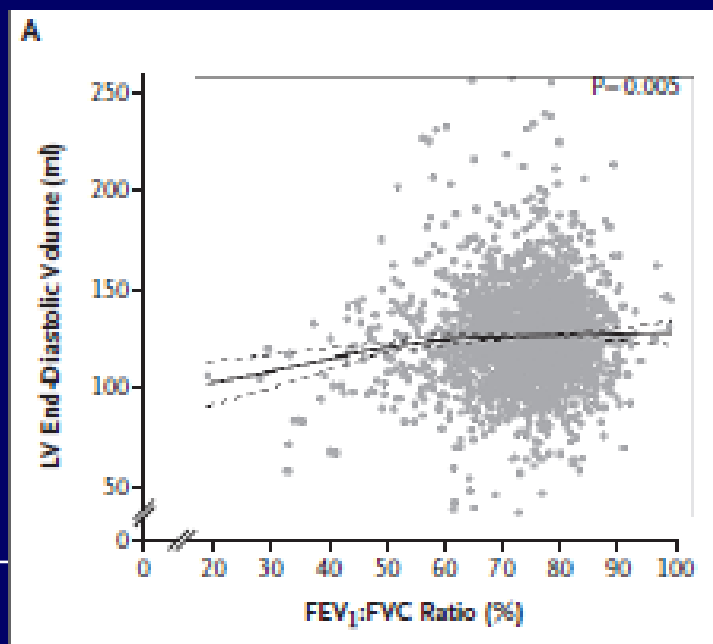
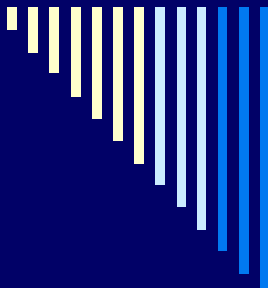


Table 4. Predicted Values for and Mean Change in Left Ventricular Structure and Function According to FEV₁:FVC Ratio.*

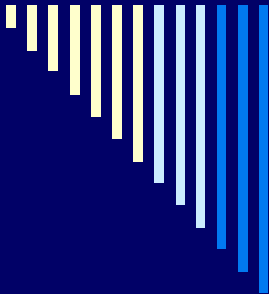
Variable	FEV ₁ :FVC Ratio					Mean Change in LV Measure (95% CI) per 10-Percentage-Point Increase in FEV ₁ :FVC Ratio	P Value
	64.6% (N= 545)	71.8% (N= 545)	75.9% (N= 546)	79.3% (N= 545)	83.6% (N= 545)		
LV end-diastolic volume — ml	126.5	127.7	127.7	129.0	128.3	1.7 (0.5 to 2.8)	0.005
LV end-systolic volume — ml	40.9	41.1	40.8	41.3	40.3	0.1 (−0.5 to 0.8)	0.72
LV stroke volume — ml	85.6	86.6	86.9	87.7	88.0	1.5 (0.8 to 2.3)	<0.001
Cardiac output — liters/min	5.57	5.58	5.67	5.67	5.74	0.10 (0.04 to 0.17)	0.002
LV ejection fraction — %	68.6	68.6	68.8	68.7	69.2	0.2 (−0.1 to 0.5)	0.22
LV mass — g	151.0	149.0	149.2	148.7	149.2	−0.7 (−1.9 to 0.5)	0.24





Conclusión:

1. El incremento del grado de enfisema se relaciona de forma lineal con:
 - a. reducción de los volúmenes telediastólicos del VI
 - b. reducción de los volúmenes sistólicos
 - c. reducción del gasto cardiaco.
 2. Estas variaciones también están relacionadas con la obstrucción y con el tabaquismo, con de mayor magnitud en los fumadores activos.
-

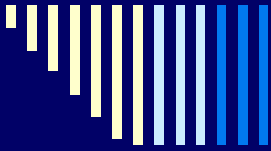


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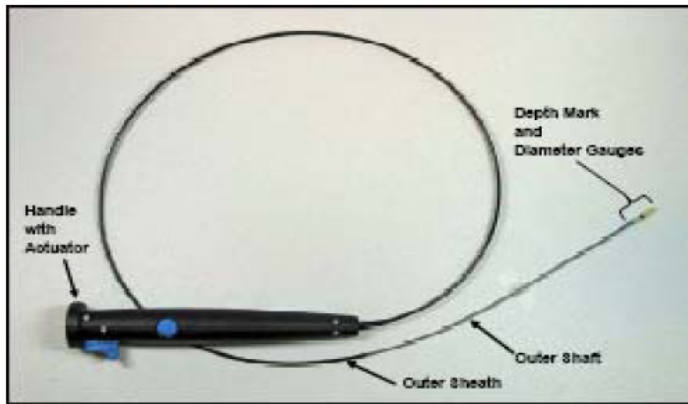
A Randomized Study of Endobronchial Valves for Advanced Emphysema

Frank C. Sciurba, M.D., Armin Ernst, M.D., Felix J.F. Herth, M.D.,
Charlie Strange, M.D., Gerard J. Criner, M.D., Charles H. Marquette, M.D., Ph.D.,
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Jonathan Goldin, M.D., Ph.D., and Geoffrey McLennan, M.D., Ph.D.,
for the VENT Study Research Group*



□ Antecedentes.

- Cirugía de resección de volumen. Poco utilizada por la mortalidad perioperatoria y por las complicaciones.
- La que se colocan válvulas en el interior del bronquio mediante broncofibroscopia (que permiten la salida del aire pero no su entrada) disminuyen la **hipersuflación**.
- Los resultados prelimares parecen mejorar la función pulmonar y los síntomas, con un moderado riesgo de complicaciones: neumonía distal y neumotórax.”.



Catéter portador de la válvula Zephyr

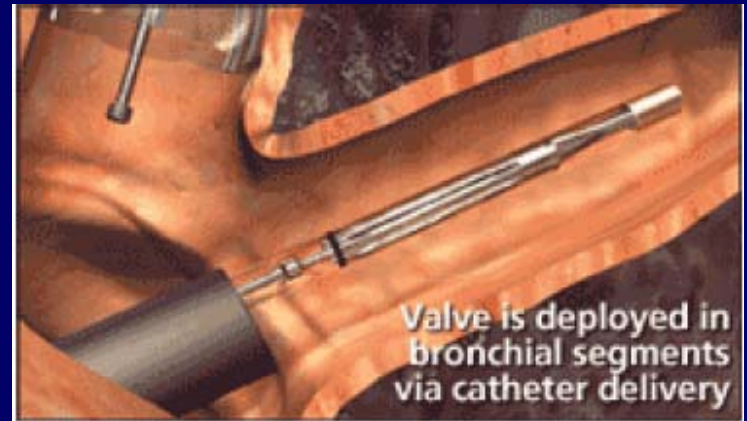
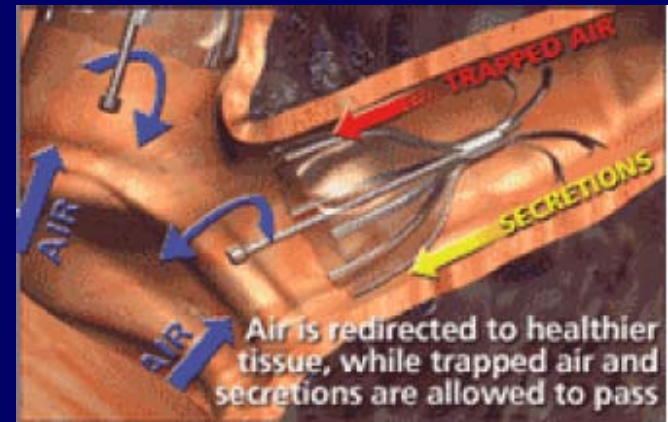
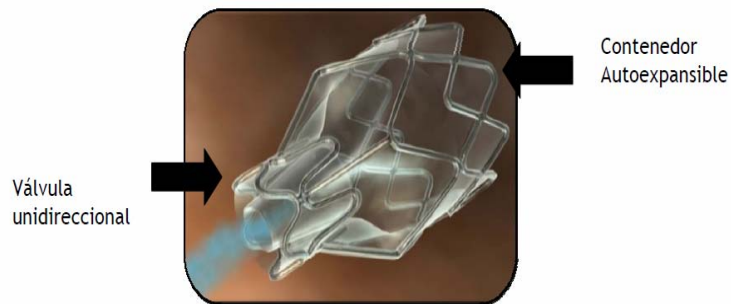
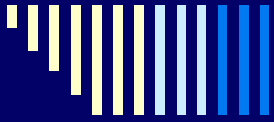


Figura 6: Válvula Zephyr
Fuente: (28)





□ Estudio:

- Estudio VENT (Endobronchial Valve for Emphysema Palliation Trial)

□ Hipótesis:

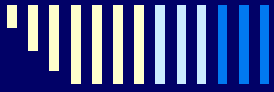
- Seguridad y eficacia de tratamiento unilateral con válvula endobronquial, comparado con tratamiento médico estándar.

■ ■ □ **Diseño:**

- Randomizado, prospectivo, multicéntrico.
- Pacientes con enfisema en estadio avanzado.
- 6-8 semanas de preinclusión (rehabilitación + optimización del tto)
- Grupo intervención: 220 paciente. Grupo control: 101 pacientes.
- Duración: 6 meses.

□ **Variable/s principal/es:**

- Cambios en el el FEV1.
- Distancia en el Test de la marcha de los 6 minutos.
- Calidad de vida.
- Complicaciones, variable combinada formada por 6 variables:
Muerte, empiema, hemoptisis masiva, neumonía distal a la válvula,
neumotórax o insuficiencia respiratoria.

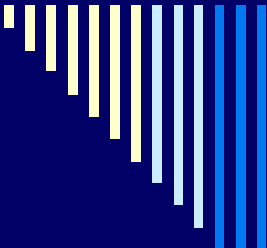


- Método:
 - Se realizaron TACAR para:
 - Determinar distribución del enfisema y su gravedad
 - Determinar lóbulos diana.
 - Evaluar cambios a los 6 meses de la intervención.
- **Densidad de Enfisema:** se calcula de forma automatizada a partir de la TACAR, por un programa informático.
- El **grado de Heterogeneidad:** la diferencia en porcentaje entre los grados de densidad del lóbulo diana y los demás lóbulos. Este porcentaje se se convirtió en una escala Likert (1=1 a 25%, 2 = 26-50%, 3 = 51-75-% y 4 = 76-100%)

Resultados

Table 2. Primary and Secondary Efficacy Outcomes in the Intention-to-Treat Population (Change from Baseline at 6 Months).*

Outcome	Endobronchial-Valve Therapy (N=220)	Control (N=101)	Between-Group Difference in Change from Baseline	P Value
	number (95% confidence interval)			
Primary outcome				
FEV ₁				
Mean absolute percent change from baseline	4.3 (1.4 to 7.2)	-2.5 (-5.4 to 0.4)	6.8 (2.1 to 11.5)	0.005
Mean change in value from baseline — ml	34.5 (10.8 to 58.3)	-25.4 (-48.3 to -2.6)	60.0 (21.5 to 98.4)	0.002
Mean absolute percent change in predicted value from baseline	1.0 (0.2 to 1.8)	-0.9 (-1.7 to -0.1)	1.9 (0.5 to 11.2)	0.007
Distance on 6-min walk test†				
Median absolute percent change from baseline	2.5 (-1.1 to 6.1)	-3.2 (-8.9 to 2.4)	5.8 (0.5 to 11.2)	0.04
Median change from baseline — m	9.3 (-0.5 to 19.1)	-10.7 (-29.6 to 8.1)	19.1 (1.3 to 36.8)	0.02
Secondary outcome				
Mean change in score on SGRQ from baseline‡	-2.8 (-4.7 to -1.0)	0.6 (-1.8 to 3.0)	-3.4 (-6.7 to 0.2)	0.04
Mean change in score on Modified Medical Research Council dyspnea scale from baseline§	-0.1 (-0.21 to 0.09)	0.2 (0.01 to 0.37)	-0.3 (-0.50 to -0.01)	0.04
Mean change in cycle ergometry peak workload from baseline — W	0.6 (-1.5 to 2.7)	-3.2 (-4.5 to -1.9)	3.8 (0.1 to 7.5)	0.05
Median change in supplemental oxygen use from baseline — liters/day†	0.0 (-117.3 to 117.3)	0.0 (-148.2 to 148.2)	-12.0 (-76.7 to 52.7)	0.005



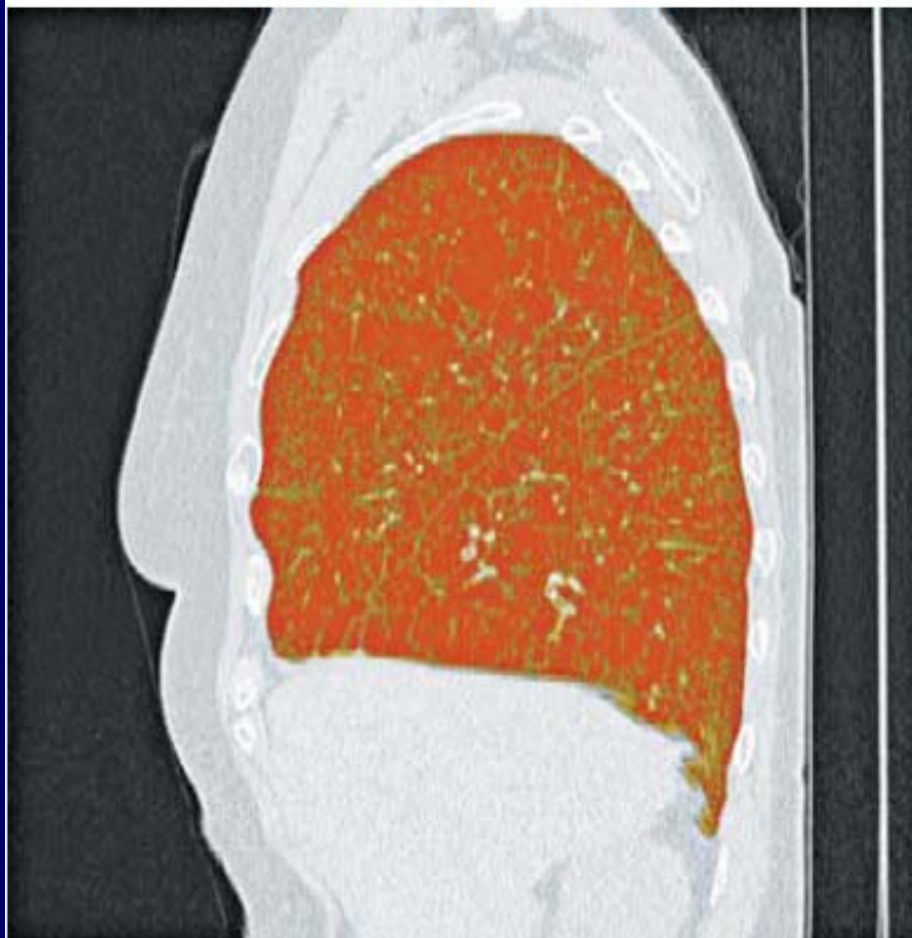
Resultados: efectos adversos

Table 3. Major Adverse Events at 90 Days.*

Event	Endobronchial-Valve Therapy (N=214)	Control (N=87)	P Value†
	no. (% [95% CI])	no. (% [95% CI])	
Patients with any event in the composite of major complications	9 (4.2 [1.9–7.8])	0 (0 [0.0–4.2])	0.06
Death‡	2 (0.9 [0.1–3.3])	0 (0 [0.0–4.2])	1.00

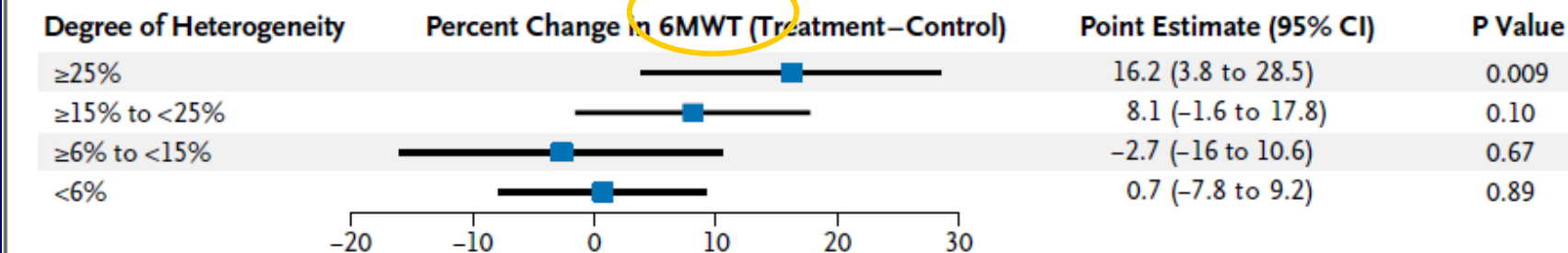
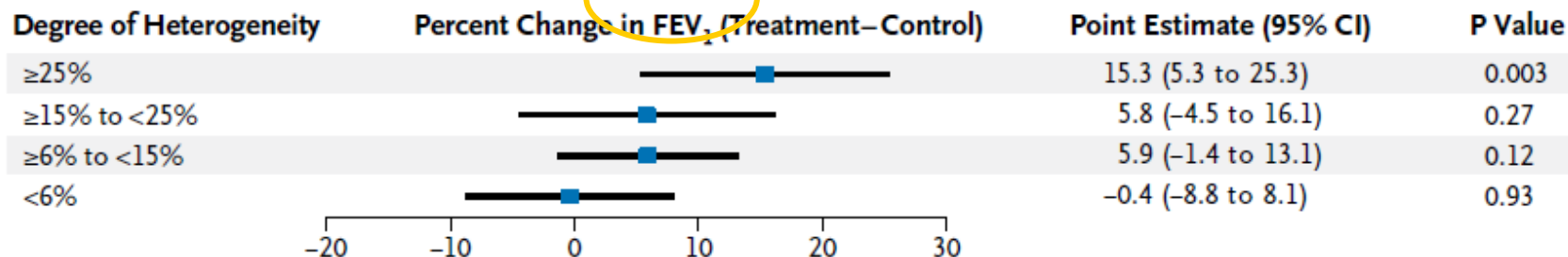
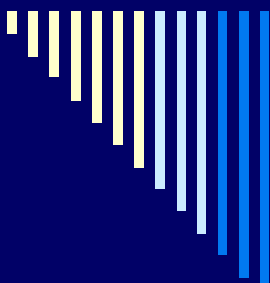
Event	Endobronchial-Valve Therapy (N=214) <i>no. (% [95% CI])</i>	Control (N= 87) <i>no. (% [95% CI])</i>	P Value [†]
Pulmonary or thoracic event			
COPD exacerbation			
With hospitalization	17 (7.9 [4.7–12.4])	1 (1.1 [0.0–6.2])	0.03
Without hospitalization	3 (1.4 [0.3–4.0])	0 (0 [0.0–4.2])	0.56
Pulmonary infection	4 (1.9 [0.5–4.7])	0 (0 [0.0–4.2])	0.33
Respiratory failure‡	3 (1.4 [0.3–4.0])	0 (0 [0.0–4.2])	0.56
Pneumonia			
Not distal to valve	5 (2.3 [0.8–5.4])	2 (2.3 [0.3–8.1])	1.00
Distal to valve‡	2 (0.9 [0.1–3.3])	NA	NA
New or worsening hypercapnia§	2 (0.9 [0.1–3.3])	0 (0 [0.0–4.2])	1.00
Hypoxemia	3 (1.4 [0.3–4.0])	0 (0 [0.0–4.2])	0.56
Hemoptysis			
Massive‡	1 (0.5 [0.0–2.6])	0 (0 [0.0–4.2])	1.00
Any	12 (5.6 [2.9–9.6])	0 (0 [0.0–4.2])	0.02
Pneumothorax or air leak			
Duration of >7 days‡	3 (1.4 [0.3–4.0])	0 (0 [0.0–4.2])	0.56
Expanding	3 (1.4 [0.3–4.0])	0 (0 [0.0–4.2])	0.56
Stable	3 (1.4 [0.3–4.0])	0 (0 [0.0–4.2])	0.56
Empyema‡	0 (0 [0.0–1.7])	0 (0 [0.0–4.2])	NA
Noncardiac chest pain	1 (0.5 [0.0–2.6])	0 (0 [0.0–4.2])	1.00

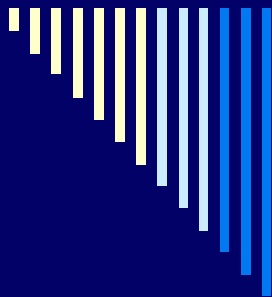
Heterogeneity Score, 6%



Heterogeneity Score, 25%

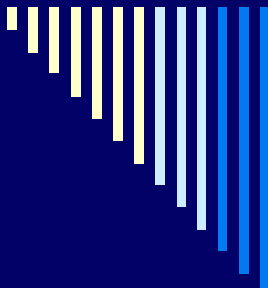






CONCLUSIONS

Endobronchial-valve treatment for advanced heterogeneous emphysema induced modest improvements in lung function, exercise tolerance, and symptoms at the cost of more frequent exacerbations of COPD, pneumonia, and hemoptysis after implantation. (Funded by Pulmonx; ClinicalTrials.gov number, NCT00129584.)

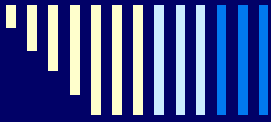


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ORIGINAL ARTICLE

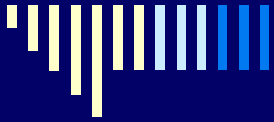
Susceptibility to Exacerbation in Chronic Obstructive Pulmonary Disease

John R. Hurst, M.B., Ch.B., Ph.D., Jørgen Vestbo, M.D., Antonio Anzueto, M.D.,
Nicholas Locantore, Ph.D., Hana Müllerova, Ph.D., Ruth Tal-Singer, Ph.D.,
Bruce Miller, Ph.D., David A. Lomas, Ph.D., Alvar Agusti, M.D., Ph.D.,
William MacNee, M.B., Ch.B., M.D., Peter Calverley, M.D.,
Stephen Rennard, M.D., Emiel F.M. Wouters, M.D., Ph.D.,
and Jadwiga A. Wedzicha, M.D., for the Evaluation of COPD Longitudinally
to Identify Predictive Surrogate Endpoints (ECLIPSE) Investigators*



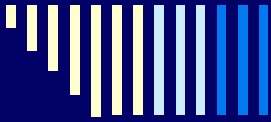
□ Situación actual del tema:

- El control de las exacerbaciones es CLAVE. Son más frecuentes y graves a medida que la enfermedad es más grave.
- ¿existe “fenotipo exacerbador”?



□ Población:

- Procedente del estudio ECLIPSE (Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points) patrocinado por industria farmacéutica (Glaxo)
- Hombres y mujeres de 40-75 años
- Epoc por criterios Gold
- Duración 3 años. 7 visitas



□ Tipo de estudio:

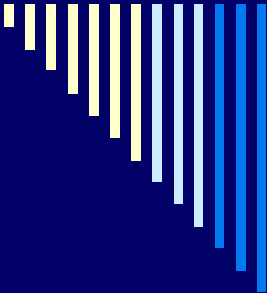
- De no intervención
- Prospectivo
- Ambito Atención Primaria.
- Multinacional
- Con grupo control (no fumadores y fumadores)

□ Conceptos:

- Exacerbación: empeoramiento que requiere tratamiento (antibióticos o GC sistémicos)
 - Exacerbación grave: que precisa ingreso
 - Exacerbador frecuente: 2 o más exac/año.
 - Exacerbador infrecuente: 0 ó 1 exac/año
-

Table 1. Characteristics of the Patients According to the Severity of

Characteristic	All Patients (N=2138)
Age (yr)	63±7
Female sex (%)	35
Current smoker (%)	36
Body-mass index†	27±6
FEV ₁ after bronchodilator use (liters)	1.35±0.52
FEV ₁ after bronchodilator use (% of predicted value)	48±16
FEV ₁ :FVC (%)	45±12
Distance walked in 6 min (m)	370±121
BODE index‡	3.2±2.1



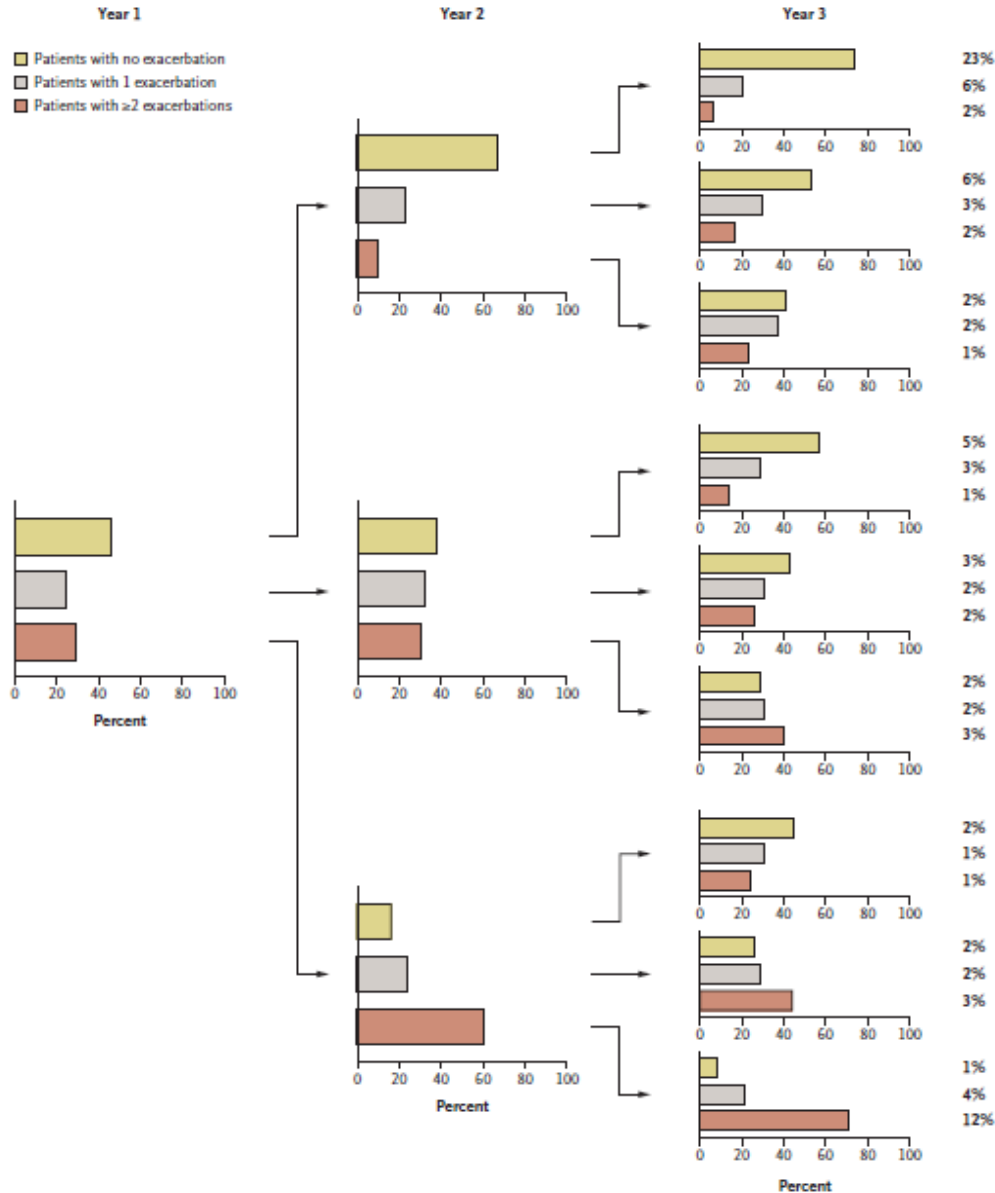
Resultados

Characteristic	All Patients (N=2138)	Moderate — GOLD Stage 2 (N=945)	Severe — GOLD Stage 3 (N=900)	Very Severe — GOLD Stage 4 (N=293)
Exacerbations				
≥1 in preceding yr (%)	47	39	52	62
≥2 in study yr 1 (%)	29	22	33	47

Table 3. Factors Associated with Increased Exacerbation Frequency in the Stepwise Multivariate Model.*

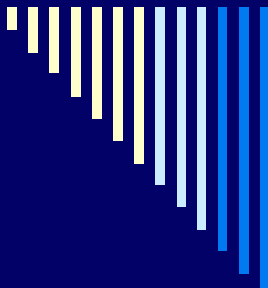
Factor	Number of Exacerbations						P Value for Overall Model
	≥2 vs. 0		1 vs. 0		≥2 vs. 1		
	<i>odds ratio</i> (95% CI)	<i>P value</i>	<i>odds ratio</i> (95% CI)	<i>P value</i>	<i>odds ratio</i> (95% CI)	<i>P value</i>	
Exacerbation during previous yr — any vs. none	5.72 (4.47–7.31)	<0.001	2.24 (1.77–2.84)	<0.001	2.55 (1.96–3.31)	<0.001	<0.001
FEV ₁ — per 100-ml decrease	1.11 (1.08–1.14)	<0.001	1.06 (1.03–1.08)	<0.001	1.05 (1.02–1.09)	<0.001	<0.001
SGRQ score for COPD — per increase of 4 points	1.07 (1.04–1.10)	<0.001	1.01 (0.99–1.04)	0.38	1.06 (1.03–1.09)	<0.001	<0.001
History of reflux or heartburn — yes vs. no	2.07 (1.58–2.72)	<0.001	1.61 (1.23–2.10)	<0.001	1.29 (0.97–1.70)	<0.005	<0.001
White-cell count — per increase of 1×10 ³ /mm ³	1.08 (1.03–1.14)	0.002	1.02 (0.97–1.08)	0.45	1.06 (1.01–1.12)	<0.001	0.007

Factor	≥ 2 vs. 0	
	<i>odds ratio</i> (95% CI)	<i>P value</i>
Women (N=376)		
Exacerbation during previous year — yes vs. no	8.89 (4.32–18.29)	<0.001
Men (N=569)		
Exacerbation during previous yr —	7.38 (4.44–12.27)	<0.001



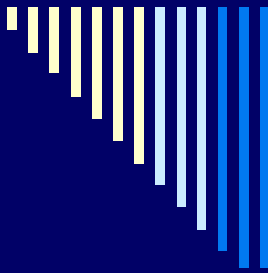
patients who had moderate COPD: 22% had frequent exacerbations

patients who had very severe COPD, 29% had resistance to exacerbations



Conclusión:

- Más exacerbaciones a mayor obstrucción **PERO**
- Existe dos subtipos extremos:
 - ▣ un fenotipo (o subtipo) de paciente “exacerbador” que ya se manifiesta desde estadios moderados de la enfermedad.
 - ▣ un fenotipo (o subtipo) “no exacerbador” que se mantiene incluso en estadios graves.
- La categorización de ambos se hace en base al **historial de exacerbaciones.**

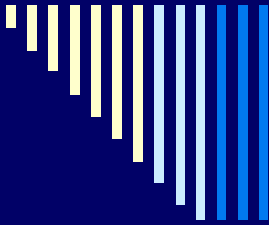


Resumen:

- El funcionalismo cardiaco puede jugar un importante papel en la clínica de los pacientes con enfisema.



nuevas dianas terapéuticas

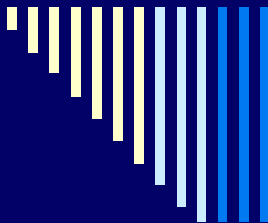


Resumen:

- Las limitaciones actuales del tratamiento médico obligan a ser imaginativos a la hora de abordar la Epoc.

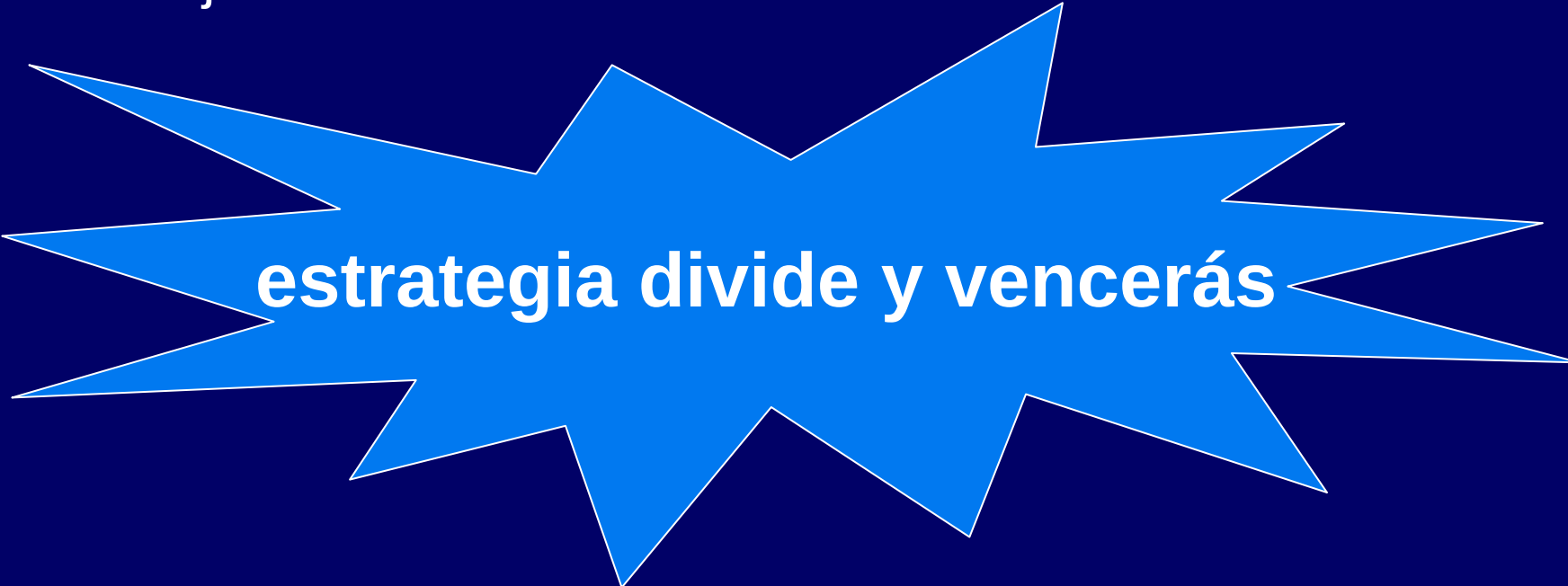


Abandono definitivo del NIHILISMO

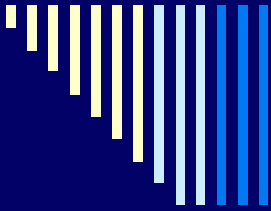


Resumen:

- La estrategia de la caracterización/subagrupación de los pacientes con Epoc puede reportar nuevas líneas de abordaje más eficientes.



estrategia divide y vencerás



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