



Societat Catalana de Medicina Intensiva i Crítica  
**Els professionals del malalt crític**



VII CONFERENCIA D'EXPERTS : INSUFICIÈNCIA RESPIRATÒRIA AGUDA

17 gener 2012

# Ventilació alveolar com a índex pronòstic en la SDRA

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# SDRA: criterios diagnósticos

- Infiltrados bilaterales en la Rx. de tórax
- $\text{PaO}_2 / \text{FiO}_2 \leq 200$
- PCP  $\leq 18$  mmHg o ausencia de HAI

# SDRA: características fisiopatológicas

- ↑ Shunt intrapulmonar derecha-izquierda
- ↓ Compliance sistema respiratorio
- ↑ Espacio muerto ( $VD/VT$ )

# SDRA: causas de elevación $V_D/V_T$

- Lesión capilares pulmonares  
Mecanismos inflamatorios y trombóticos
- Obstrucción flujo sangre extra-alveolar
- Áreas con elevada relación V/Q

# Concepto de espacio muerto y ventilación alveolar

$$\dot{V}_A = f(V_T - V_D)$$

Volumen de aire efectivo: intercambia gases

Volumen de aire sin intercambio de gases

# Métodos de medición del espacio muerto

- Fórmulas (bolsa de *Douglas*)
- Capnografía volumétrica
- MIGET  
(técnica de eliminación múltiple de gases inertes)

# Fórmulas

*Bohr -1891-*

$$\dot{V}_{CO_2} = \dot{V}_A \times F_{ACO_2}$$

$$V_{D_{anat}}/V_T = \frac{F_{ACO_2} - F_{ECO_2}}{F_{ACO_2}}$$

# Fórmulas

*Enghoff -1938-*

$$V_{D_{fisiol}} / V_T = \frac{PaCO_2 - PECO_2}{PaCO_2}$$

$$V_{D_{fisiol}} = V_{D_{anat}} + V_{D_{alv}}$$



PECO<sub>2</sub>



PaCO<sub>2</sub>





PECO<sub>2</sub>  
PetCO<sub>2</sub>  
V'CO<sub>2</sub>  
V'O<sub>2</sub>



PaCO<sub>2</sub>

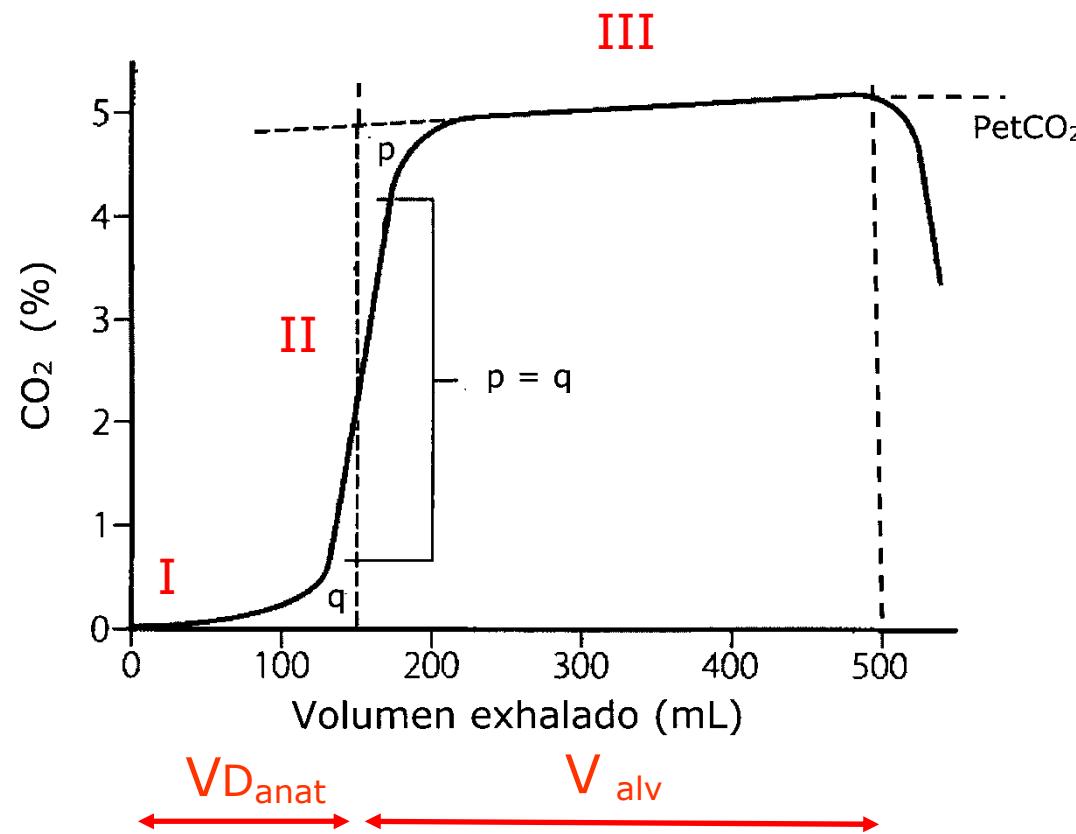


# Fórmulas: problemas con la ventilación mecánica

- Normalizar:  $V_T$ , nivel de PEEP
- Volumen comprensible de los circuitos
- Fugas: circuitos, tubo OT, fistulas

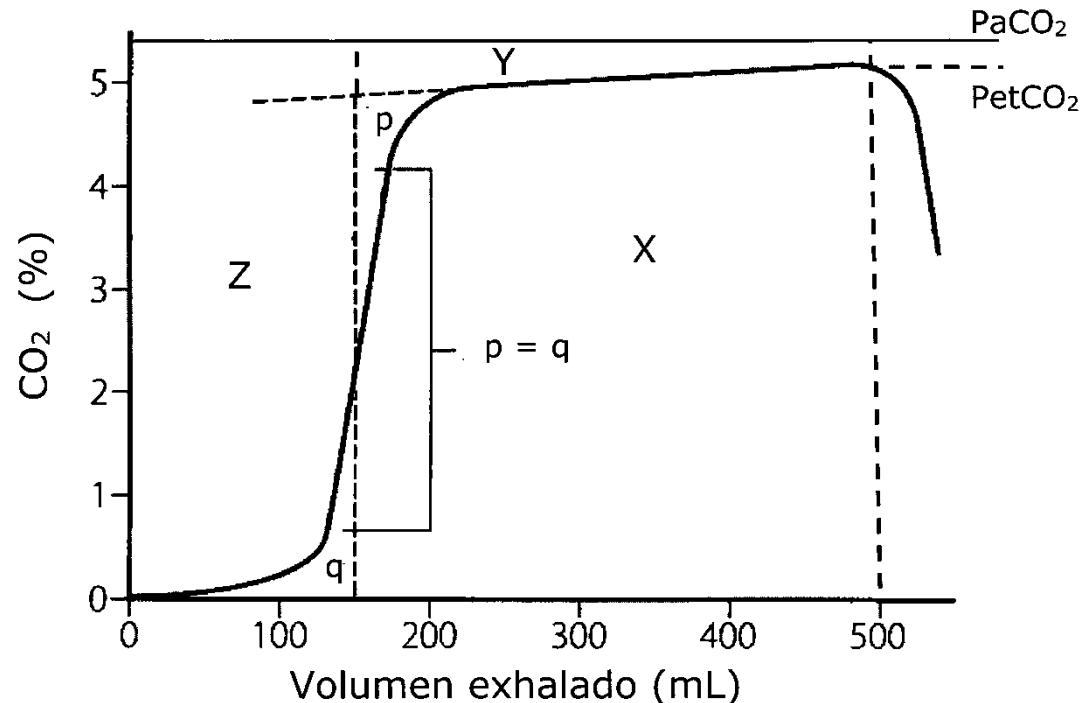
# Capnografía volumétrica

Fowler - 1948-  $[N_2]$   
Bartels - 1954-  $[CO_2]$



# Capnografía volumétrica

Fletcher - 1984-

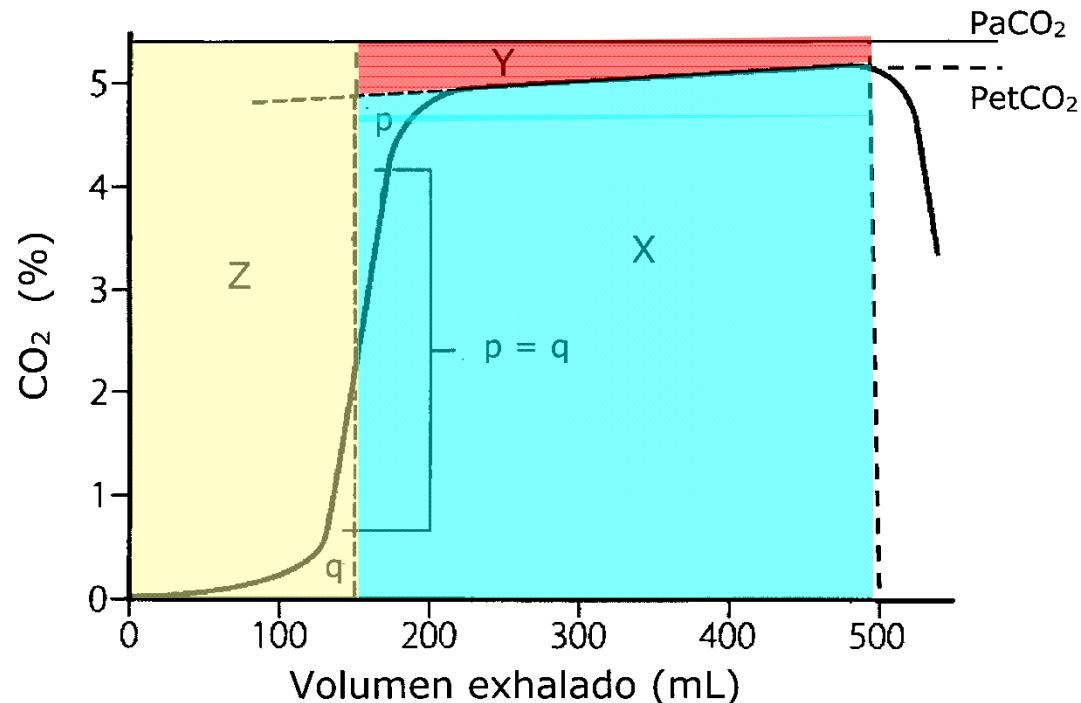


$$V_{D_{\text{anat}}}/V_T = Z / (X + Y + Z)$$

$$V_{D_{\text{alv}}}/V_T = Y / (X + Y + Z)$$

$$V_{D_{\text{fisiol}}}/V_T = (Y + Z) / (X + Y + Z)$$

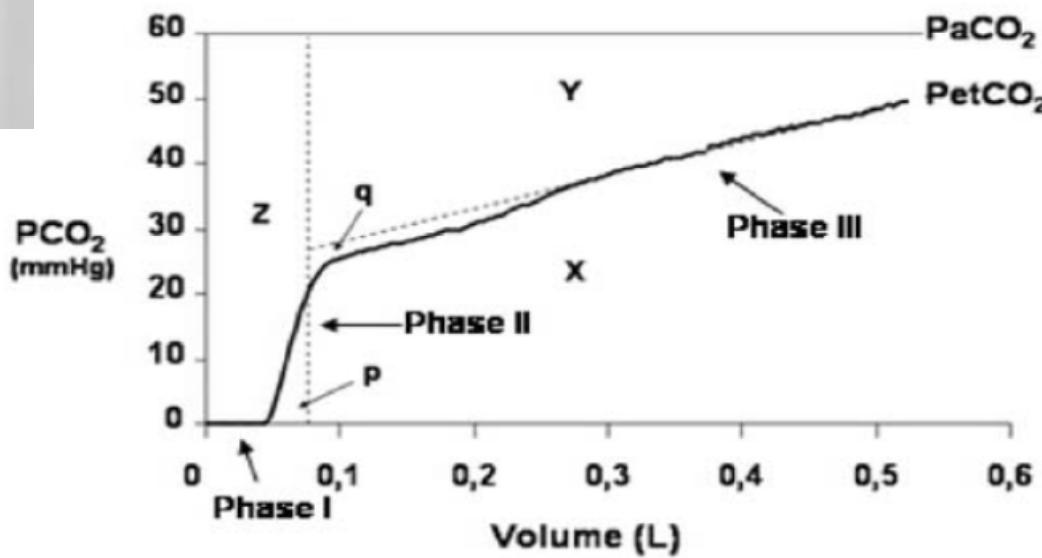
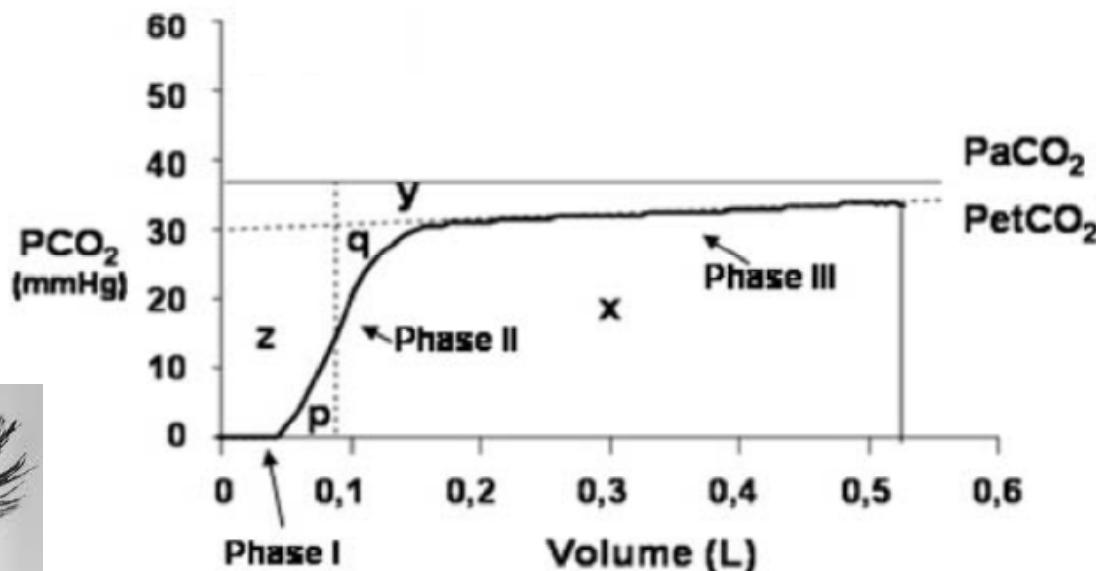
# Capnografía volumétrica



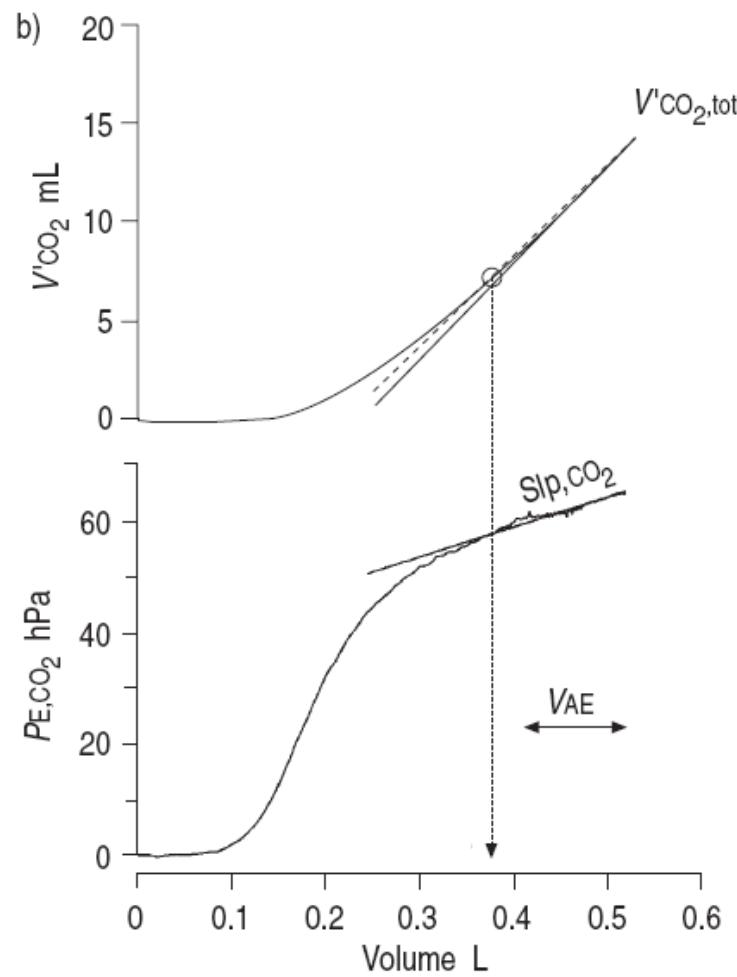
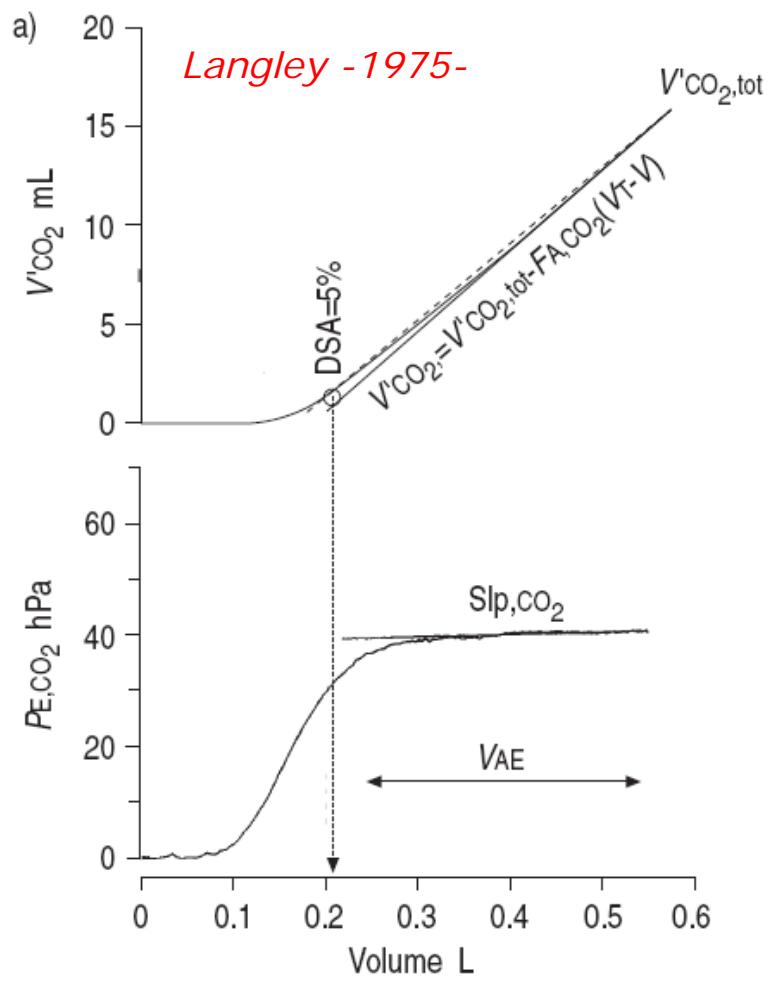
$$V_{D_{\text{anat}}}/V_T = Z / (X + Y + Z)$$

$$V_{D_{\text{alv}}}/V_T = Y / (X + Y + Z)$$

$$V_{D_{\text{fisiol}}}/V_T = (Y + Z) / (X + Y + Z)$$



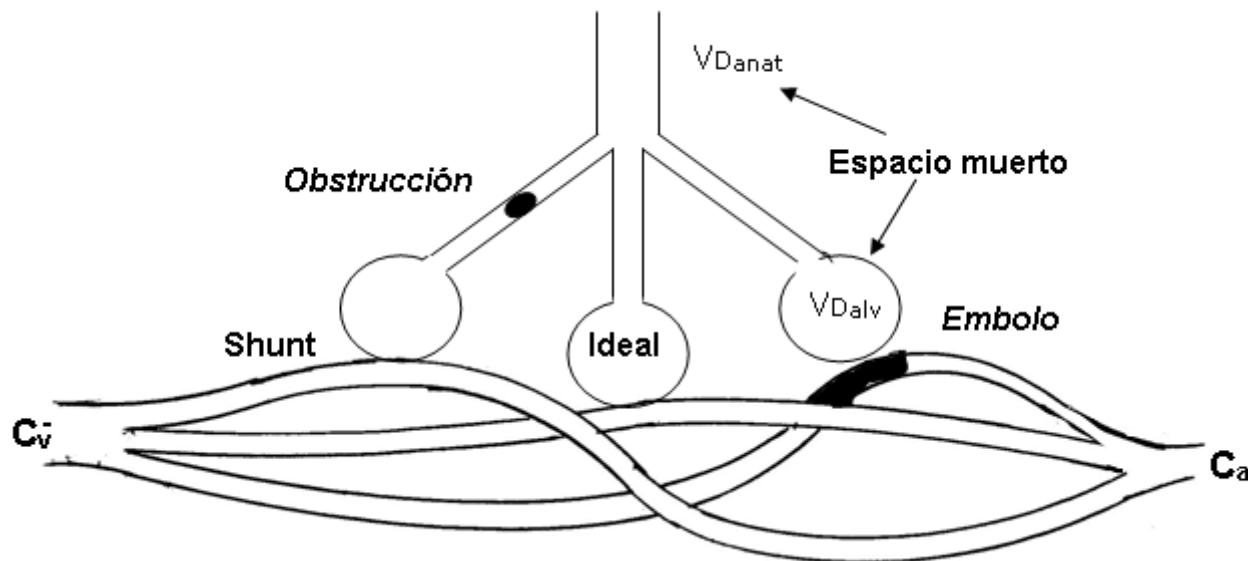
Lucangelo U and Blanch L. ICM 2004; 30: 576



*Romero PV. Eur Resp J 1997; 10: 1309*

# Modelo pulmonar tri-compartmental

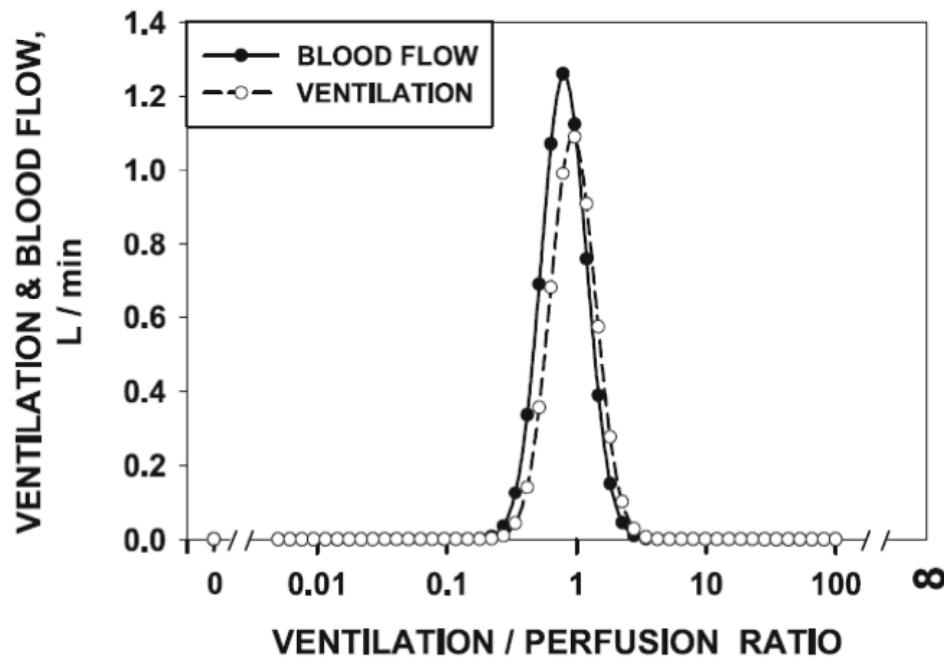
Riley -1949-



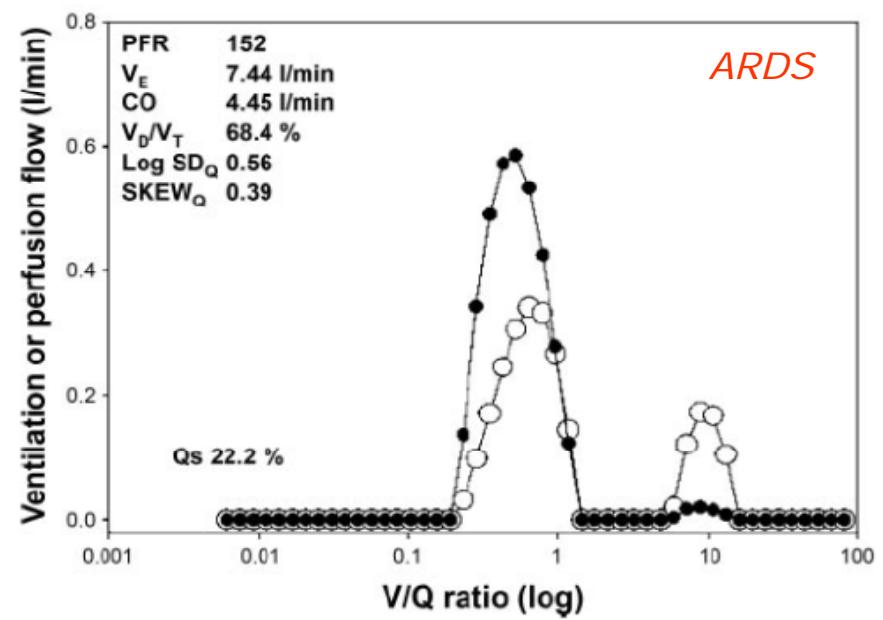
Riley RL, Cournand A. J Appl Physiol 1949; 1:825

# MIGET

## técnica de eliminación múltiple de gases inertes



Wagner PD. ICM 2008; 34:994



Batchinsky AY. JAP 2007; 103:895

Chest. 1979 Aug;76(2):180-6.

## **Evaluation of the progress and prognosis of adult respiratory distress syndrome. Simple respiratory physiologic measurement.**

Shimada Y, Yoshiya I, Tanaka K, Sone S, Sakurai M.

### **Abstract**

In our study of 14 patients with adult respiratory distress syndrome (ARDS), we measured A-aDO<sub>2</sub>, VD/VT, arterial-to-end tidal PCO<sub>2</sub> ), effective dynamic compliance, and pulmonary vascular resistance on a daily basis. At the onset of ARDS, all patients showed bilateral interstitial edema on the chest X-ray films, P(A-a)O<sub>2</sub> of more than 500 mm Hg, marked decrease in effective dynamic compliance, a moderate increase in VD/VT, and a normal value of a-etPCO<sub>2</sub>. Pulmonary vascular resistance was low. After seven days, all of those who subsequently died and developed persistent elevation of P(A-a)O<sub>2</sub>, significant increase in VD/VT, a-etPCO<sub>2</sub> and pulmonary vascular resistance, and significant decrease in effective dynamic compliance compared to the values at the onset of ARDS. Those abnormalities diverged significantly from the findings in those who survived. By evaluating sequential changes of those parameters, we might be able to predict an accurate prognosis of ARDS.

PMID: 456058 [PubMed - indexed for MEDLINE]

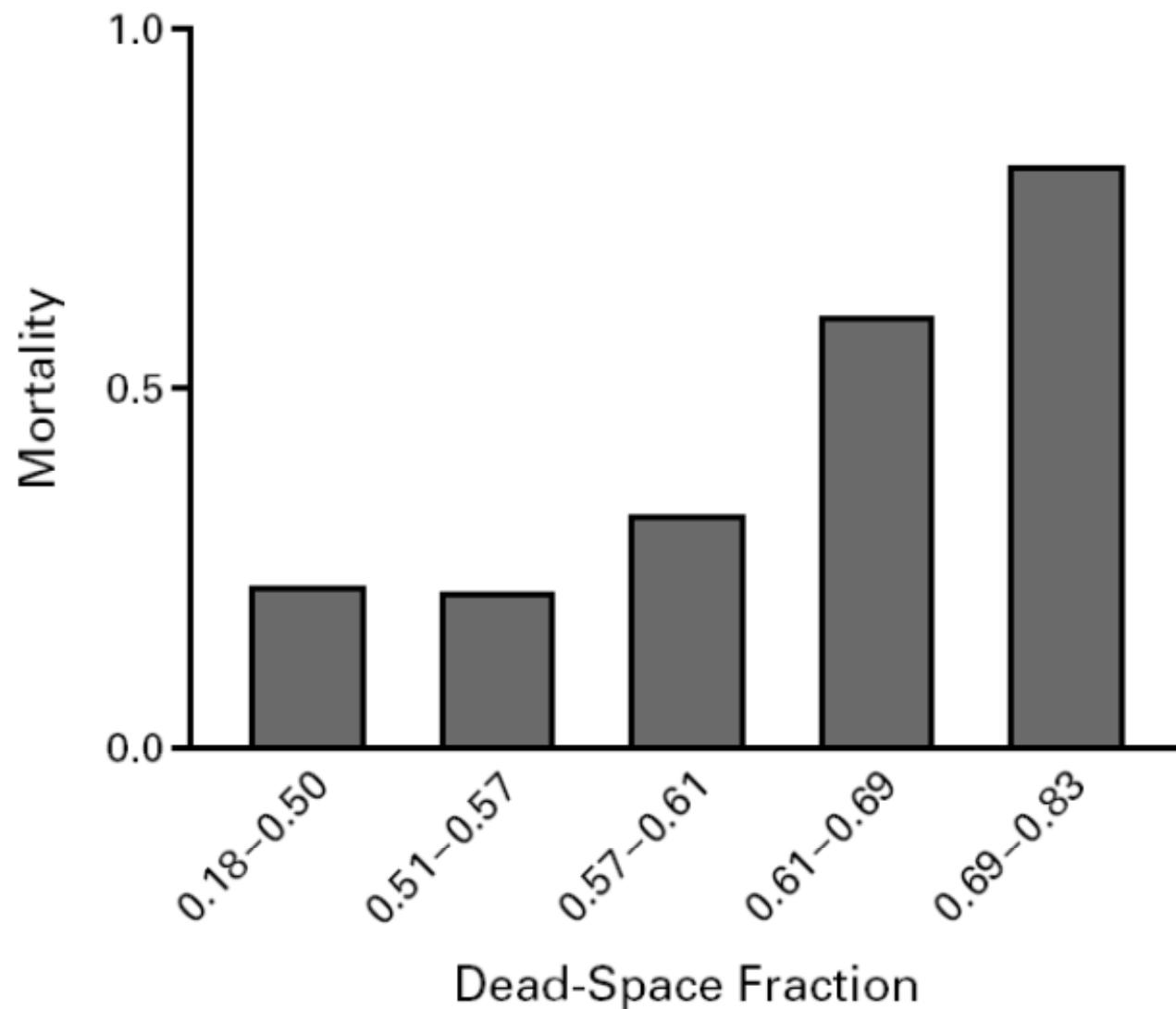
PULMONARY DEAD-SPACE FRACTION AS A RISK FACTOR FOR DEATH  
IN THE ACUTE RESPIRATORY DISTRESS SYNDROME

TABLE 1. CLINICAL CHARACTERISTICS OF 179 PATIENTS

CHARACTERISTIC	VALUE
Age — yr	48±15
PaO <sub>2</sub> :FiO <sub>2</sub>	147±61
SAPS II†	47±17
Clinical disorder associated with the acute respiratory distress syndrome — no. of patients (%)	
Sepsis	45 (25)
Aspiration	19 (11)
Pneumonia	55 (31)
Trauma, overdose, fat emboli, or idiopathic	60 (34)
Tidal volume — ml/kg of ideal body weight§	10.0±1.4
Quasistatic respiratory compliance — ml/cm of water	30.9±11.1
Minute ventilation — liters/min	12.1±4.3
Dead-space fraction¶ [Deltatrac]	0.58±0.10

Nuckton TJ. NEJM 2002; 346:1281

PULMONARY DEAD-SPACE FRACTION AS A RISK FACTOR FOR DEATH  
IN THE ACUTE RESPIRATORY DISTRESS SYNDROME



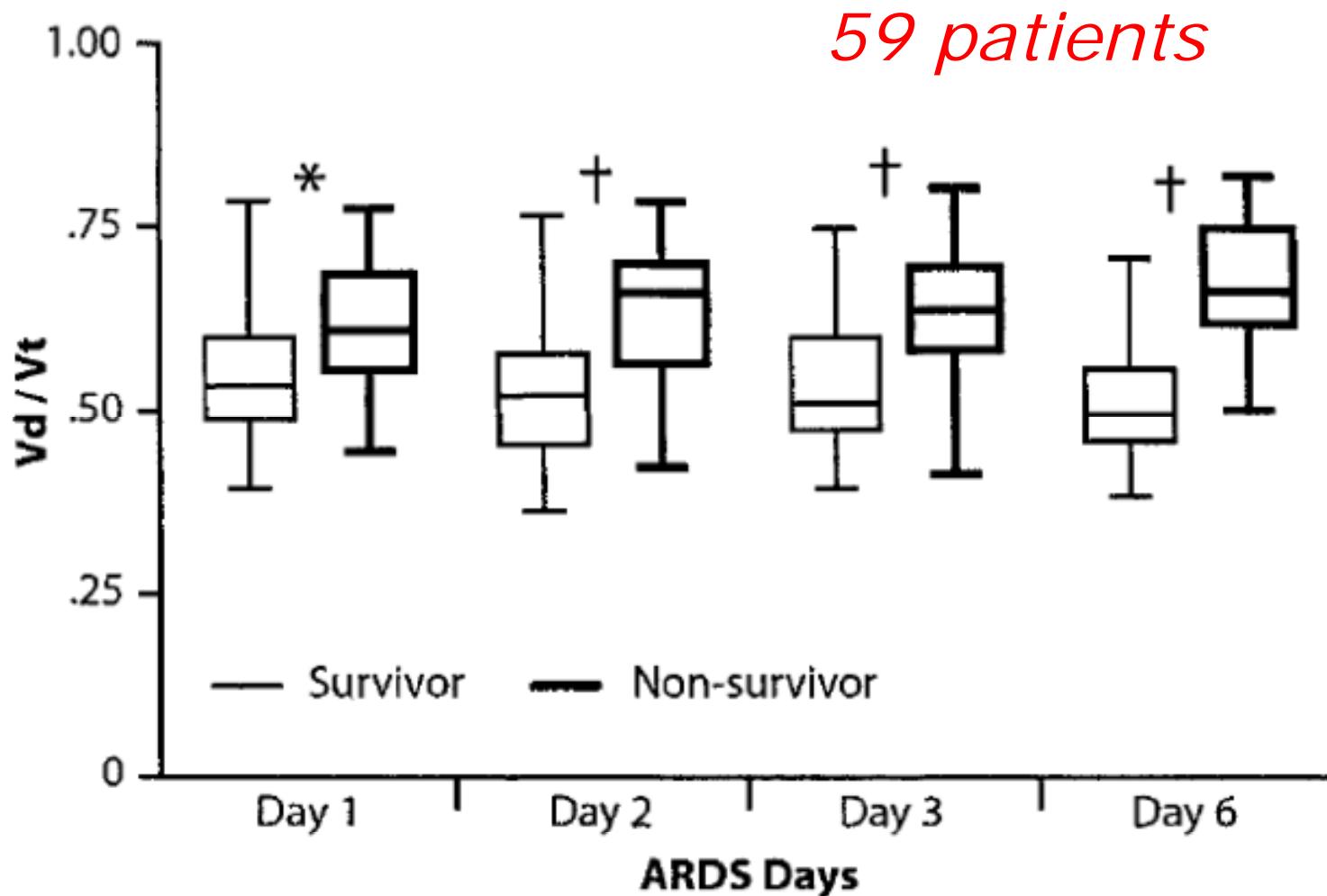
Nuckton TJ. NEJM 2002; 346:1281

PULMONARY DEAD-SPACE FRACTION AS A RISK FACTOR FOR DEATH  
IN THE ACUTE RESPIRATORY DISTRESS SYNDROME

**TABLE 3.** ODDS RATIOS FOR VARIABLES INDEPENDENTLY  
ASSOCIATED WITH AN INCREASED RISK OF DEATH.\*

VARIABLE	ODDS RATIO (95% CI)	P VALUE
Dead-space fraction (per increase of 0.05)†	1.45 (1.15–1.83)	0.002
SAPS II (per 1-point increase)	1.06 (1.03–1.08)	<0.001
Quasistatic respiratory compliance (per decrease of 1 ml/cm of water)	1.06 (1.01–1.10)	0.01

Prognostic Value of the Pulmonary Dead-Space Fraction During the First 6 Days of Acute Respiratory Distress Syndrome



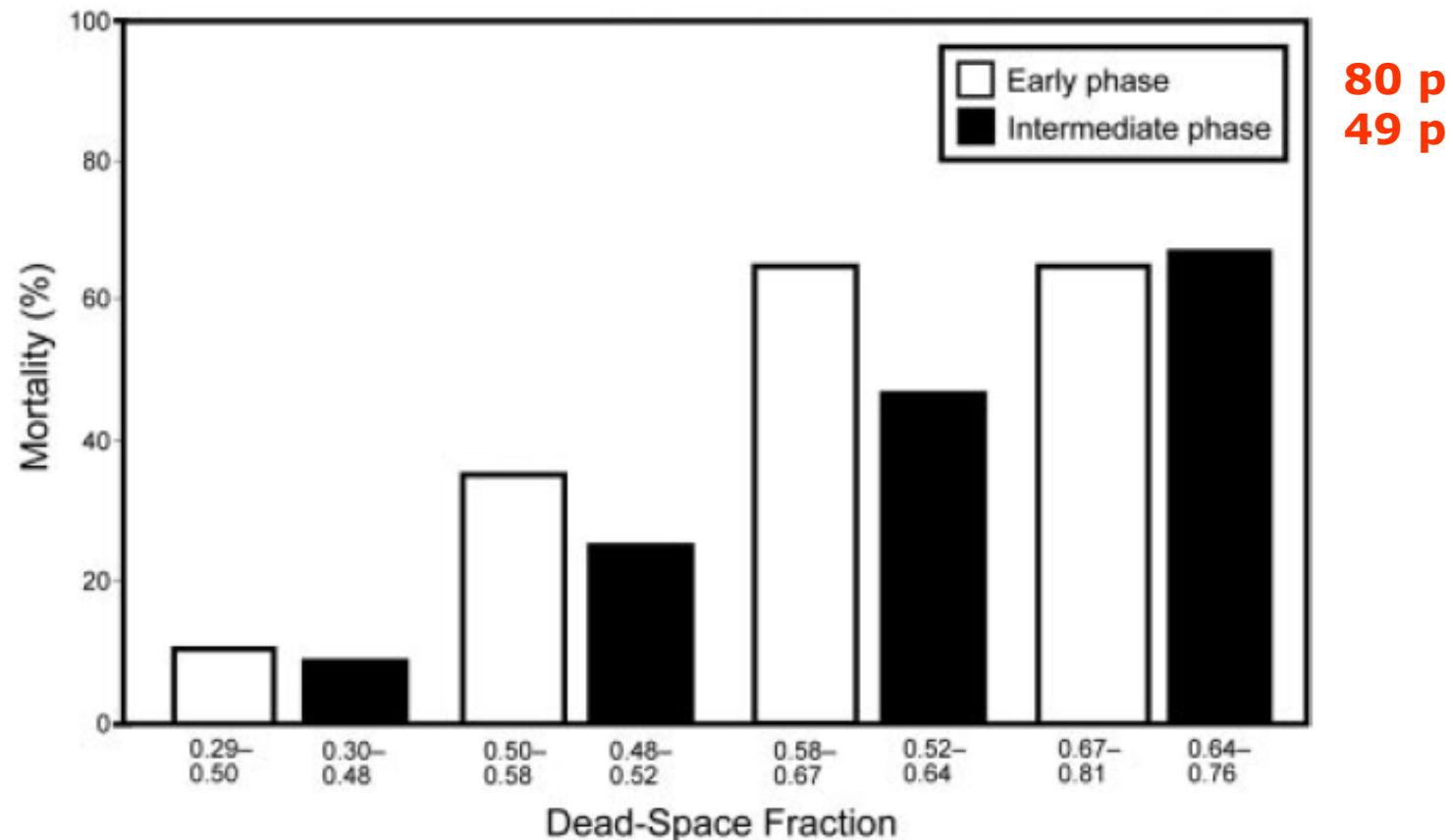
Kallet RH. Respir Care 2004; 49: 1008

# Prognostic Value of the Pulmonary Dead-Space Fraction During the Early and Intermediate Phases of Acute Respiratory Distress Syndrome

Table 1. Clinical Characteristics of 80 Patients

Age (mean $\pm$ SD y)	51 $\pm$ 18
Male ( <i>n</i> , %)	54 (68)
SAPS II score (mean $\pm$ SD)	45 $\pm$ 16
SOFA score (mean $\pm$ SD)	9.6 $\pm$ 3.4
Lung injury score (mean $\pm$ SD)	2.8 $\pm$ 0.5
P <sub>aO<sub>2</sub></sub> /F <sub>IO<sub>2</sub></sub> (mean $\pm$ SD mm Hg)	153 $\pm$ 55
Direct lung injury ( <i>n</i> , %)	66 (82)
Cause of ARDS ( <i>n</i> , %)*	
Pneumonia	55 (69)
Aspiration	7 (9)
Sepsis	11 (14)
Trauma, or other	7 (9)

# Prognostic Value of the Pulmonary Dead-Space Fraction During the Early and Intermediate Phases of Acute Respiratory Distress Syndrome



Raurich JM. *Respir Care* 2010; 55:282

Prognostic Value of the Pulmonary Dead-Space Fraction  
During the Early and Intermediate Phases  
of Acute Respiratory Distress Syndrome

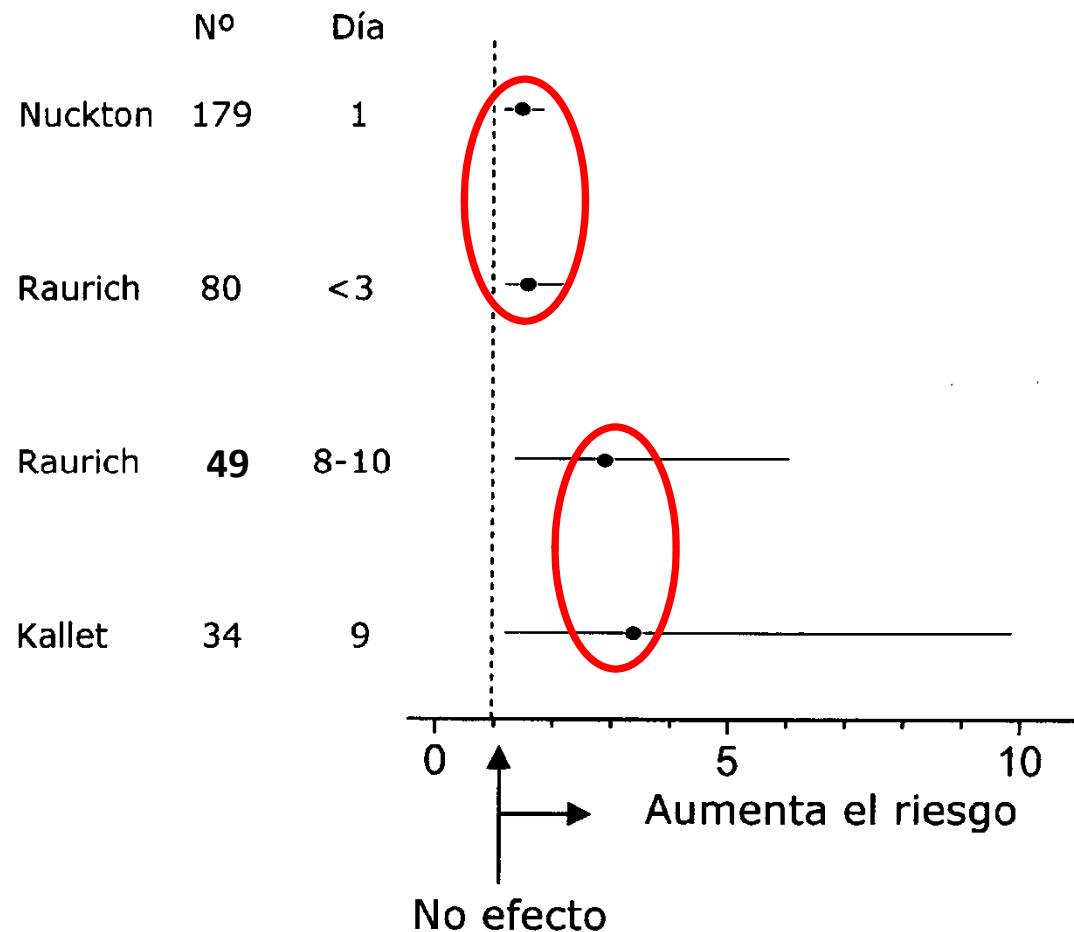
Table 3. Odds Ratios for Variables Independently Associated With a Greater Risk of Death in the Early Phase of Acute Respiratory Distress Syndrome

	Odds Ratio	95% CI	P
Dead-space fraction, per increase of 0.05	1.59	1.18–2.16	.003
Age, per 1-year increase	1.06	1.02–1.10	.004
SOFA, per 1-point increase	1.44	1.17–1.77	.001

Prognostic Value of the Pulmonary Dead-Space Fraction  
During the Early and Intermediate Phases  
of Acute Respiratory Distress Syndrome

Table 5. Odds Ratios for Variables Independently Associated With a Greater Risk of Death in the Intermediate Phase of Acute Respiratory Distress Syndrome

	Odds Ratio	95% CI	P
Dead-space fraction, per increase of 0.05	2.87	1.36–6.04	.005
Age, per 1-year increase	1.09	1.01–1.18	.03
SOFA, per 1-point increase	2.35	1.22–4.53	.01



*Nuckton TJ. NEJM 2002; 346:1281  
Raurich JM. Respir Care 2010; 55:282  
Kallet RH. Respir Care 2010; 55:350*

## **Prognostic Value of Different Dead Space Indices in Mechanically Ventilated Patients With Acute Lung Injury and ARDS\***

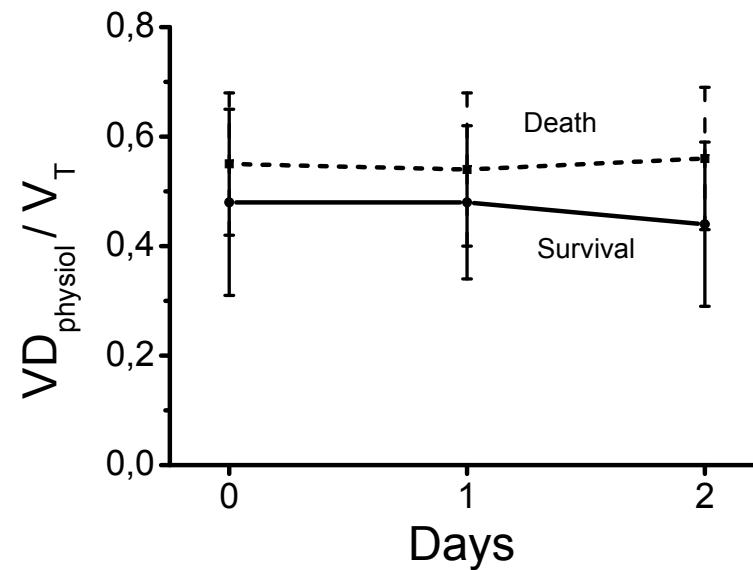
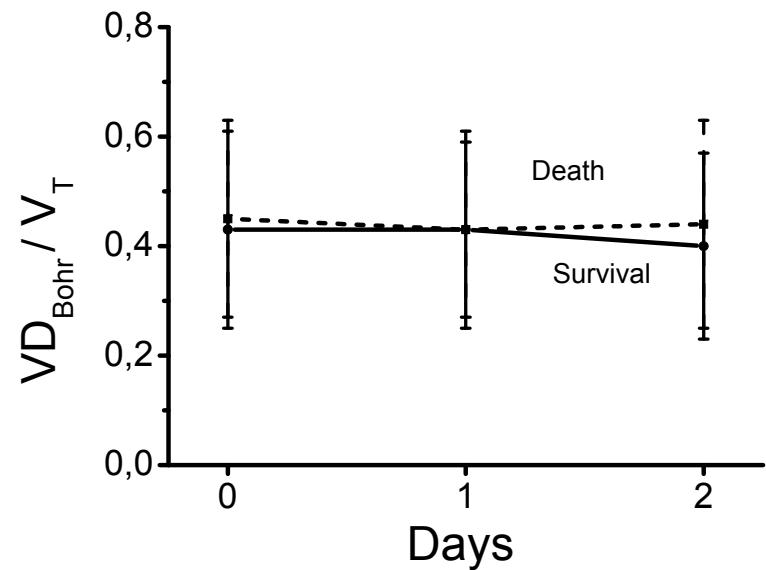
Variables	Survivors (n = 22)	Nonsurvivors (n = 14)	p Value
SAPS II	37.5 (32–45)	49 (36–54)	0.144
SOFA score	7 (6–9)	8.5 (5–10)	0.463
Lung injury score	1.63 (1.25–2)	2.38 (1.25–3)	0.112
Crs, mL/cm H <sub>2</sub> O	38 ± 11.7	32 ± 11.7	0.175
Pao <sub>2</sub> /Fio <sub>2</sub> , mm Hg	201 ± 60	194 ± 96	0.799
Paco <sub>2</sub> , mm Hg	38 ± 9.2	40 ± 10.2	0.481
Minute volume, L	8.3 ± 2.3	9.2 ± 4.2	0.432
Respiratory rate, breaths/min	15 ± 3.7	20 ± 7.8	0.028†
VT, mL/kg	7.0 ± 1.2	6.4 ± 1.1	0.178
Plateau pressure, cm H <sub>2</sub> O	25 ± 3.5	24 ± 7	0.795
PEEP, cm H <sub>2</sub> O	9 ± 4	8.3 ± 2.6	0.645

## **Prognostic Value of Different Dead Space Indices in Mechanically Ventilated Patients With Acute Lung Injury and ARDS\***

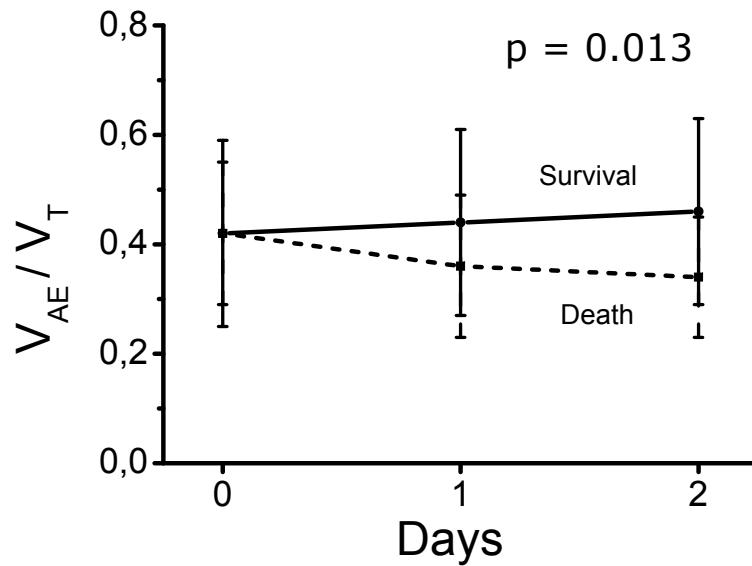
Variables	Survivors (n = 22)	Nonsurvivors (n = 14)	p Value
VDBohr/VT	0.41 ± 0.19	0.44 ± 0.17	0.610
VDphys/VT	0.47 ± 0.19	0.55 ± 0.13	0.152
VAE/VT ratio	0.42 ± 0.17	0.41 ± 0.13	0.970
Vco <sub>2</sub> , mL/min	214 ± 82	225 ± 115	0.820

*Diferencias en la gravedad del ARDS (26 ALI)*

*Diferencias en la metodología (capnografía)*



Variables	At ICU		
	Admission	At 24 h	At 48 h
VDB <sub>Bohr</sub> /V <sub>T</sub>			
D	0,45 ± 0,18	0,43 ± 0,18	0,44 ± 0,19
S	0,43 ± 0,18	0,43 ± 0,16	0,40 ± 0,17
Vd <sub>phys</sub> /V <sub>T</sub>			
D	0,55 ± 0,13	0,54 ± 0,14	0,56 ± 0,13
S	0,48 ± 0,17	0,48 ± 0,14	0,44 ± 0,15
VAE/V <sub>T</sub> ratio			
D	0,42 ± 0,13	0,36 ± 0,13	0,34 ± 0,11
S	0,42 ± 0,17	0,44 ± 0,17	0,46 ± 0,17



*Adaptado de:* Lucangelo U. CHEST 2008; 133:62

# Métodos de medición del espacio muerto

- Fórmulas (bolsa de *Douglas*)
- Capnografía volumétrica
- MIGET  
(técnica de eliminación múltiple de gases inertes)
- *Estimación* ( $V_D/V_{T_{est}}$ )

Bedside quantification of dead-space fraction using routine clinical data in patients with acute lung injury: secondary analysis of two prospective trials

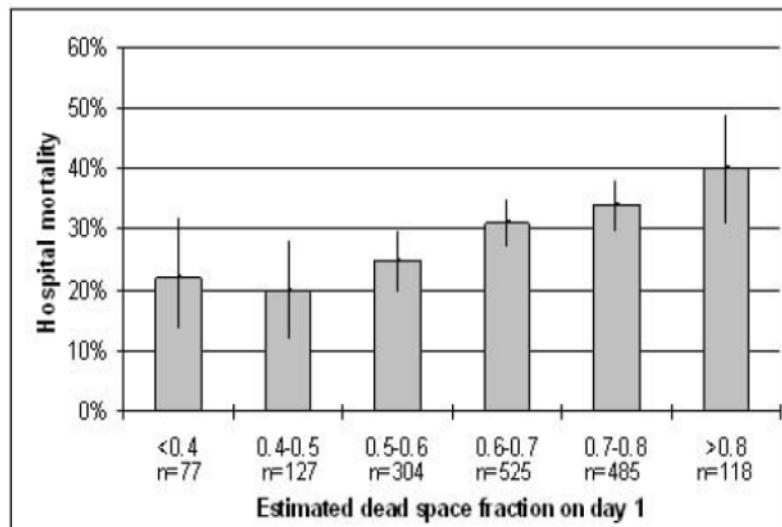
$$\text{PaCO}_2 = \frac{V'\text{CO}_2 \times 0.863}{V'A}$$

$$V'D/VT_{\text{est}} = 1 - \frac{0.863 \times V'\text{CO}_{2\text{ est}}}{\text{VE} \times \text{PaCO}_2}$$

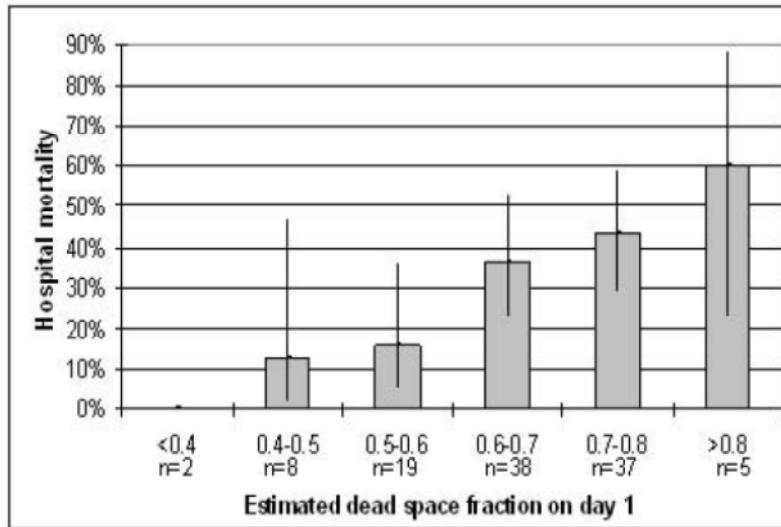
$$\text{Harris\&Benedict} = \text{GER}_{\text{HB}}$$

$$\text{GER}_{\text{HB}} = \text{GER}_{\text{Weir}} = 1,44 (V'\text{O}_2 \times 3,9 + V'\text{CO}_2 \times 1,1)$$

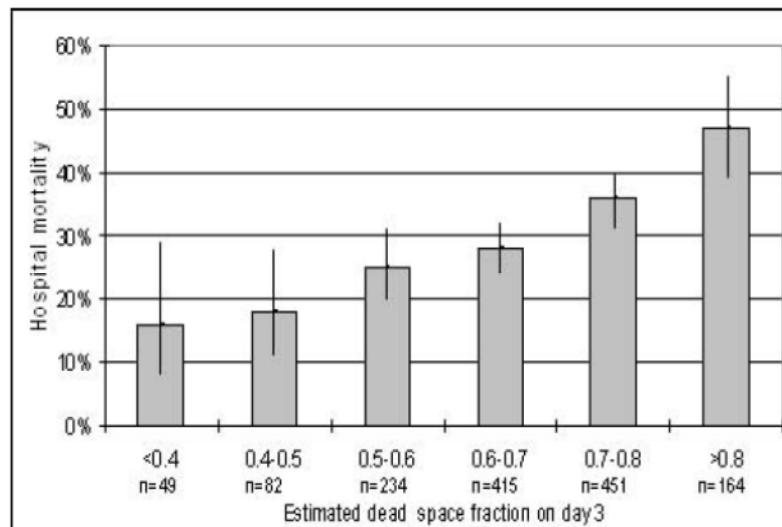
ARDS-net: 1636



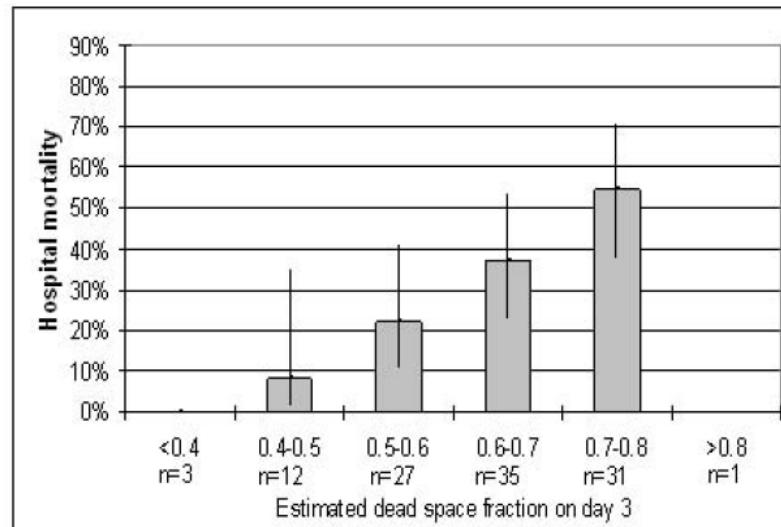
Mayo Clinic: 109



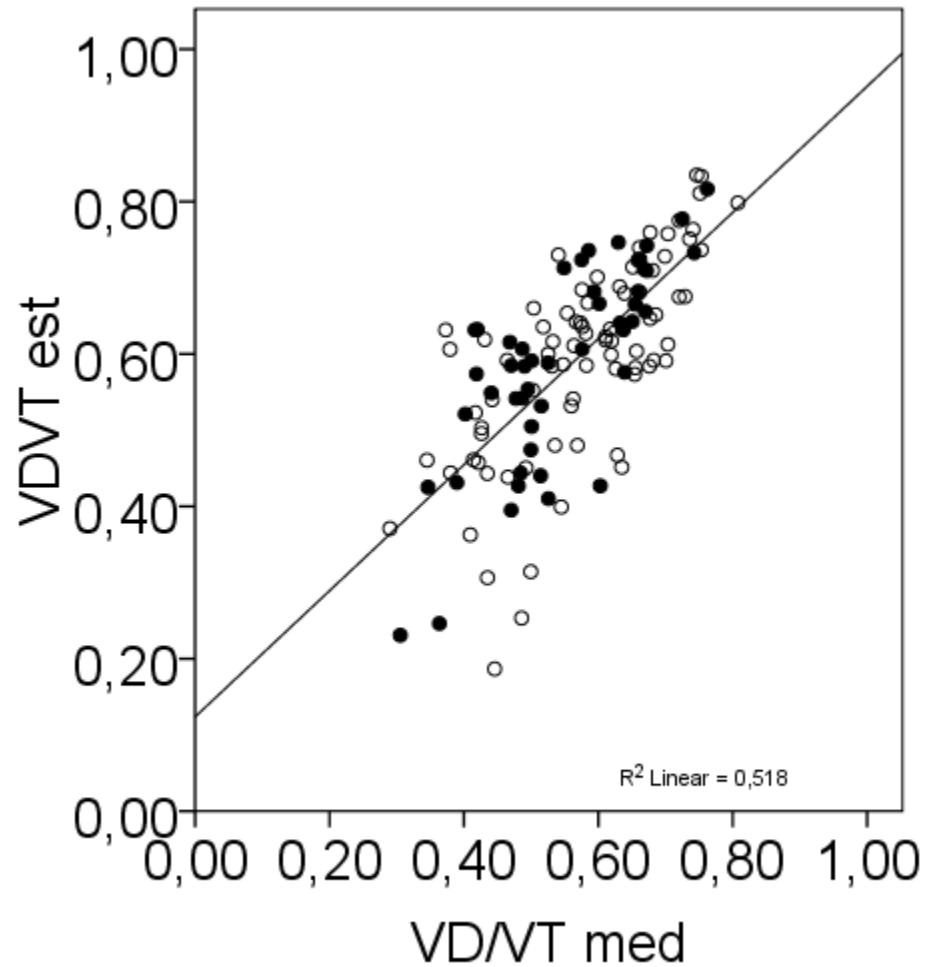
ARDS-net: 1395



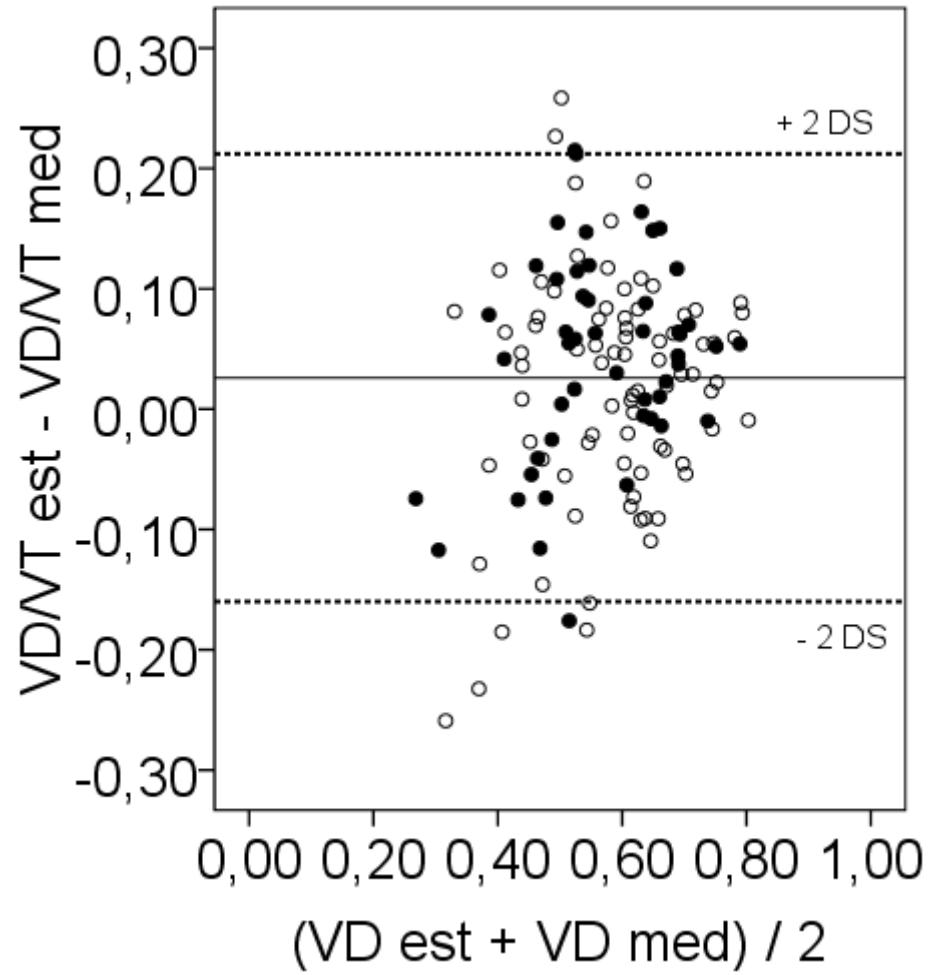
Mayo Clinic: 109



## *Correlación*

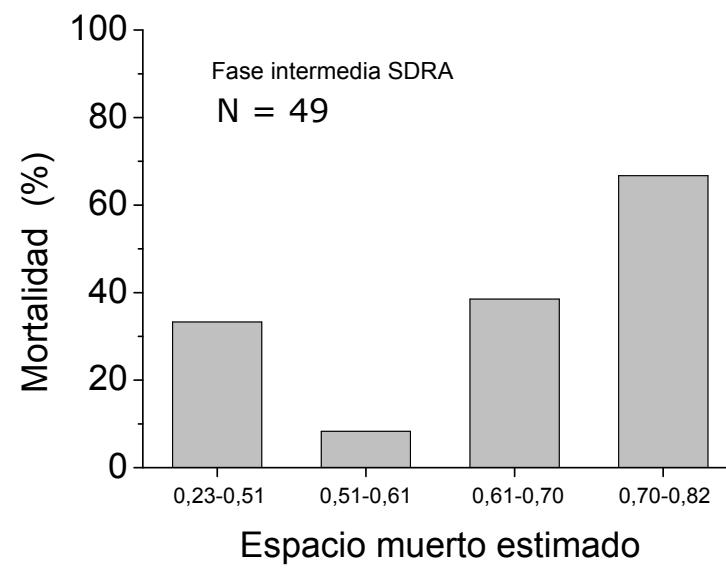
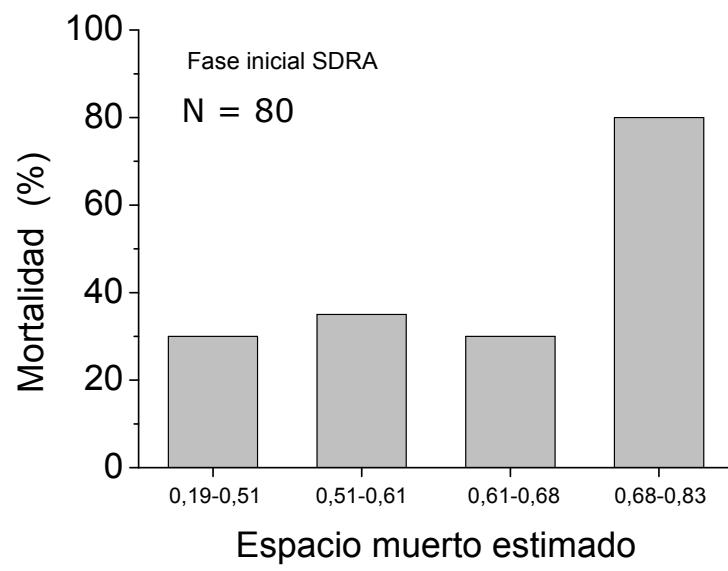


## *Límites de acuerdo*



129 mediciones

Datos no publicados



*Datos no publicados*

## PULMONARY DEAD-SPACE FRACTION AS A RISK FACTOR FOR DEATH IN THE ACUTE RESPIRATORY DISTRESS SYNDROME

Measurement of the dead-space fraction could help clinical investigators identify the patients who may benefit most from a particular therapeutic intervention. The dead-space fraction could also be used prospectively in future clinical trials, particularly when the goal is to evaluate the benefit of a treatment in the most severely ill patients.

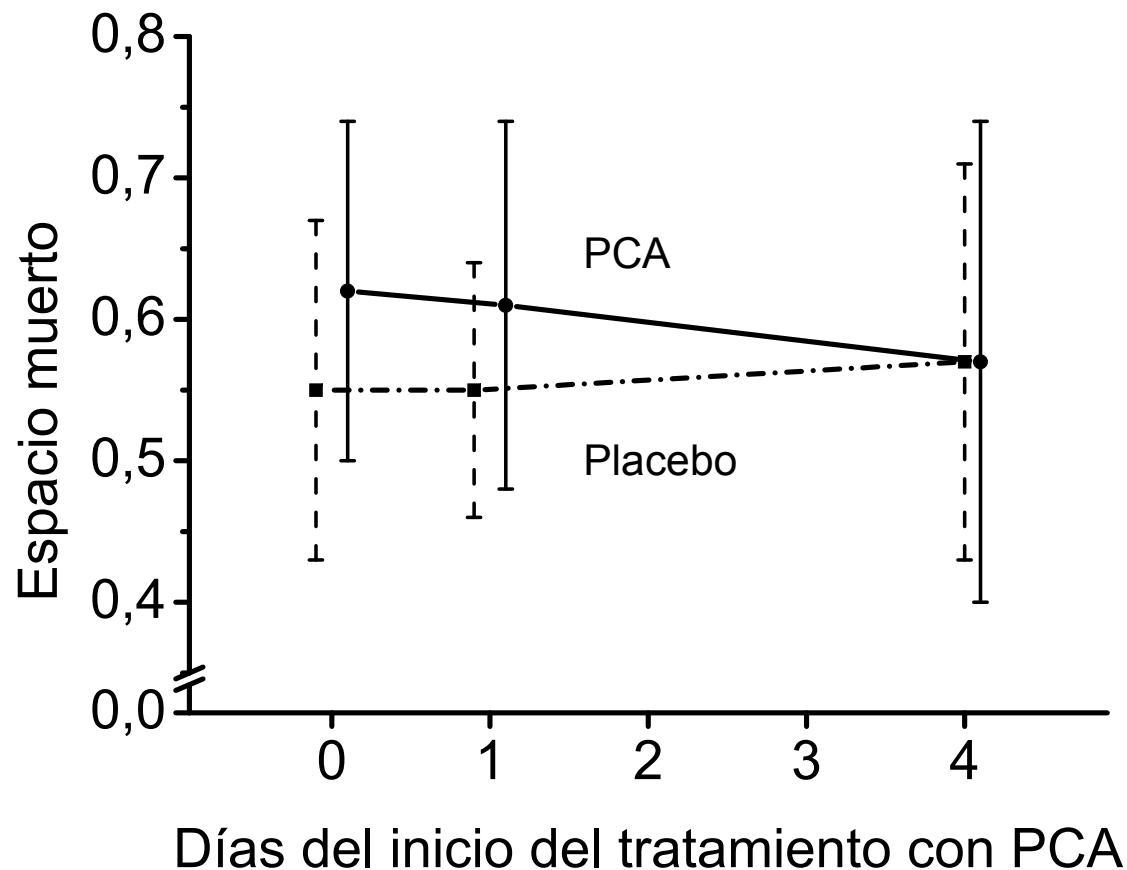
# **Randomized Clinical Trial of Activated Protein C for the Treatment of Acute Lung Injury**

*75 patients*

**TABLE 1. BASELINE CHARACTERISTICS**

	Placebo (n = 38)	APC (n = 37)	P Value
Age, yr	51.6 ± 18.6	51.6 ± 15.5	>0.99
Male sex, n (%)	26 (68)	21 (57)	0.30
Primary etiology of lung injury, n (%)			0.24
Pneumonia	16 (42)	14 (38)	
Aspiration	12 (32)	14 (38)	
Sepsis	7 (18)	4 (11)	
Drug overdose	2 (5)	0 (0)	
Other	1 (3)	5 (13)	
APACHE II score	20 ± 7	20 ± 8	0.72
SAPS II score	42 ± 14	42 ± 16	0.96
Respiratory variables			
Tidal volume, ml/kg PBW	6.9 ± 1.5	6.7 ± 1.4	0.54
Plateau pressure, cm H <sub>2</sub> O	24 ± 5	25 ± 7	0.22
PEEP, cm H <sub>2</sub> O	8.5 ± 3.2	9.4 ± 4.6	0.34
pH	7.38 ± 0.05	7.38 ± 0.07	0.82
Pa <sub>O<sub>2</sub></sub> /F <sub>IO<sub>2</sub></sub>	174 ± 63	158 ± 67	0.30
Lung injury score*	2.5 ± 0.6	2.7 ± 0.6	0.10
Dead space fraction	0.55 ± 0.12	0.62 ± 0.12	0.03

## **Randomized Clinical Trial of Activated Protein C for the Treatment of Acute Lung Injury**



*Adaptado de:* Liu KD. AJRCCM 2008; 178:618

## **Randomized Clinical Trial of Activated Protein C for the Treatment of Acute Lung Injury**

**TABLE 2. CLINICAL OUTCOMES BY GROUP**

	Placebo (n = 38)	APC (n = 37)	P Value
✓ Ventilator-free days, median (IQR)	19 (0–24)	19 (14–22)	0.78
✓ Death by Day 60, n (%)	5 (13.5)	5 (13.5)	1.00
Ventilator-free days among survivors, median (IQR)	21 (5–25)	20 (16–23)	0.36
Organ failure-free days, median (IQR)	23 (14–27)	23 (16–27)	0.46
Cardiovascular failure, median (IQR)	25 (20–28)	26 (23–28)	0.30
Coagulation failure, median (IQR)	28 (28–28)	28 (28–28)	0.57
Renal failure, median (IQR)	28 (18.5–28)	28 (28–28)	0.41
Hepatic failure, median (IQR)	28 (27–28)	28 (28–28)	0.36

*Definition of abbreviations:* APC = activated protein C; IQR = interquartile range.

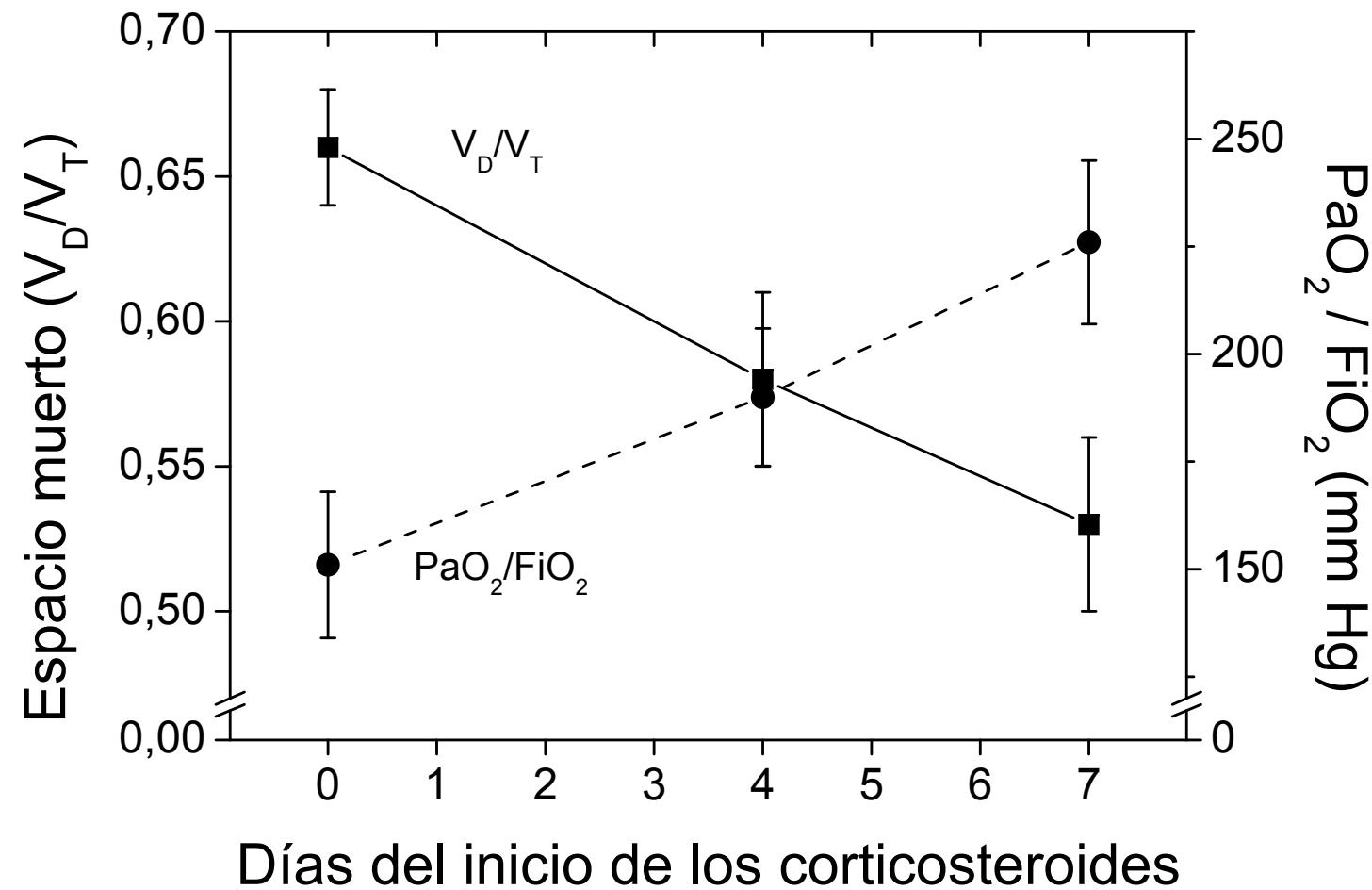
# Potential Effects of Corticosteroids in Physiological Dead Space Fraction in Acute Respiratory Distress Syndrome

<b>Variable</b>	<b>≤ 14 days onset ARDS (n: 10)</b>	<b>&gt; 14 days onset ARDS (n: 9)</b>	<b>P value</b>
Age, yr	55 ± 17	46 ± 15	0.25
SAPS II	36 ± 15	36 ± 4	0.90
SOFA	5.4 ± 3.1	5.1 ± 3.2	0.84
<b><i>Pulmonary function data</i></b>			
PaO <sub>2</sub> /FiO <sub>2</sub>	135 ± 43	156 ± 82	0.80
pH	7.40 ± 0.10	7.41 ± 0.08	0.86
PaCO <sub>2</sub> , mm Hg	52 ± 15	60 ± 32	0.53
Lung-injury score	2.5 ± 0.4	2.6 ± 0.7	0.83
PEEP, cm H <sub>2</sub> O	9.6 ± 5.9	6.8 ± 6.1	0.32
Plateau pressure, cm H <sub>2</sub> O	27.8 ± 6.0	32.1 ± 7.9	0.19
Tidal volume, mL	351 ± 70	372 ± 130	0.67
Tidal volume, mL/Kg of IBW	6.1 ± 1.5	6.3 ± 1.9	0.82
Minute ventilation, L/min	9.2 ± 1.8	10.9 ± 4.0	0.22
Corrected minute ventilation, L/min	11.8 ± 3.5	16.9 ± 12.5	0.27
Quasistatic compliance, mL/cm H <sub>2</sub> O	20.7 ± 7.6	15.1 ± 6.1	0.10
Dead-space fraction	0.63 ± 0.04	0.69 ± 0.14	0.21

$$V_{Ec} = V_E \times PaCO_2 / 40$$

Raurich JM. Respir Care 2012; 57(3)

# Potential Effects of Corticosteroids in Physiological Dead Space Fraction in Acute Respiratory Distress Syndrome



Raurich JM. Respir Care 2012; 57(3)

# Potential Effects of Corticosteroids in Physiological Dead Space Fraction in Acute Respiratory Distress Syndrome

<b>Variable</b>	<b>N</b>	<b>Day 0</b>	<b>Day 4</b>	<b>Day 7</b>	<b>p value</b>
PaO <sub>2</sub> / FiO <sub>2</sub>					
< 14 days onset ARDS	10	135 ± 43	178 ± 50	222 ± 65	0.001
≥ 14 days onset ARDS	9	156 ± 82	202 ± 86	231 ± 105	0.06
Physiological dead-space					
< 14 days onset ARDS	10	0.63 ± 0.04	0.57 ± 0.05	0.50 ± 0.06	0.001
≥ 14 days onset ARDS	9	0.69 ± 0.13	0.59 ± 0.17	0.57 ± 0.15	0.001
Quasistatic compliance, mL/cm H <sub>2</sub> O					
< 14 days onset ARDS	10	20.7 ± 7.6	29.4 ± 14.0	29.7 ± 8.8	0.06
≥ 14 days onset ARDS	9	15.1 ± 6.1	17.4 ± 4.8	22.0 ± 7.9	0.10
Lung-injury score					
< 14 days onset ARDS	10	2.6 ± 0.5	2.1 ± 0.5	1.8 ± 0.4	0.001
≥ 14 days onset ARDS	9	2.5 ± 0.7	2.2 ± 0.7	1.9 ± 0.5	0.004

Raurich JM. *Respir Care* 2012; 57(3)

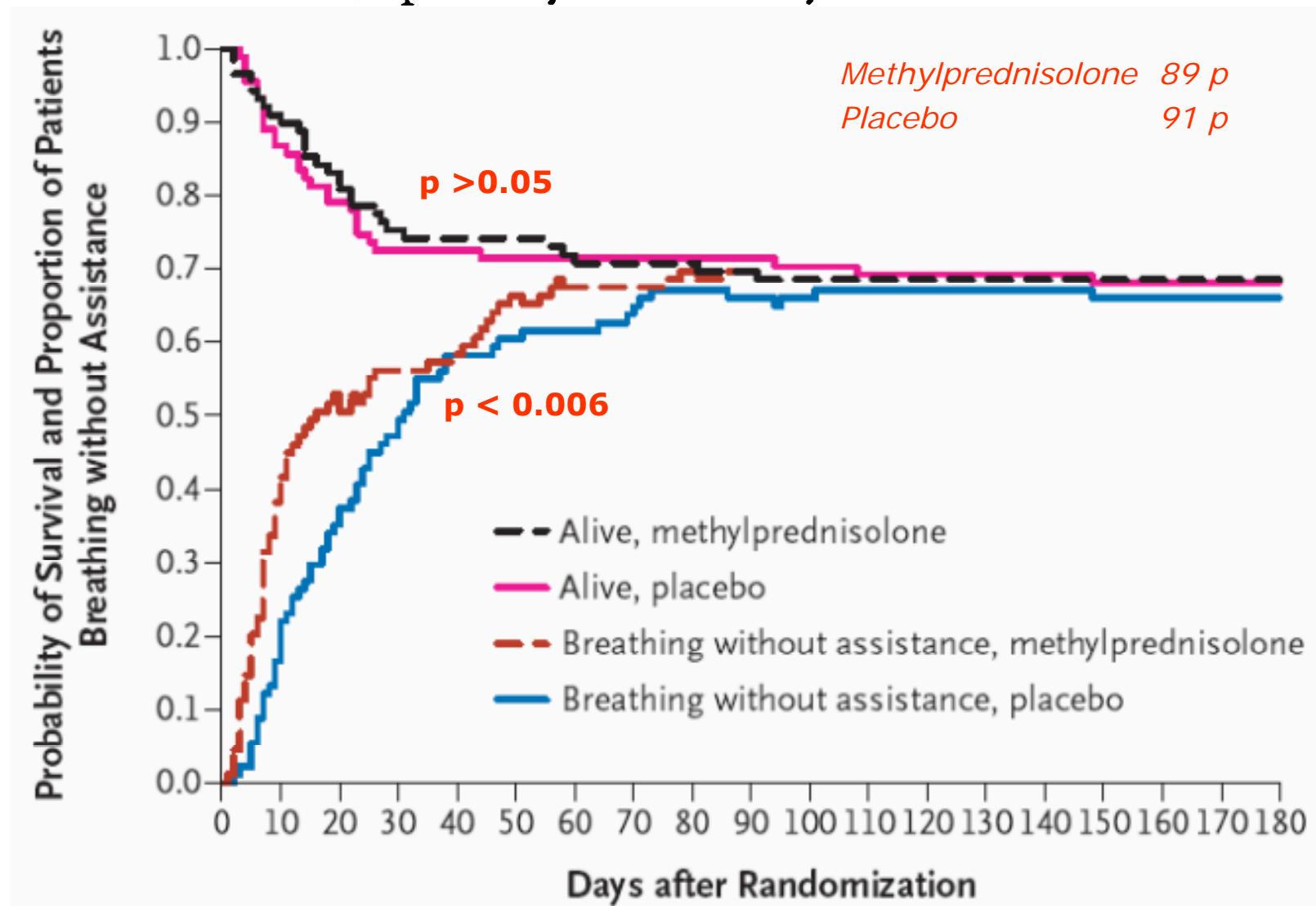
## Potential Effects of Corticosteroids in Physiological Dead Space Fraction in Acute Respiratory Distress Syndrome

	≤ 14 days onset of ARDS (n: 10)	> 14 days onset of ARDS (n: 9)	p value
Duration of mechanical ventilation, d	40 (26 – 50)	37 (29 – 45)	0.78
ICU length of stay, d	38 (30 – 50)	38 (32 – 46)	0.81
In-hospital length of stay, d	47 (34 – 70)	50 (38 – 77)	0.62
In-hospital mortality, n (%)	3 (30)	4 (44)	0.65

*Número reducido de pacientes  
Falta grupo control*

Raurich JM. Respir Care 2012; 57(3)

# Efficacy and Safety of Corticosteroids for Persistent Acute Respiratory Distress Syndrome



ARDS Network. Steinberg KP. NEJM 2006; 354: 1671

# Conclusiones

## Sobre el espacio muerto en el SDRA

- ✓ Variable independiente asociada a la mortalidad
- ✓ Permite valorar el efecto sobre el pulmón de determinados tratamientos



Gràcies per la vostra atenció

Jodhpur