

17º CONGRESO BARCELONA



22-24
marzo
2023



SOCIETAT
CATALANA DE
TRASPLANTAMENT

Biomarcadores de disfunción del injerto en el trasplante pulmonar

M^a Piedad Ussetti GIL

H. U. Puerta de Hierro Majadahonda

Biomarcadores de disfunción del injerto en el trasplante pulmonar



Citoquinas
DSA
Poblaciones celulares

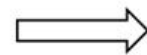
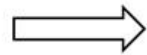
miRNA
ddcfDNA
KL6

Espiromería
Biospia

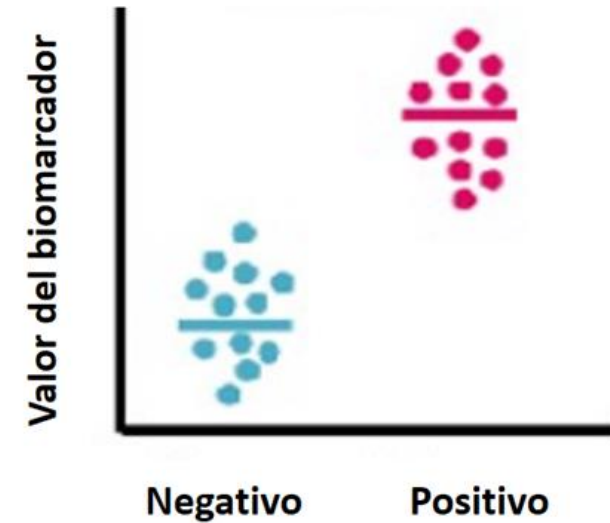
TC
torácico

FUTURO

BIOMARCADOR: Introducción



Pronóstico Diagnóstico Respuesta



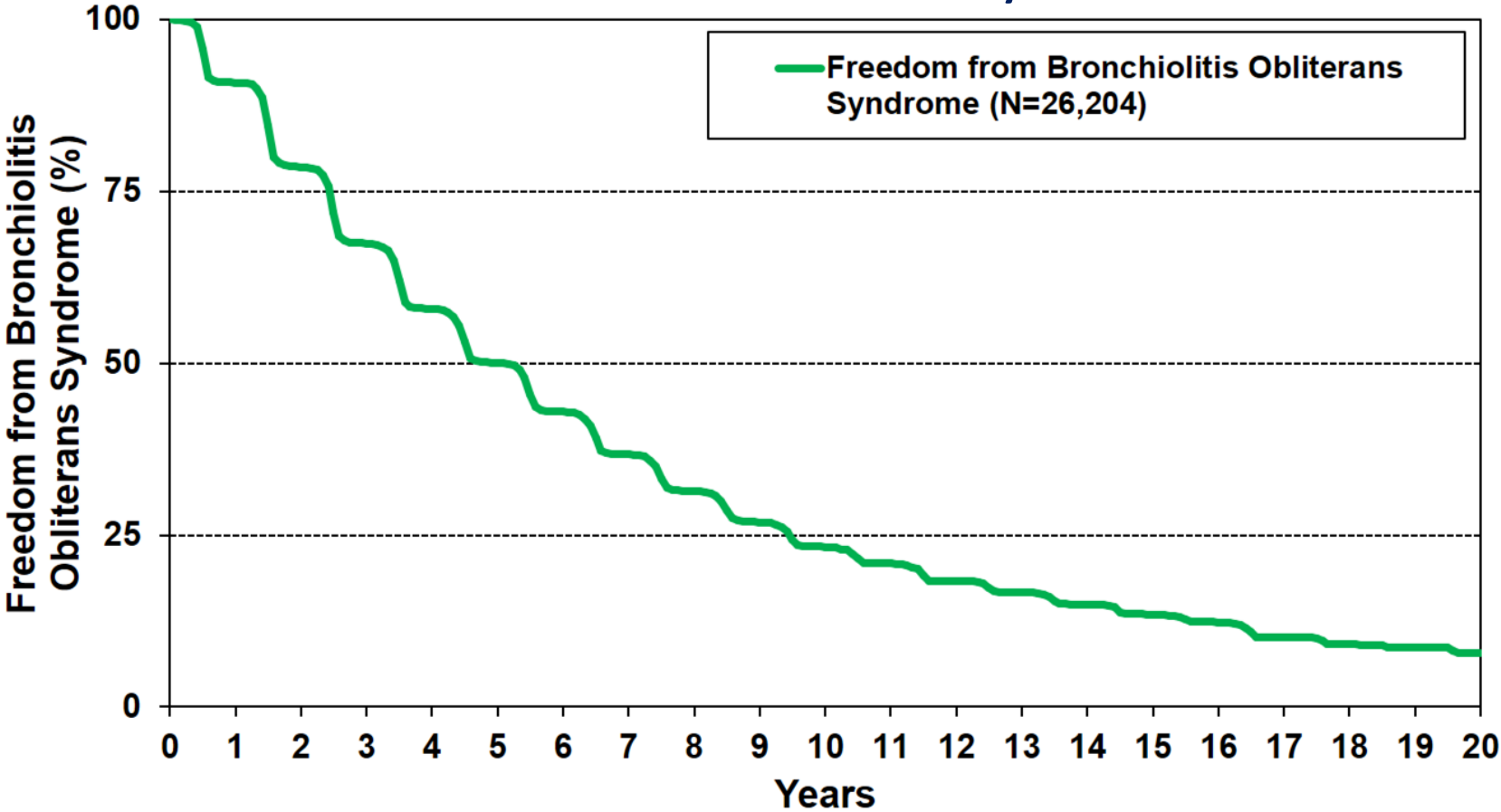
BIOMARCADOR: Introducción

- Debe estar presente en el tejido o en sangre periférica
- Su detección debe ser fácil y asequible
- Debe ser posible su cuantificación y asociarse de la forma más específica posible a la patología.

Adult Lung Transplants

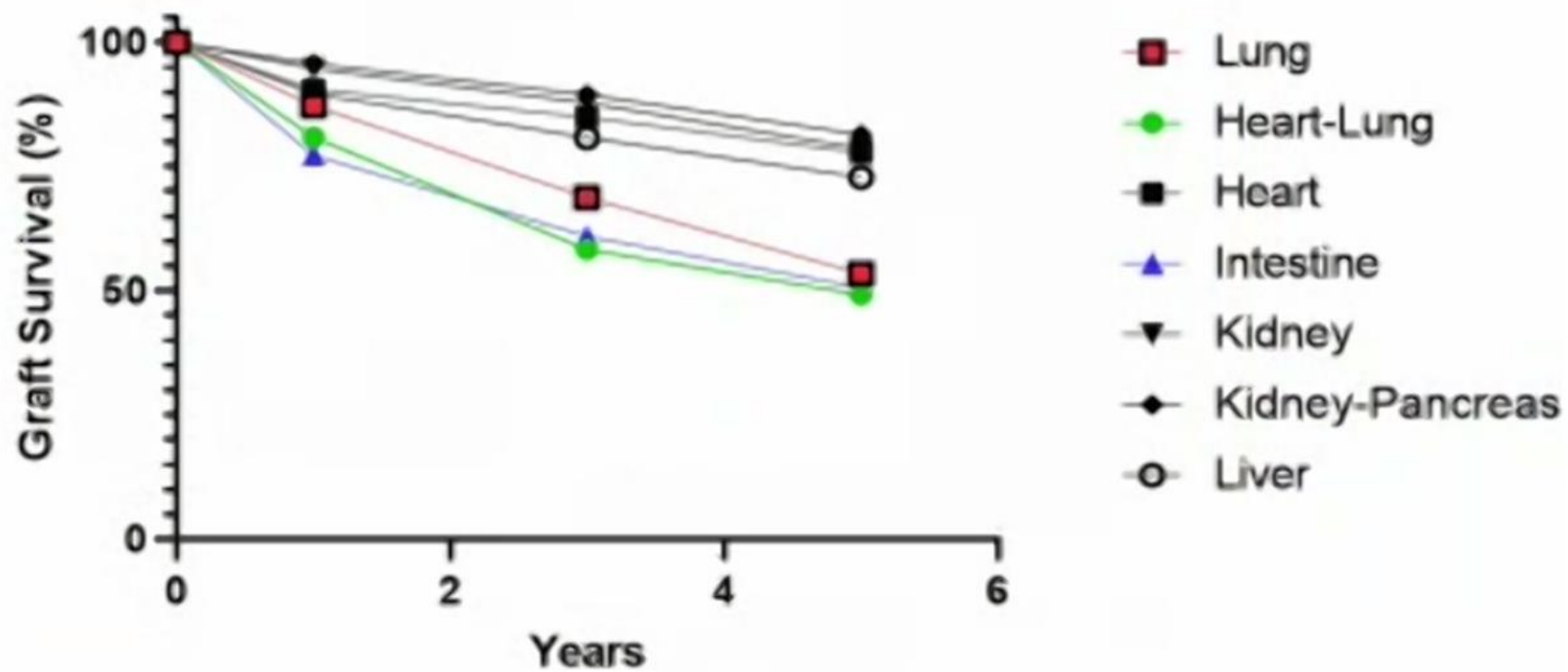
Freedom from Bronchiolitis Obliterans Syndrome

Conditional on Survival to 14 days



Lung Allograft Survival worse than Kidney, Heart & Liver

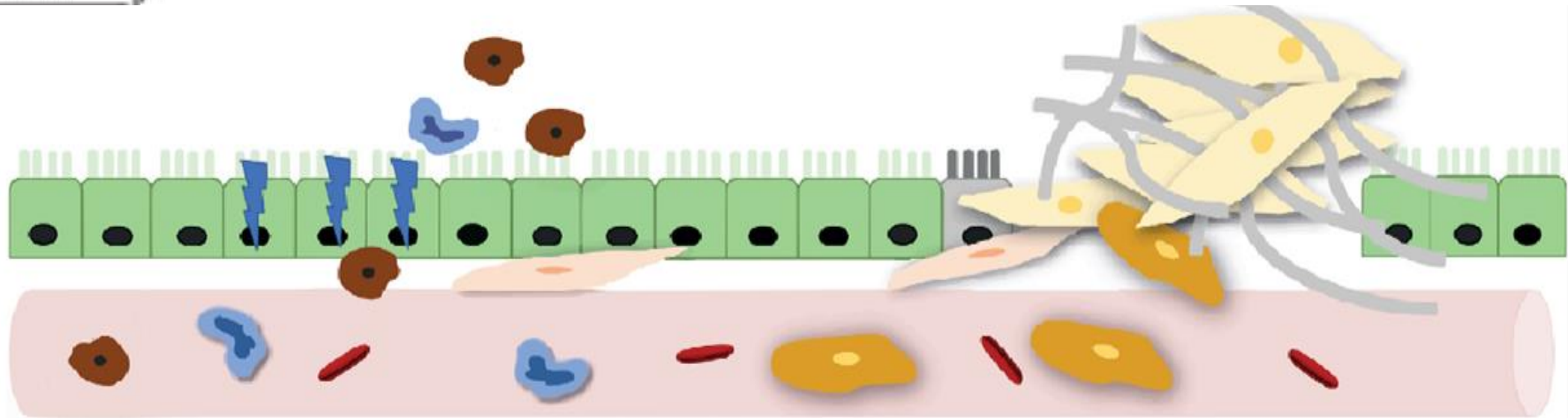
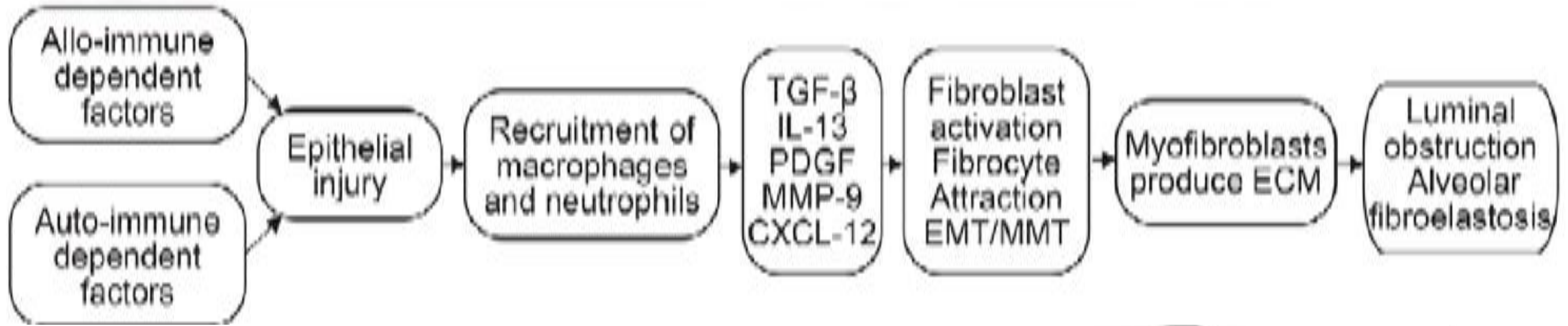
CLAD the predominant cause...



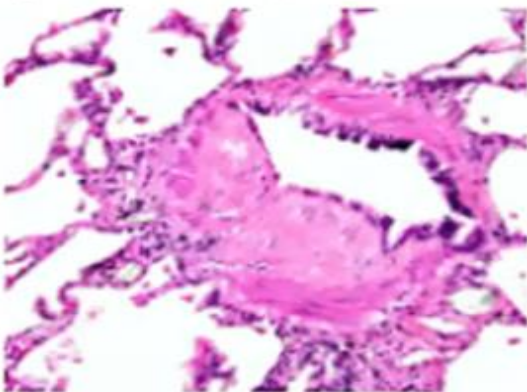
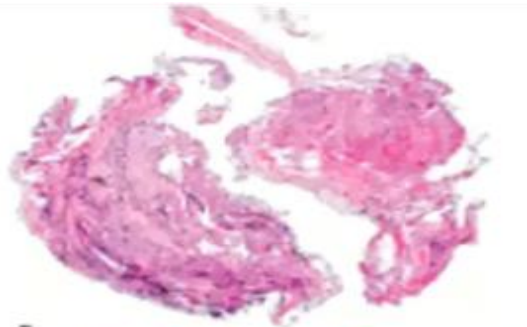
OPTN Data (1/29/2021) <https://optn.transplant.hrsa.gov/data>

The potential of biomarkers of fibrosis in chronic lung allograft dysfunction

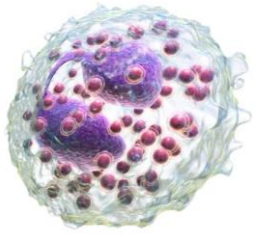
Eline A. van der Ploeg^{a,*}, Barbro N. Melgert^{b,c}, Janette K. Burgess^{c,d}, C. Tji Gan^a



BIOMARCADORES: Rechazo agudo y cónico



- Debe estar presente en el tejido o en sangre periférica
- Su detección debe ser fácil y asequible
- Debe ser posible su cuantificación y asociarse de la forma más específica posible a la patología.



BIOMARCADORES EN SANGRE: Rechazo agudo y trasplante renal

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TRANSPLANTATION
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BLOOD EOSINOPHILIA, STEROIDS, AND REJECTION¹

IRMELI LAUTENSCHLAGER, EEVA VON WILLEBRAND, AND PEKKA HÄYRY²

Transplantation Laboratory and Fourth Department of Surgery, University of Helsinki, Helsinki Finland

Un aumento de EOS > 400/mm³ en sangre periférica era un marcador precoz de rechazo del injerto en trasplante renal.

Original Paper

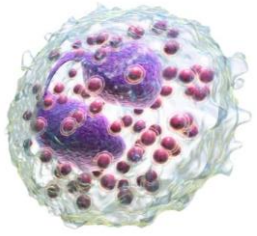
Nephron 1993;65:304-309

*Jaume Almirall^a
Josep M. Campistol^b
Manel Sole^c
Jordi Andreu^b
Lluís Revert^a*

Blood and Graft Eosinophilia as a Rejection Index in Kidney Transplant

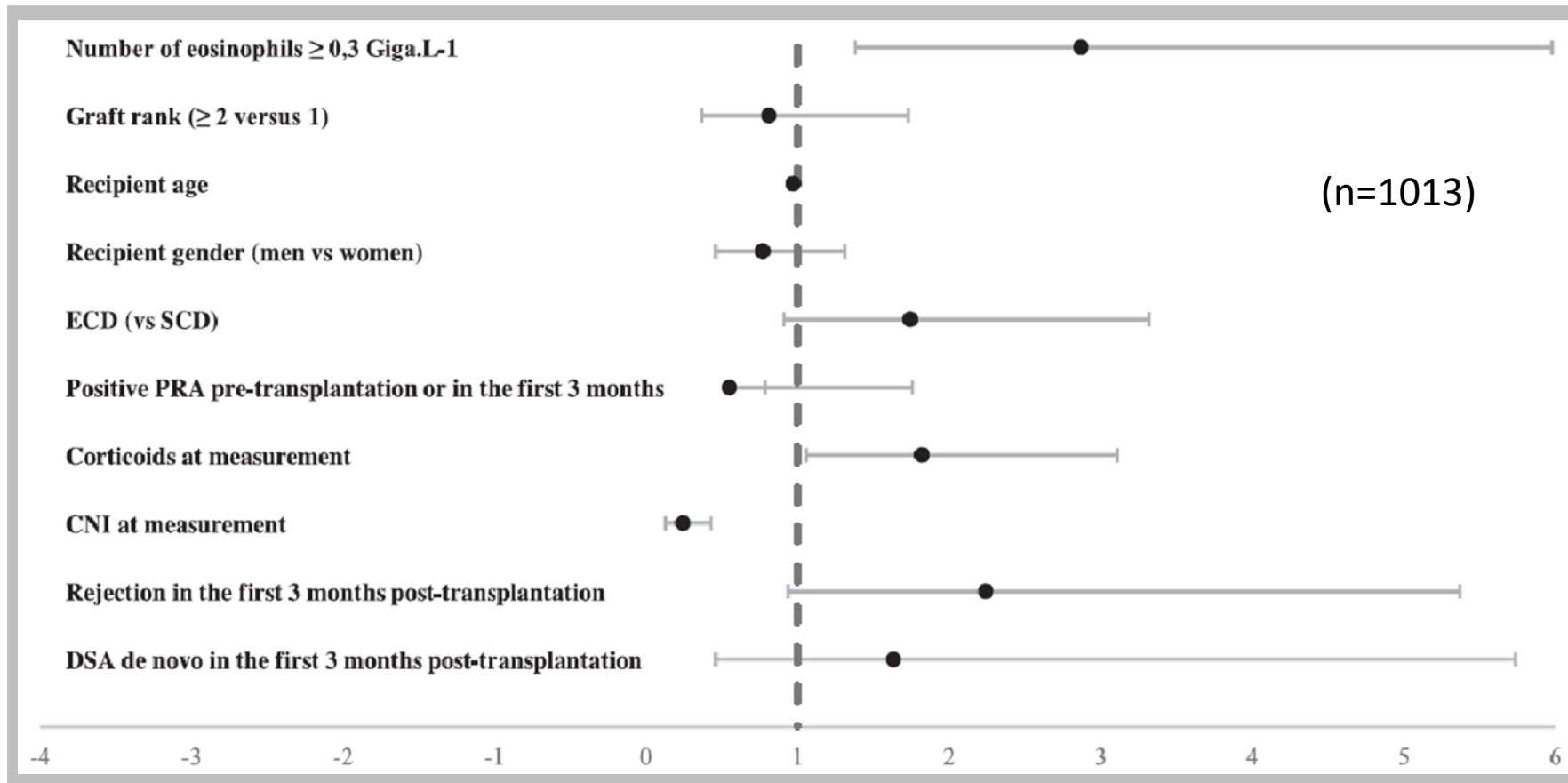
^a Nephrology Department,
^b Renal Transplant Unit and
^c Pathology Department,
Hospital Clinic i Provincial,
University of Barcelona, Spain

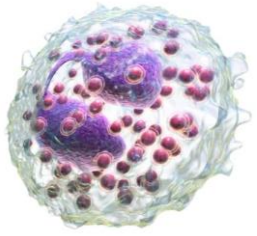
El aumento de EOS y la infiltración eosinofílica del injerto renal se considera criterios de gravedad del rechazo.



Time-dependent blood eosinophilia count increases the risk of kidney allograft rejection

Luc Colas, MD, PhD^{a,1}, Linh Bui, MD^{b,1}, Clarisse Kerleau^c, Mohamed Lemdani, PhD^d,
Karine Autain-Renaudin, MD, PhD^{a,e}, Antoine Magnan, MD^f, Magali Giral, MD, PhD^{a,c,g,h,1,*},
Sophie Brouard, VMD, PhD^{a,g,h,1,**}, for the DIVAT Consortium²





BIOMARCADORES EN SANGRE: Rechazo agudo y trasplante hepático

ORIGINAL ARTICLE

Predicting severity and clinical course of acute rejection after liver transplantation using blood eosinophil count

Manuel Rodríguez-Perálvarez,¹ Giacomo Germani,¹ Emmanuel Tsochatzis,¹ Nancy Rolando,¹ Tu Vinh Luong,² Amar Paul Dhillon,² Douglas Thorburn,¹ James O'Beirne,¹ David Patch¹ and Andrew Kenneth Burroughs¹

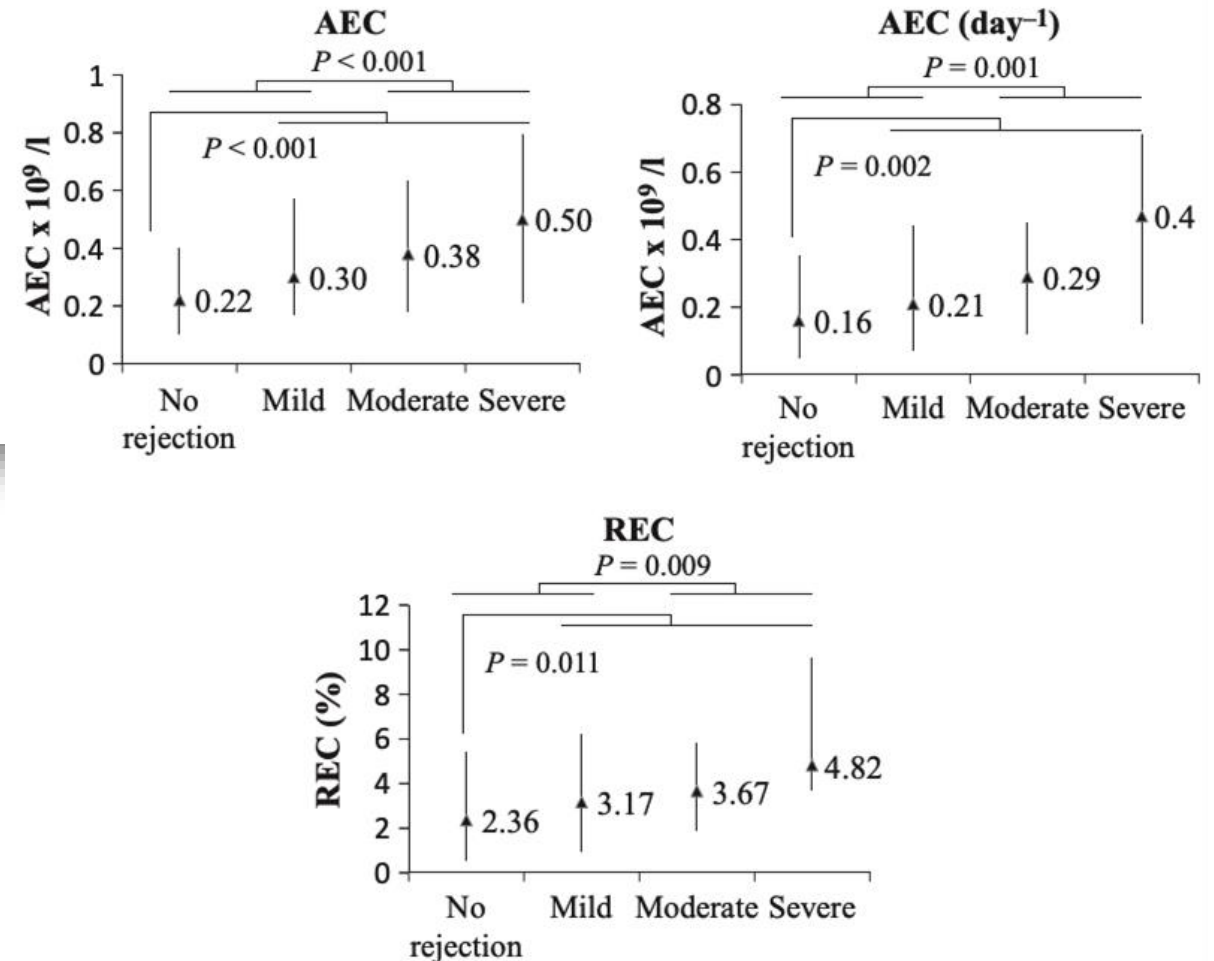
¹ The Royal Free Sheila Sherlock Liver Centre and University Department of Surgery, Royal Free Hospital London, UK

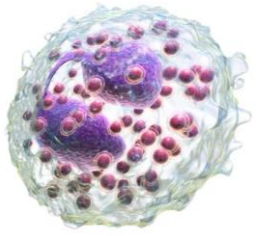
² Department of Histopathology, Royal Free Hospital, London, UK

Correlación entre la severidad del rechazo y EOS.

Aumento de EOS es el signo mas específico y confiable de la presencia de rechazo en pacientes Tx hepático

Transpl Int. 2012 May;25(5):555-63





BIOMARCADORES EN SANGRE: Rechazo agudo y trasplante hepático

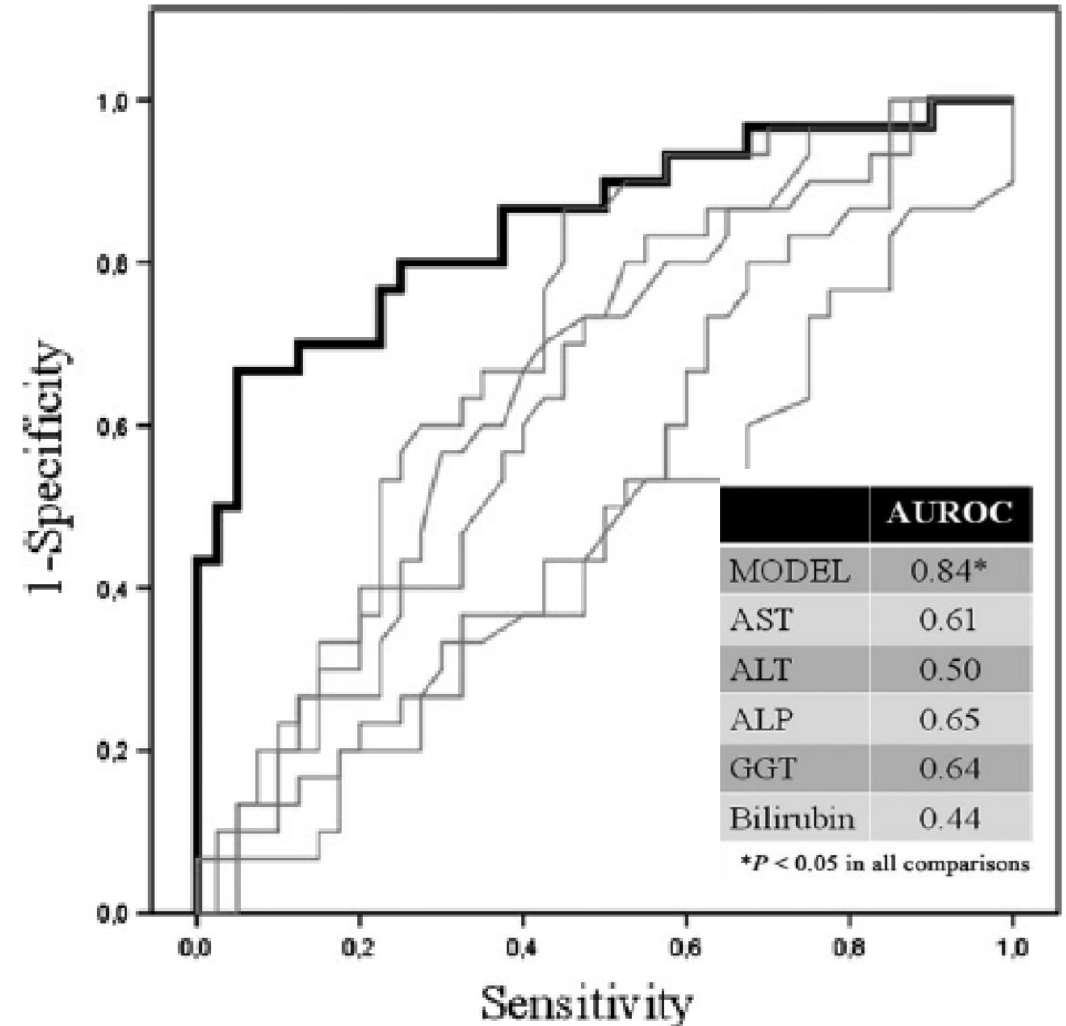
ORIGINAL ARTICLE

Lack of agreement for defining 'clinical suspicion of rejection' in liver transplantation: a model to select candidates for liver biopsy

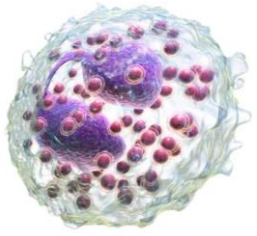
Manuel Rodríguez-Perálvarez,¹ Carmen García-Caparrós,¹ Emmanuel Tsochatzis,² Giacomo Germani,^{2,3} Brian Hogan,² Antonio Poyato-González,¹ James O'Beirne,² Marco Senzolo,³ Marta Guerrero-Misas,¹ Jose L. Montero-Álvarez,¹ David Patch,² Pilar Barrera,¹ Javier Briceño,¹ Amar P. Dhillon,² Patrizia Burra,³ Andrew K. Burroughs² and Manuel De la Mata¹

¹ Department of Hepatology and Liver Transplantation, Reina Sofía University Hospital, IMBIC, CIBERehd, Córdoba, Spain

$$\text{Score} = \frac{e^{(-0.07093)+0.00206 \times (\text{Age} \times \text{MELD}) - 2.43720 \times (\text{Red_Immunos}) - 0.00407 \times (\Delta \text{EOS})}}{1 + e^{(-0.07093)+0.00206 \times (\text{Age} \times \text{MELD}) - 2.43720 \times (\text{Red_Immunos}) - 0.00407 \times (\Delta \text{EOS})}}$$





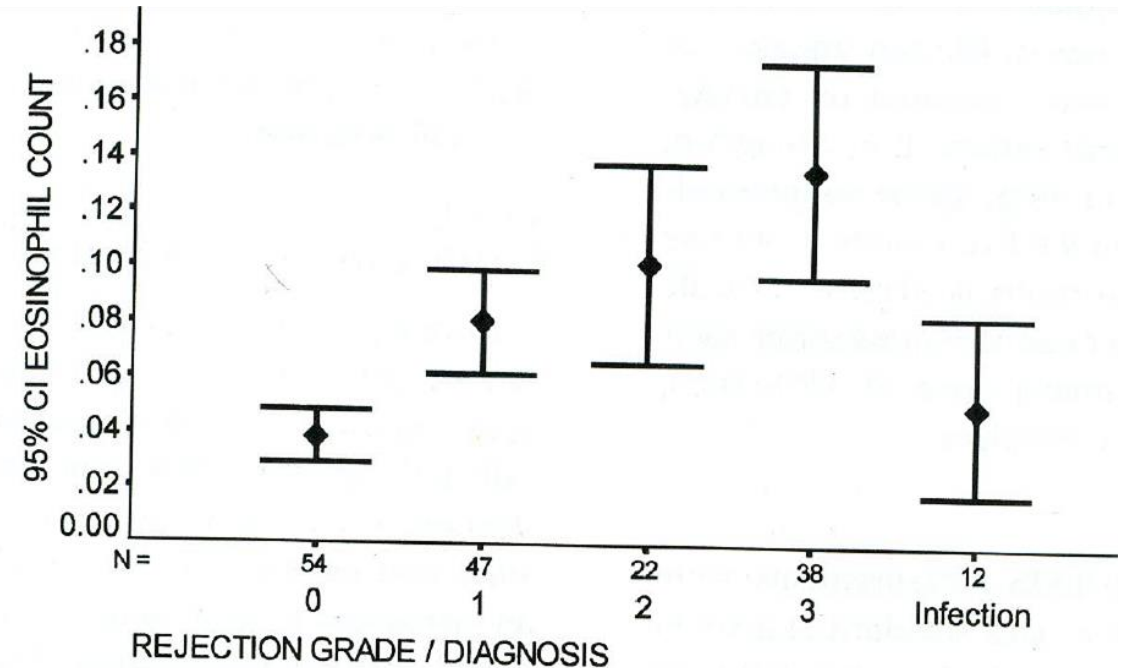


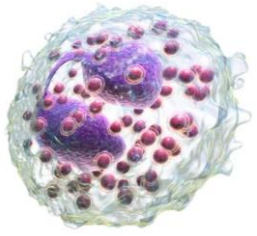
BIOMARCADORES EN SANGRE: Rechazo agudo y trasplante pulmonar

Association Between Blood Eosinophil Counts and Acute Cardiac and Pulmonary Allograft Rejection

Andrew Trull, PhD,^a Louise Steel,^a Jacqueline Cornelissen,^a Teresa Smith, PhD,^b Linda Sharples, PhD,^{b,c} Nathaniel Cary, FRCPATH,^d Susan Stewart, FRCPATH,^d Stephen Large, FRCS,^e John Wallwork, FRCS^e

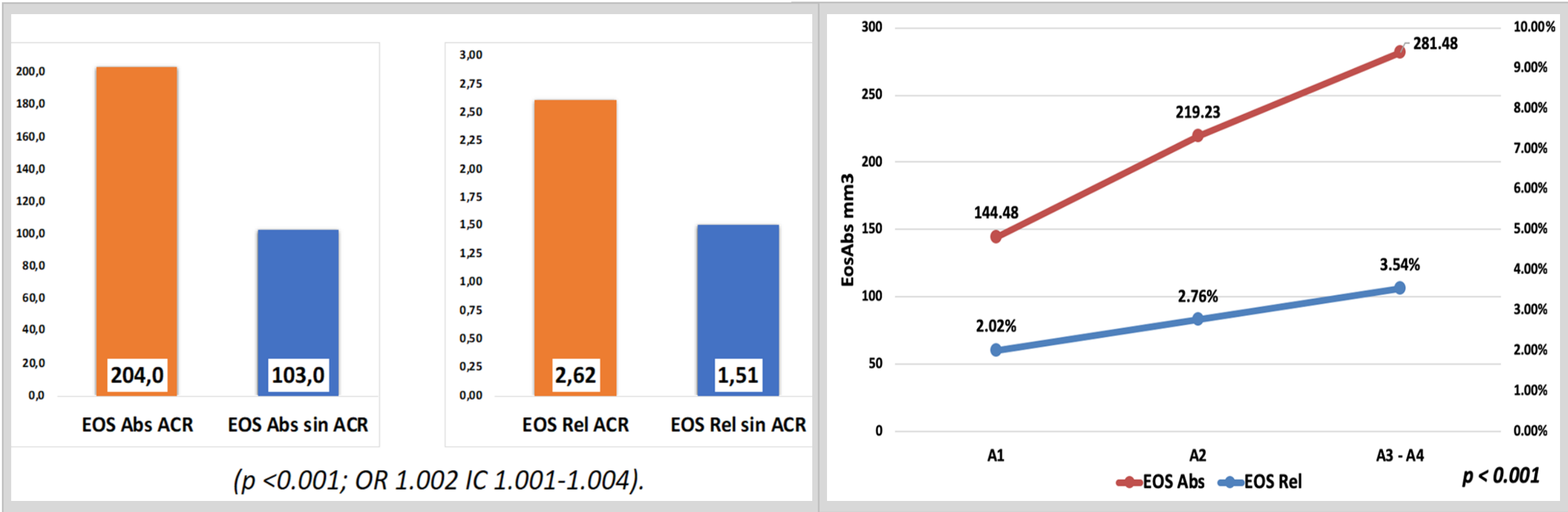
Asociación entre EOS > 140/mm³ y ACR en BTB en pacientes trasplantados pulmonares

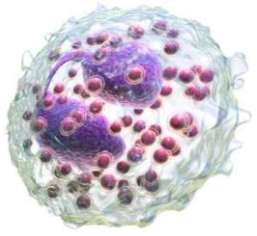




BIOMARCADORES EN SANGRE : Rechazo agudo

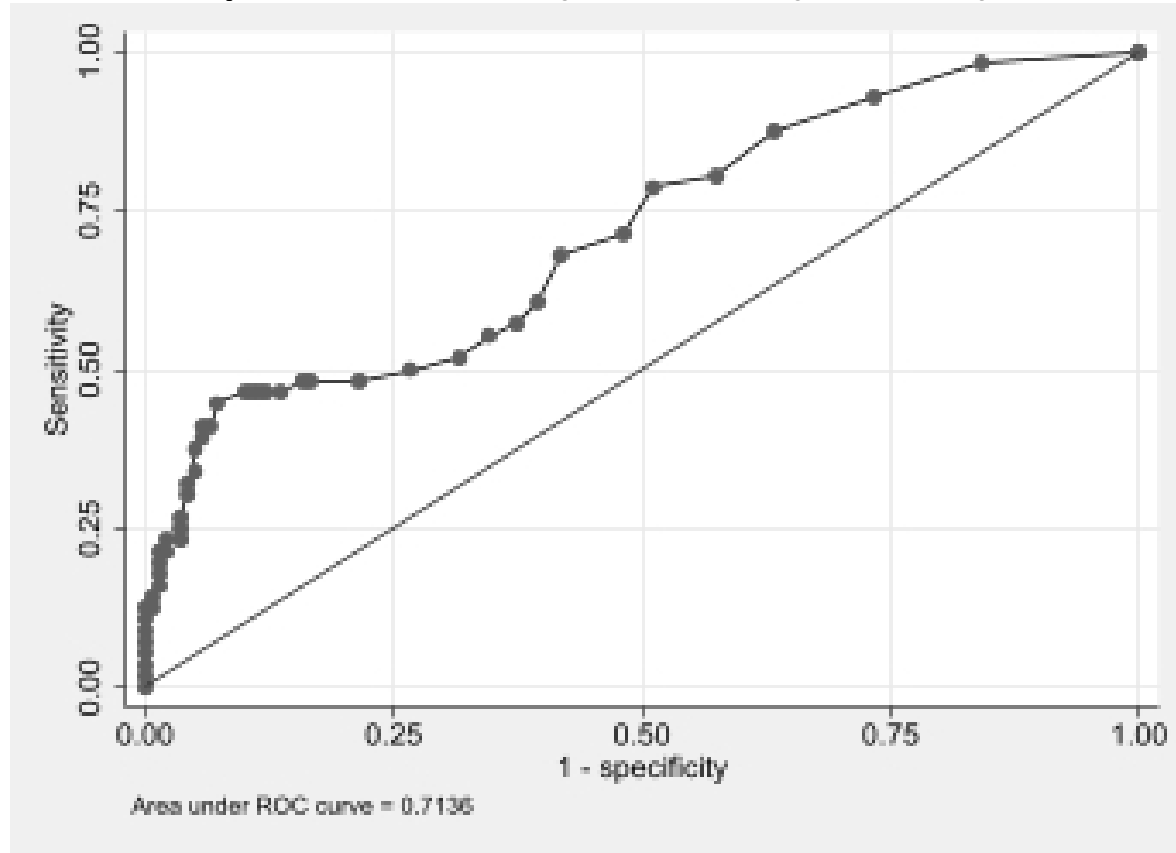
- 583 biopsias transbronquiales (29% con rechazo agudo)
- 256 pacientes Tx pulmonares



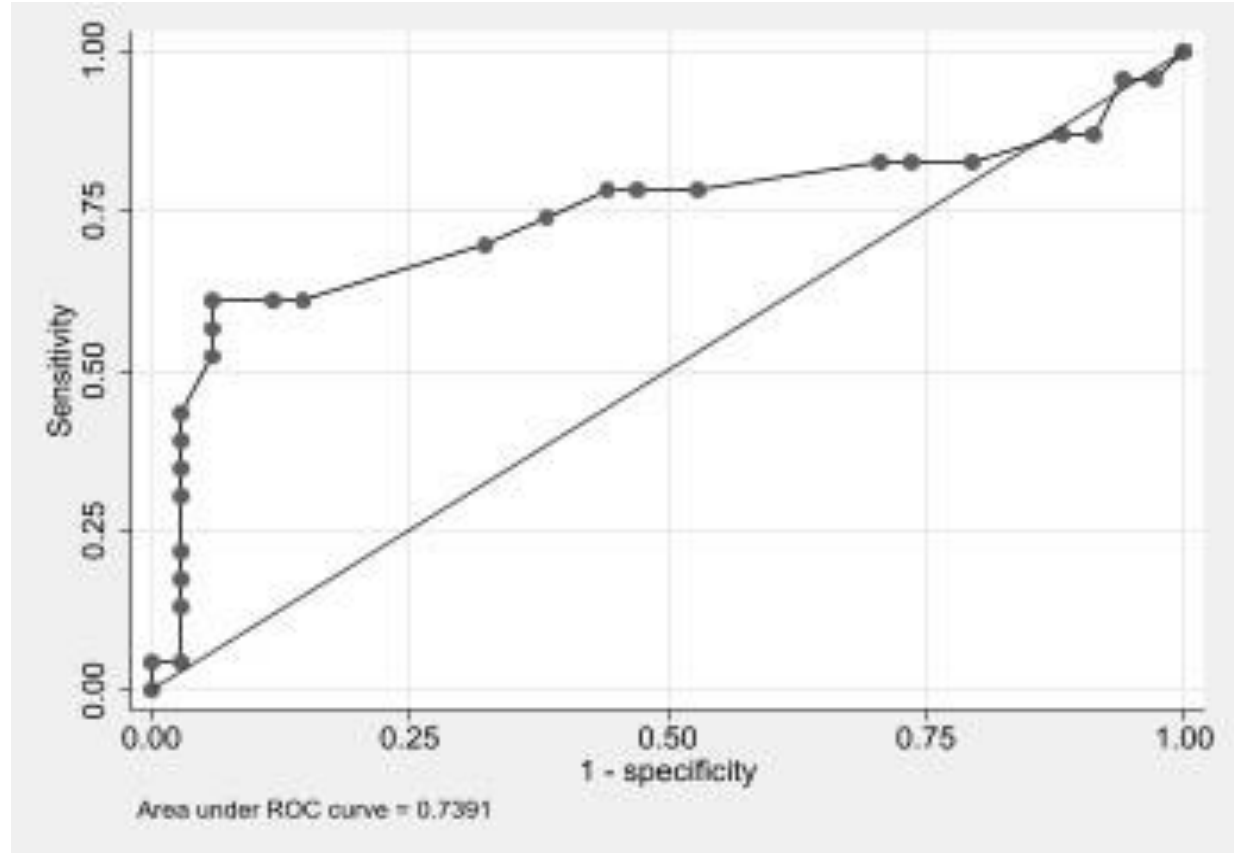


BIOMARCADORES EN SANGRE : Rechazo agudo

Especificidad 90% (195/mm³ (12meses)



Especificidad 94% (180/mm³) (>12meses)





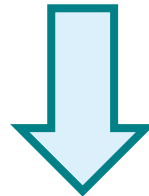
BIOMARCADORES EN LAVADO BRONCOALVEOLAR (BAL)

CELULARIDAD



Ventana al microambiente del injerto pulmonar

Mecanismos fisiopatológicos que contribuyen a la presencia de rechazo



Método para el diagnóstico y detección precoz

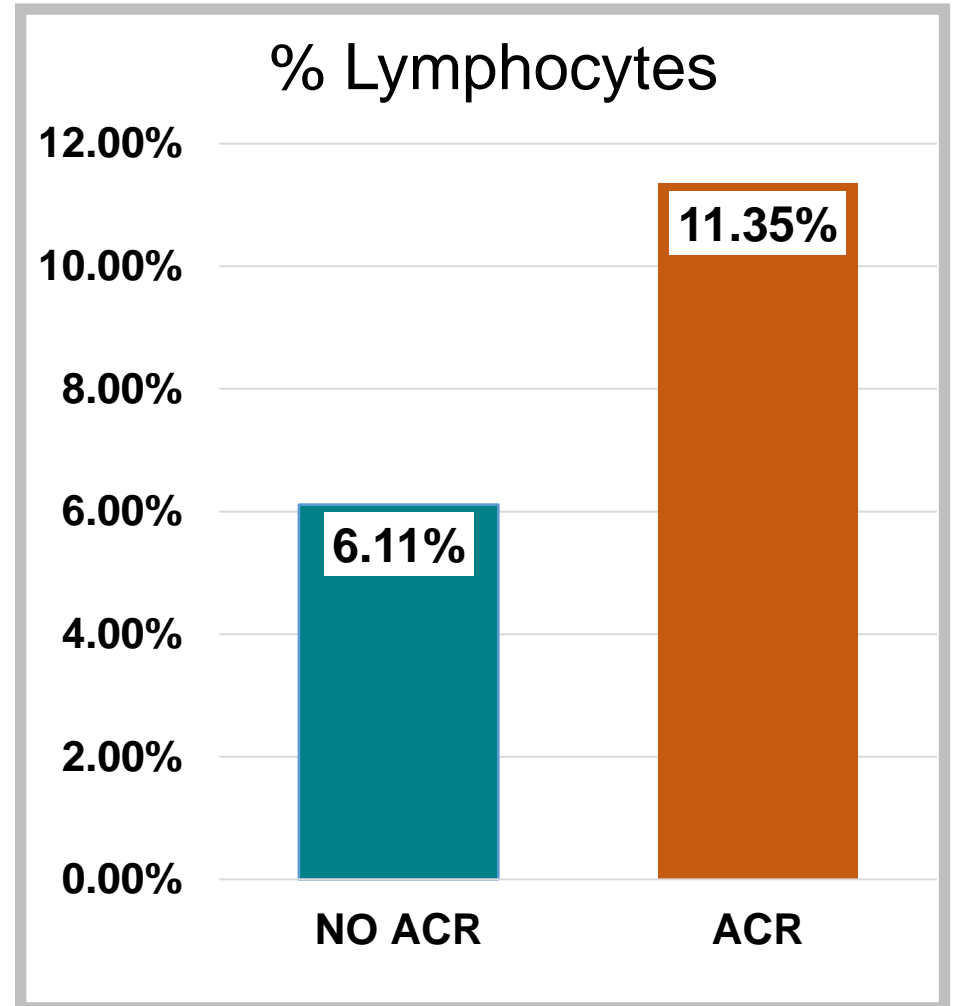


BIOMARCADORES EN LAVADO BRONCOALVEOLAR (BAL): Rechazo agudo

- 887 biopsias transbronquiales (29% rechazo agudo)
- 362 pacientes con Tx Pulmonar

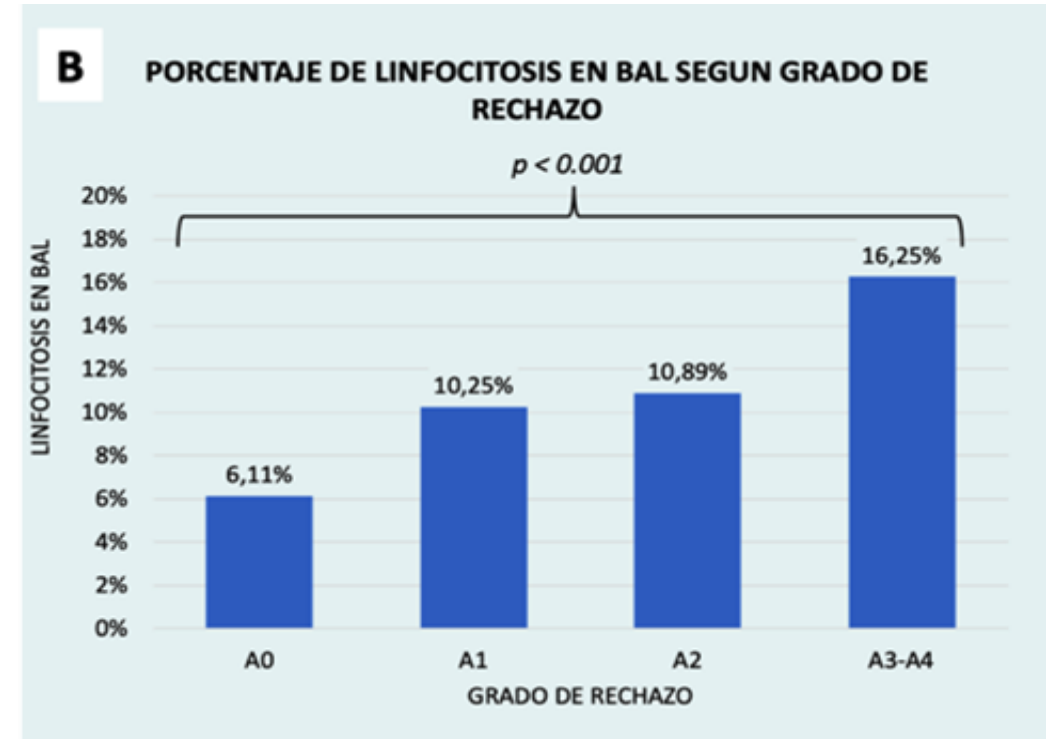
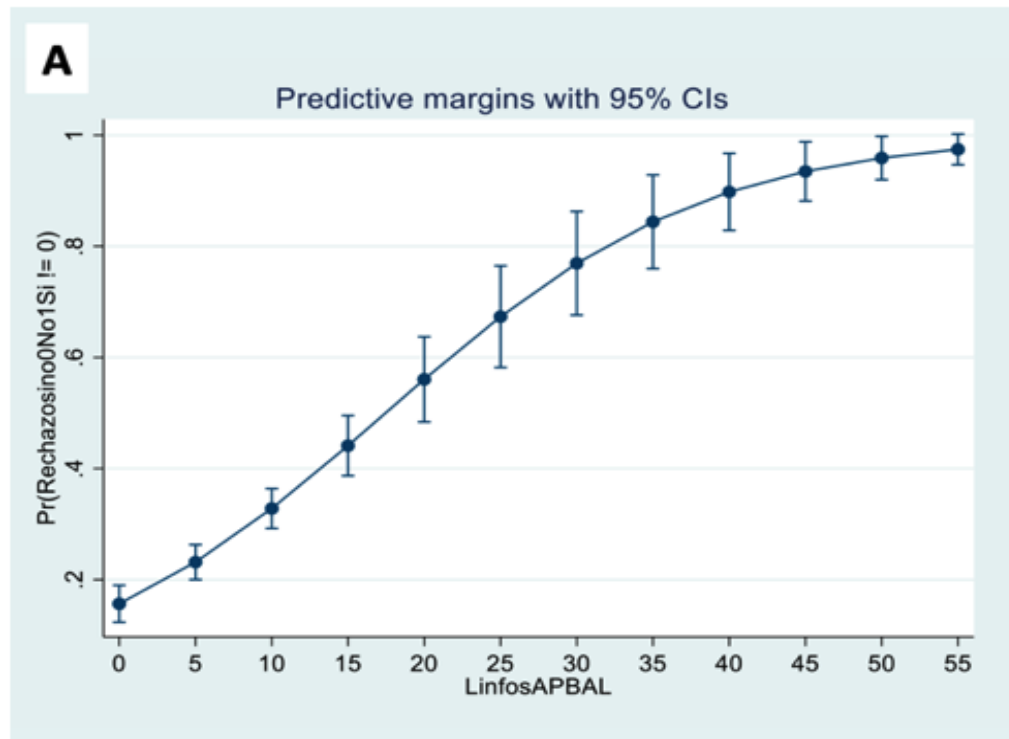
TBB	Total (N = 887)	No ACR (n = 628; 70.8%)	ACR (n = 259; 29.2%)	p
Differential cell count in BALF				
% Neutrophils	9.04 ± 13.08	7.48 ± 11.04	12.90 ± 16.49	p=.106
% Lymphocytes	7.64 ± 7.38	6.11 ± 5.83	11.35 ± 9.25	p<.001
% Macrophages	82.92 ± 16.71	85.94 ± 14.26	75.49 ± 19.73	p=.107
% Eosinophils	0.36 ± 2.12	0.31 ± 1.97	0.48 ± 2.44	p=.311

ACR: acute cellular rejection; CF: cystic fibrosis; COPD: chronic obstructive pulmonary disease; DILD: diffuse interstitial lung disease; IPF: idiopathic pulmonary fibrosis; TBB: transbronchial biopsy; BE: bronchiectasis; BALF: bronchoalveolar lavage fluid.





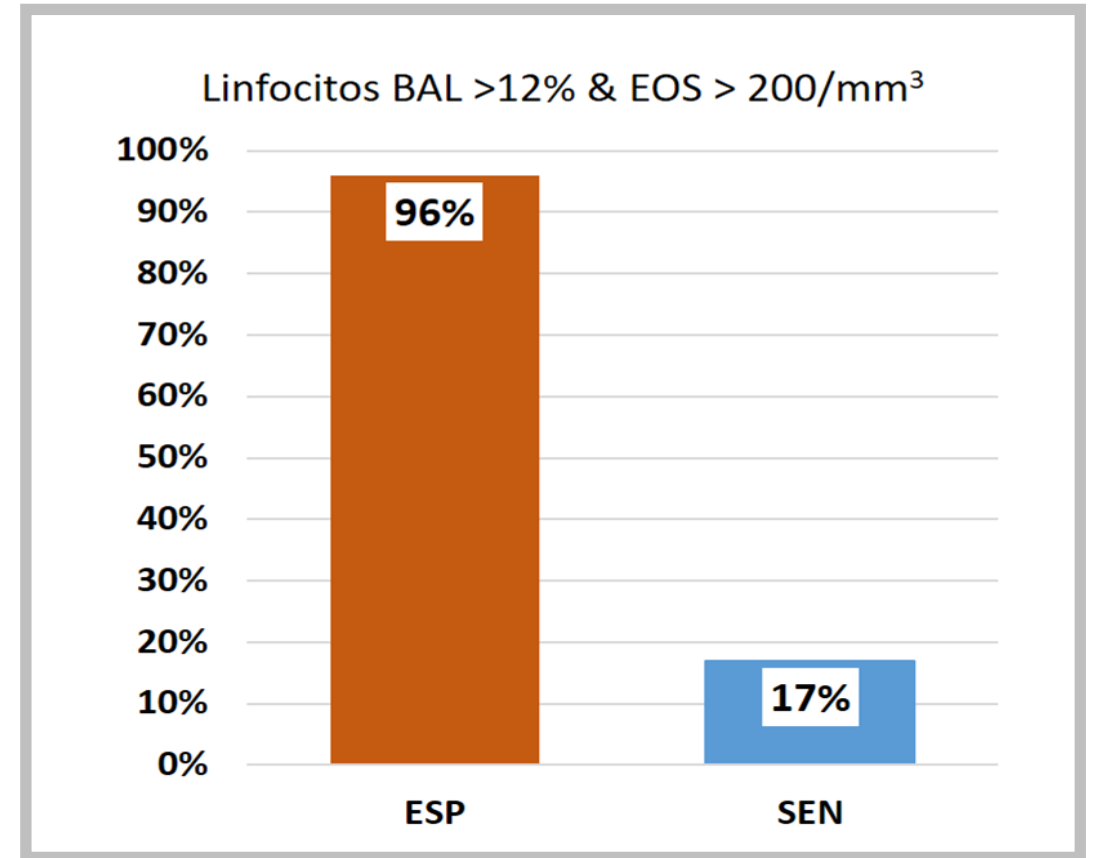
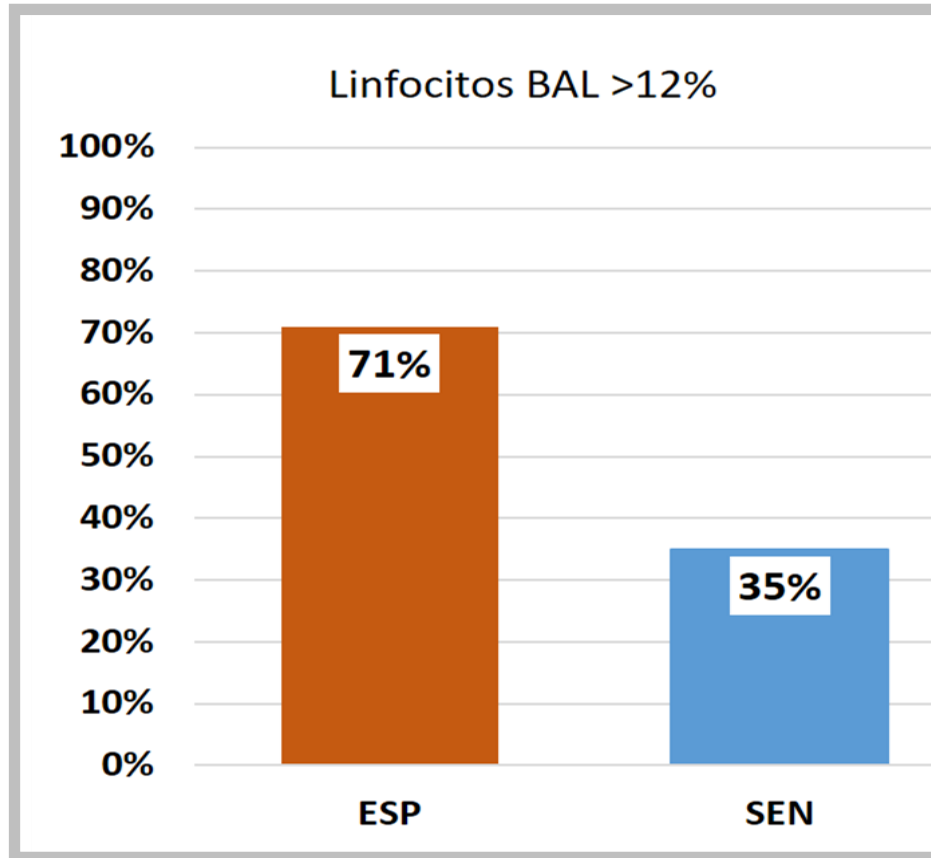
BIOMARCADORES EN LAVADO BRONCOALVEOLAR (BAL): Rechazo agudo



A mayor porcentaje de linfocitos, mayor riesgo de presentar ACR ((OR 1.10 IC 95% 1.080-1.131)



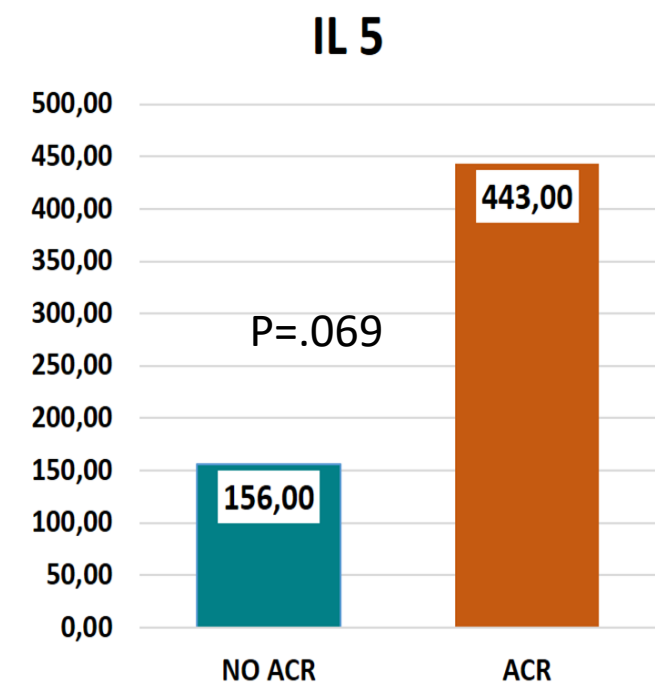
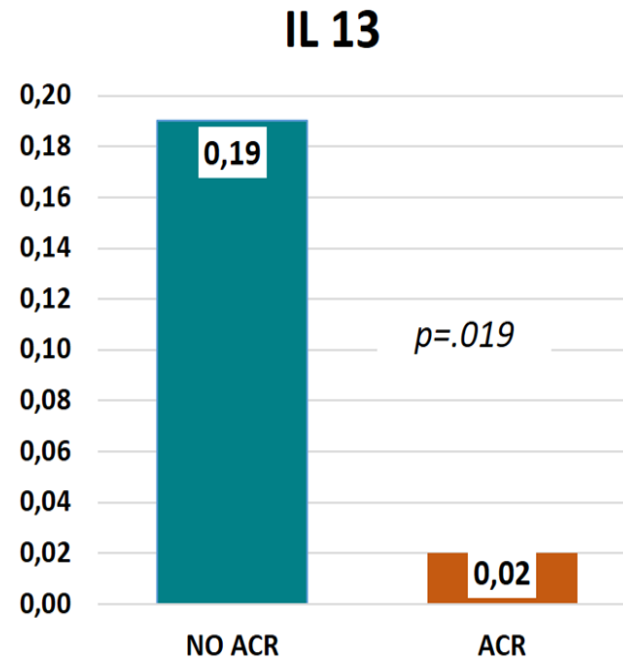
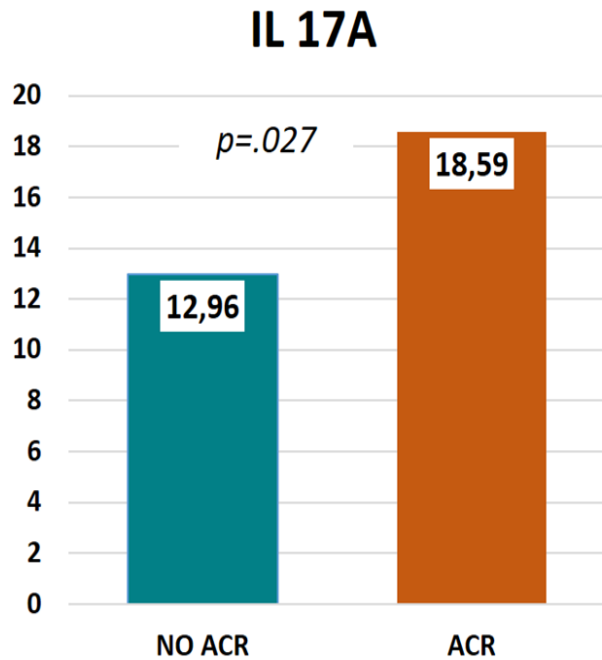
BIOMARCADORES EN LAVADO BRONCOALVEOLAR (BAL): Rechazo agudo





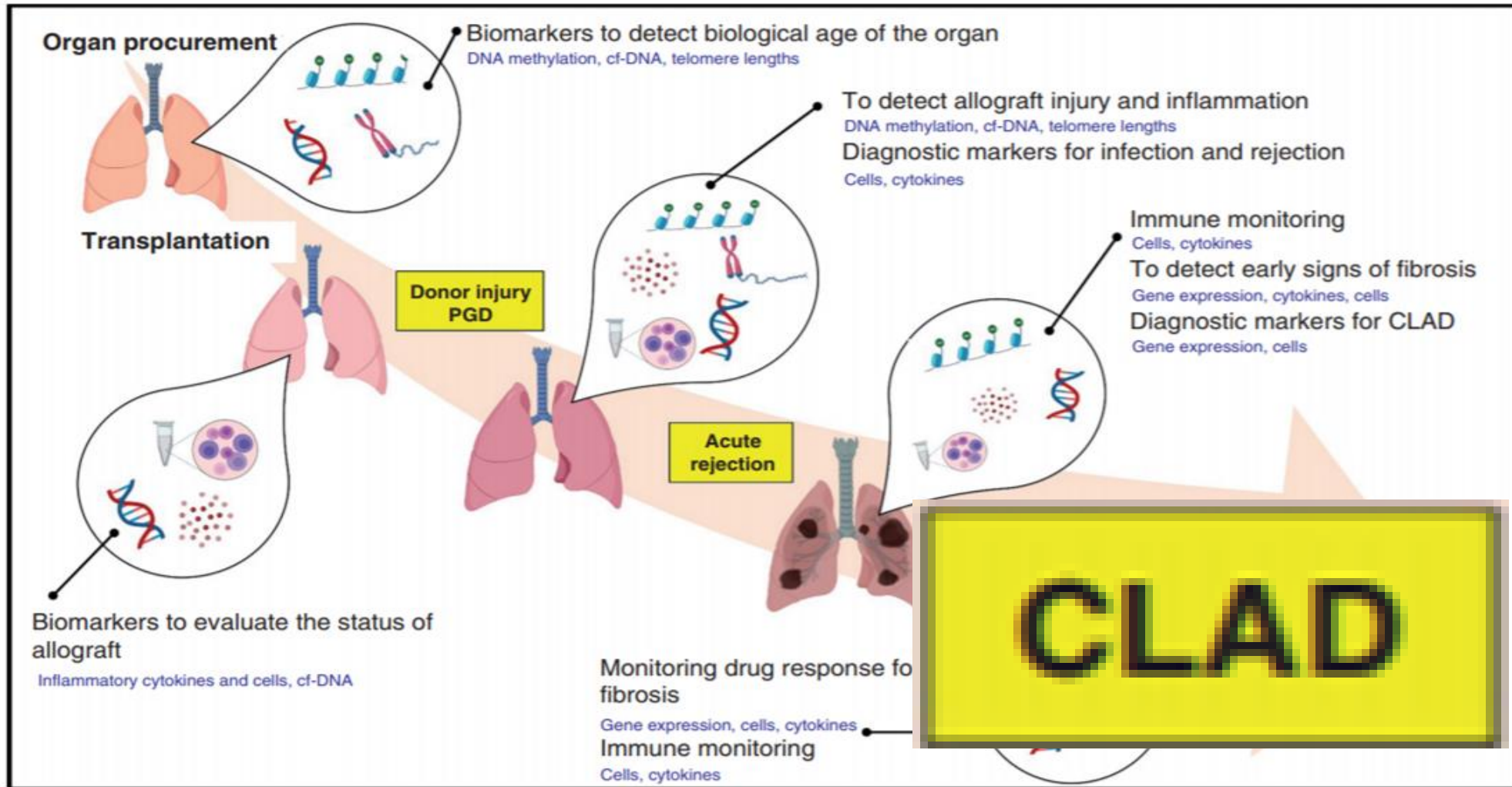
BIOMARCADORES EN LAVADO BRONCOALVEOLAR (BAL): Rechazo agudo

	Total (N = 108)	No ACR (n = 628; 70.8%)	ACR (n = 259; 29.2%)	<i>p</i>
IL 17A (pg/ml)	15.92 ± 12.55	12.96 ± 7.96	18.59 ± 15.17	<i>p</i> =.027
IL-13 (pg/ml)	0.10 ± 0.37	0.19 ± 0.51	0.02 ± 0.11	<i>p</i> =.019
IL-5 (fentogr/ml)	306.98 ± 775.04	156.18 ± 205.83	443.00 ± 1037.02	<i>p</i> =.069



Markers of rejection of a lung allograft: state of the art

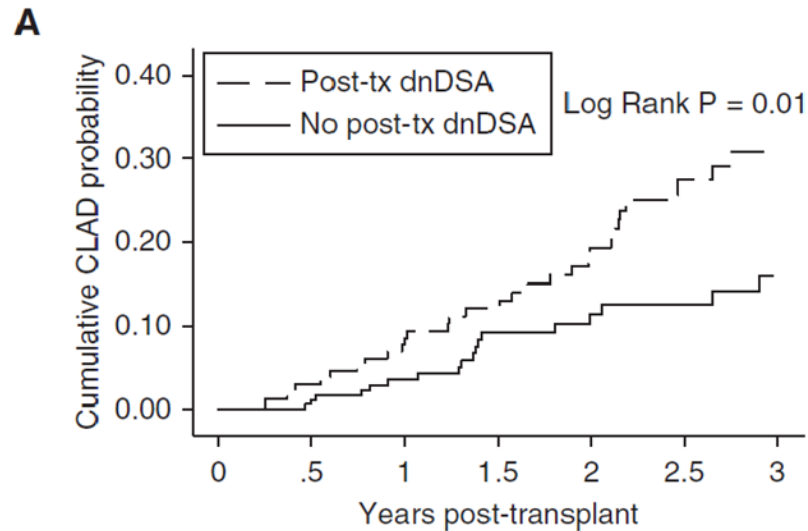
Tharushi de Silva^{1,2}  Joanne Voisev¹  Peter Hopkins^{2,3} Simon Ante^{2,3}  Daniel



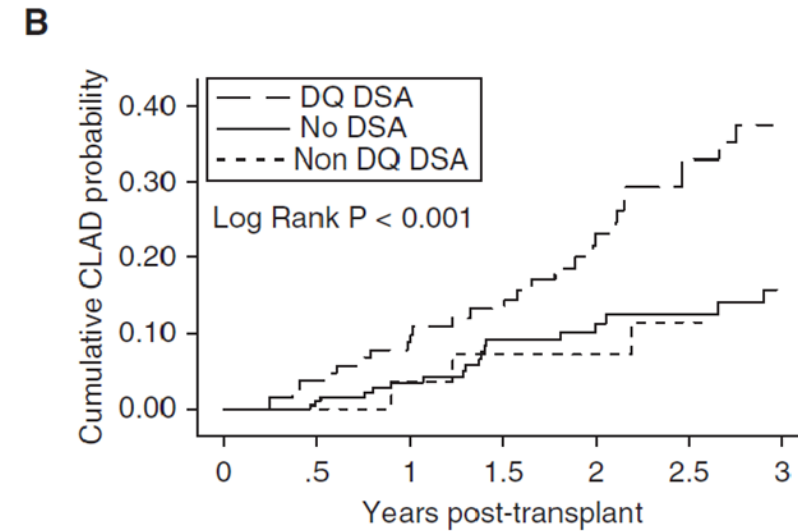
De Novo DQ Donor-Specific Antibodies Are Associated with Chronic Lung Allograft Dysfunction after Lung Transplantation

Jussi M. Tikkanen¹, Lianne G. Singer¹, S. Joseph Kim², Yanhong Li², Matthew Binnie¹, Cecilia Chaparro¹, Chung-Wai Chow¹, Tereza Martinu¹, Sassan Azad¹, Shaf Keshavjee¹, and Kathryn Tinckam^{2,3}

¹Toronto Lung Transplant Program, ²Division of Nephrology, Department of Medicine, and ³HLA Laboratory, Laboratory Medicine



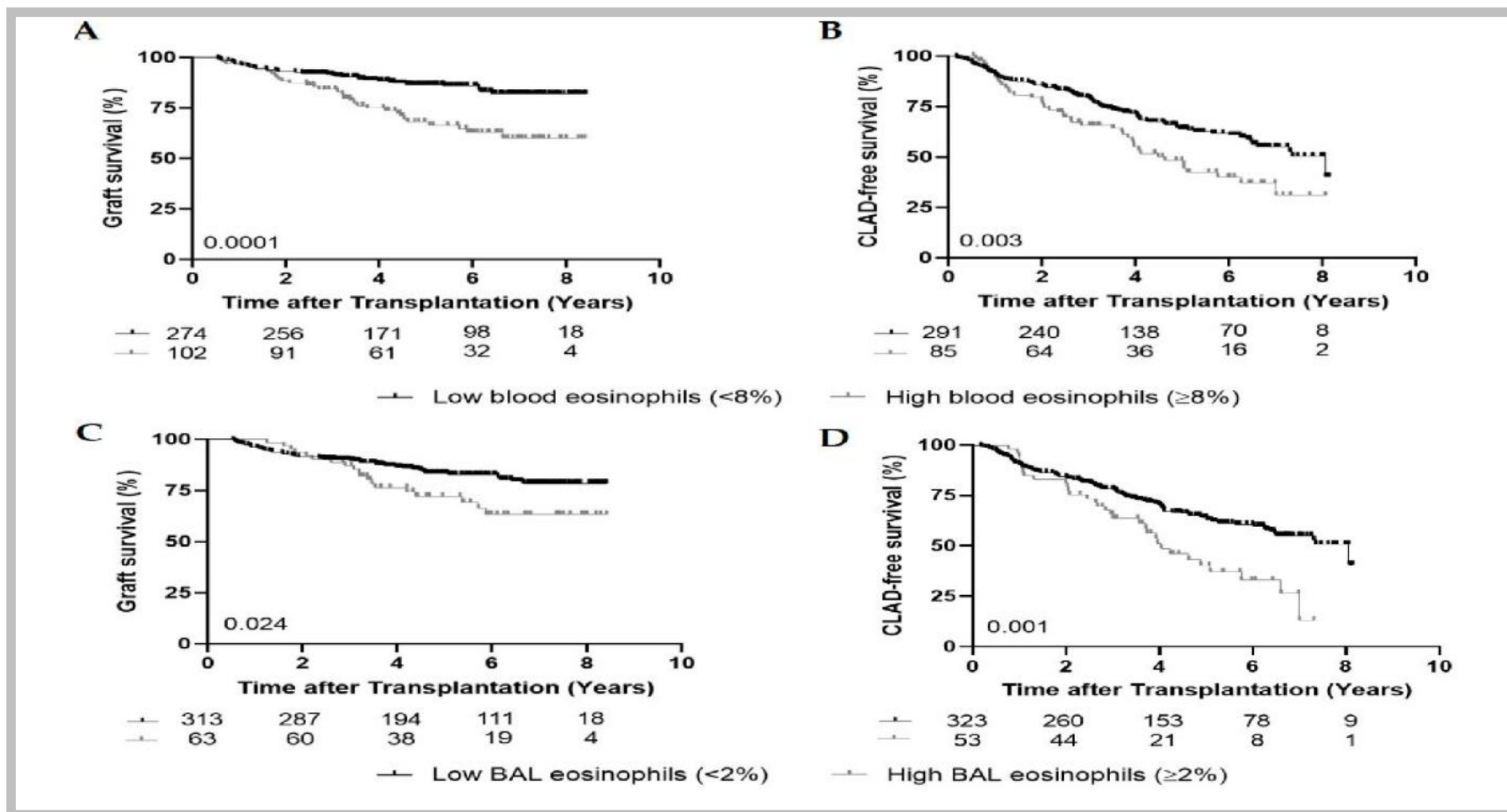
Number at risk		0	.5	1	1.5	2	2.5	3
Post-tx dnDSA		0	114	112	95	73	57	36
No post-tx dnDSA		340	196	134	97	75	57	45



Number at risk		0	.5	1	1.5	2	2.5	3
DQ DSA		0	89	86	72	50	37	22
No DSA		340	196	134	97	75	57	45
Non DQ DSA		0	25	26	23	23	20	14

Peripheral Blood Eosinophilia Is Associated with Poor Outcome Post-Lung Transplantation

Janne Kaes ¹ , Elise Van der Borgh ¹, Arno Vanstapel ^{1,2}, Anke Van Herck ^{1,3},

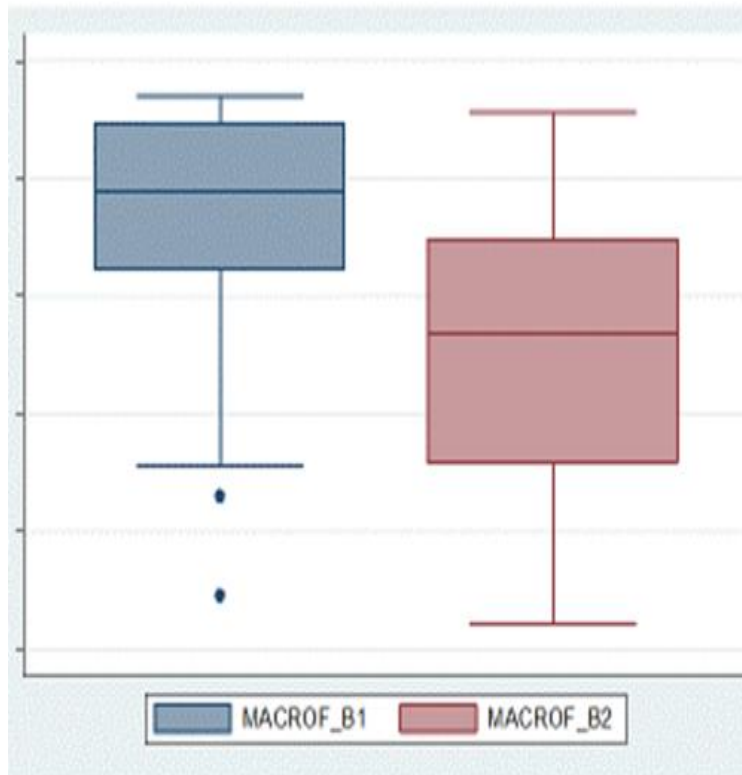




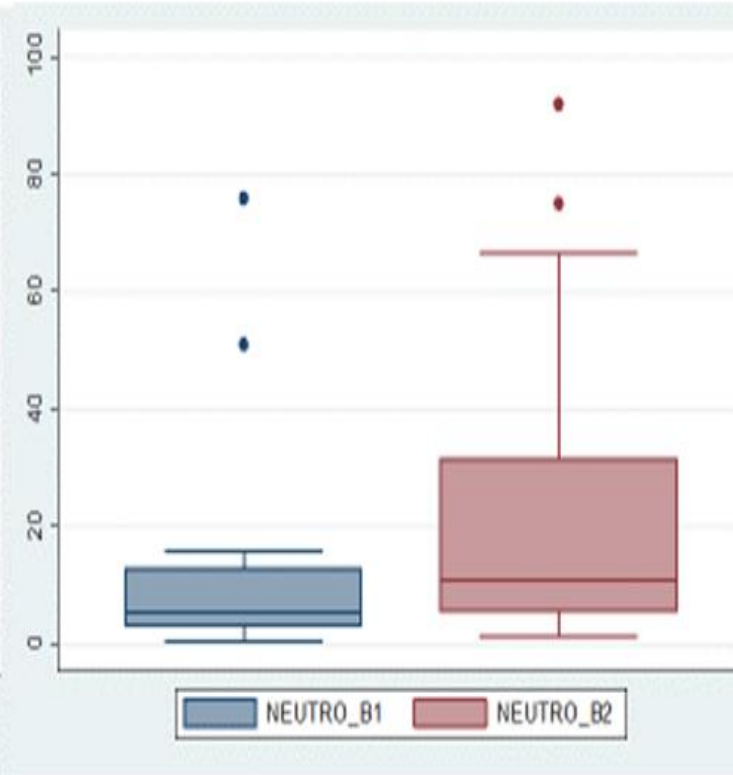
BIOMARCADORES EN LAVADO BRONCOALVEOLAR (BAL): Rechazo crónico

(n= 27 pacientes con BOS)

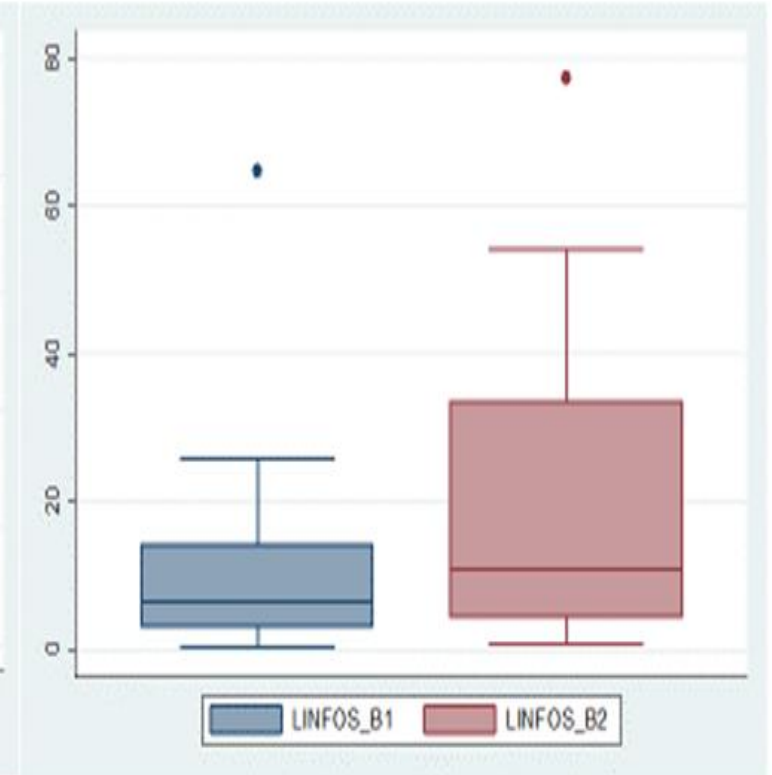
MACROFAGOS



NEUTROFILOS



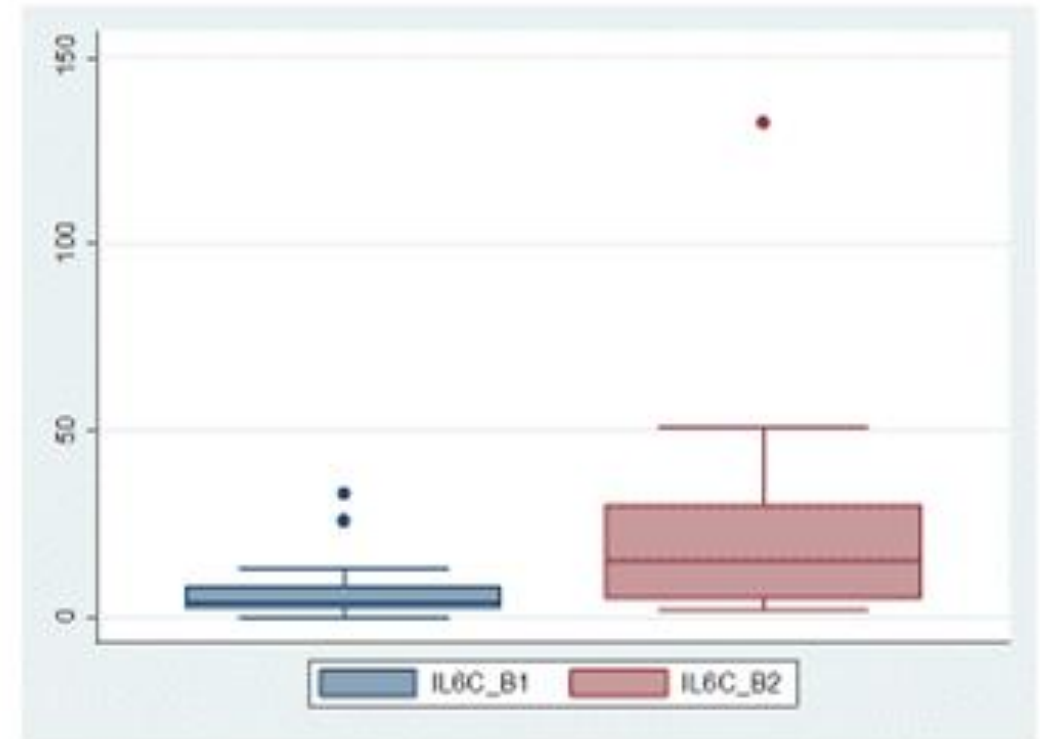
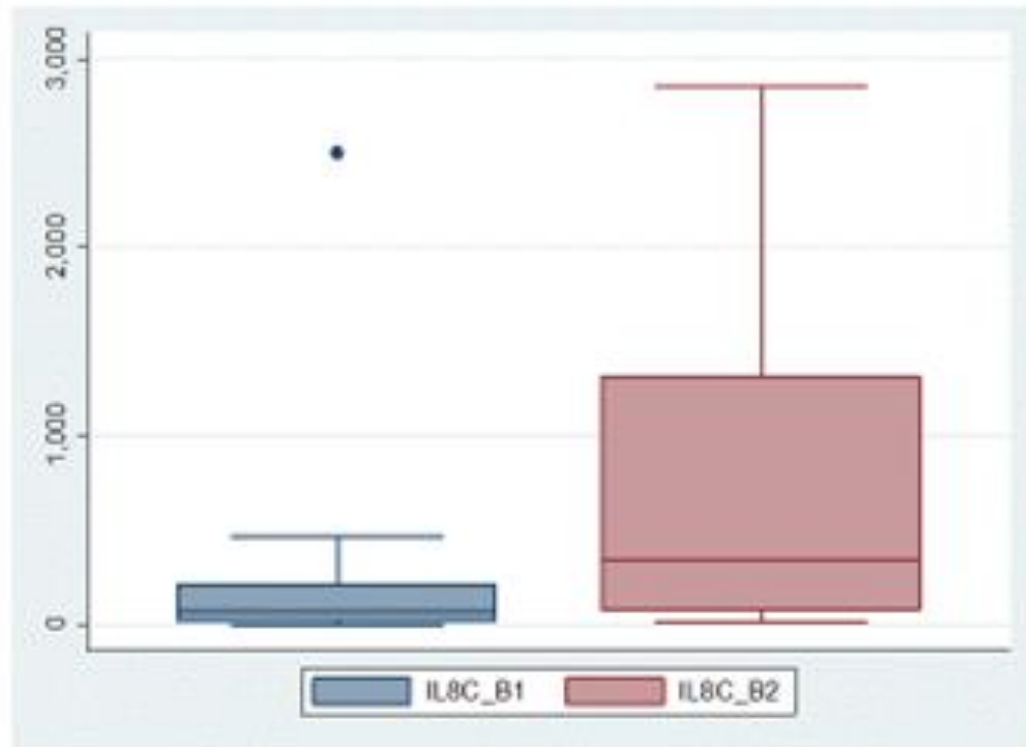
LINFOCITOS





BIOMARCADORES EN LAVADO BRONCOALVEOLAR (BAL): Rechazo crónico

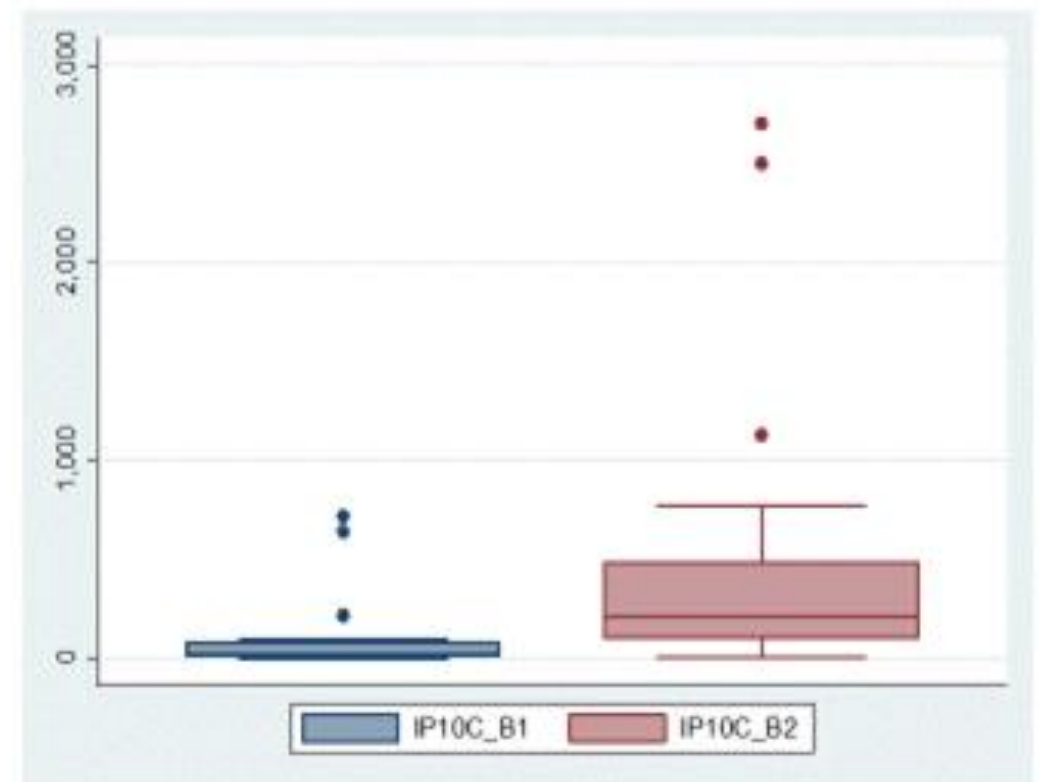
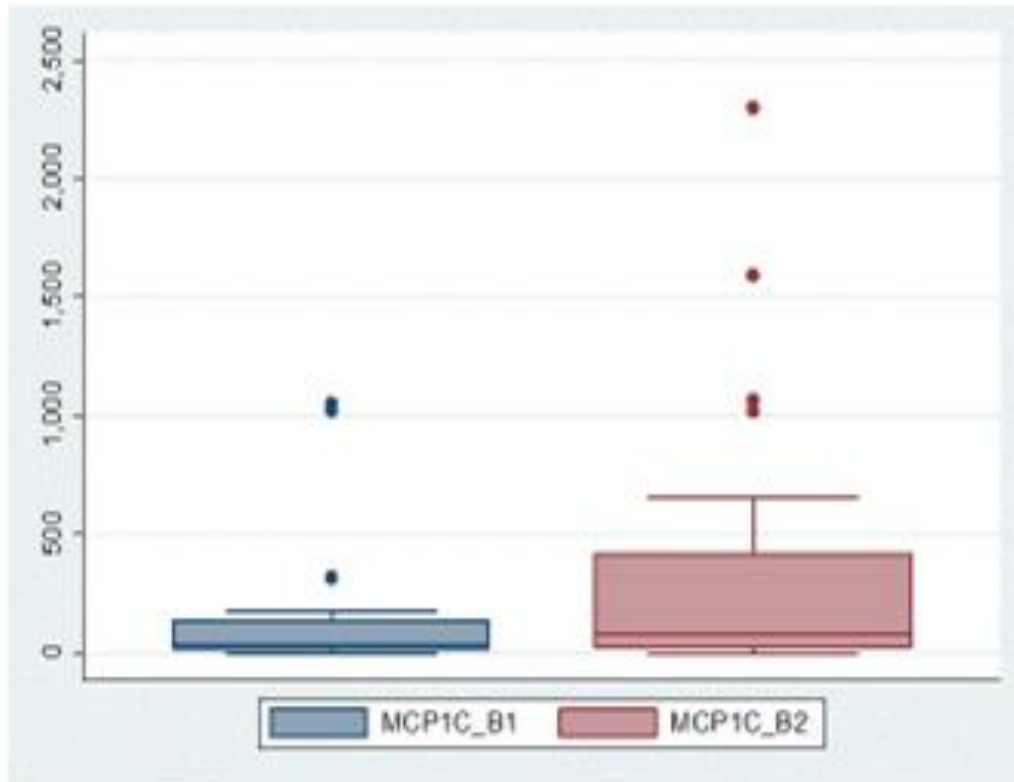
(n= 27 pacientes con BOS)





BIOMARCADORES EN LAVADO BRONCOALVEOLAR (BAL): Rechazo crónico

(n= 27 pacientes con BOS)



Biomarcadores de disfunción del injerto en el trasplante pulmonar

