BIOPSIA DEL IMPLANTE RENAL: ¿TIENE VALOR PRONÓSTICO?

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REVIEWS

Clinical role of the renal transplant biopsy

Winfred W. Williams, Diana Taheri, Nina Tolkoff-Rubin and Robert B. Colvin

Abstract | Percutaneous needle core biopsy is the definitive procedure by which essential diagnostic and prognostic information on acute and chronic renal allograft dysfunction is obtained. The diagnostic value of the information so obtained has endured for over three decades and has proven crucially important in shaping strategies for therapeutic intervention. This Review provides a broad outline of the utility of performing kidney graft biopsies after transplantation, highlighting the relevance of biopsy findings in the immediate and early post-transplant period (from days to weeks after implantation), the first post-transplant year, and the late period (beyond the first year). We focus on how biopsy findings change over time, and the wide variety of pathological features that characterize the major clinical diagnoses facing the clinician. This article also includes a discussion of acute cellular and humoral rejection, the toxic effects of calcineurin inhibitors, and the widely varying etiologies and characteristics of chronic lesions. Emerging technologies based on gene expression analyses and proteomics, the *in situ* detection of functionally relevant molecules, and new bioinformatic approaches that hold the promise of improving diagnostic precision and developing new, refined molecular pathways for therapeutic intervention are also presented.

Williams, W. W. *et al. Nat. Rev. Nephrol.* **8**, 110–121 (2012); published online 10 January 2012; doi:10.1038/nrneph.2011.213

http://www.senefro.org

artículo especial

Recomendaciones para la indicación, obtención, procesamiento y evaluación de biopsias en el trasplante renal

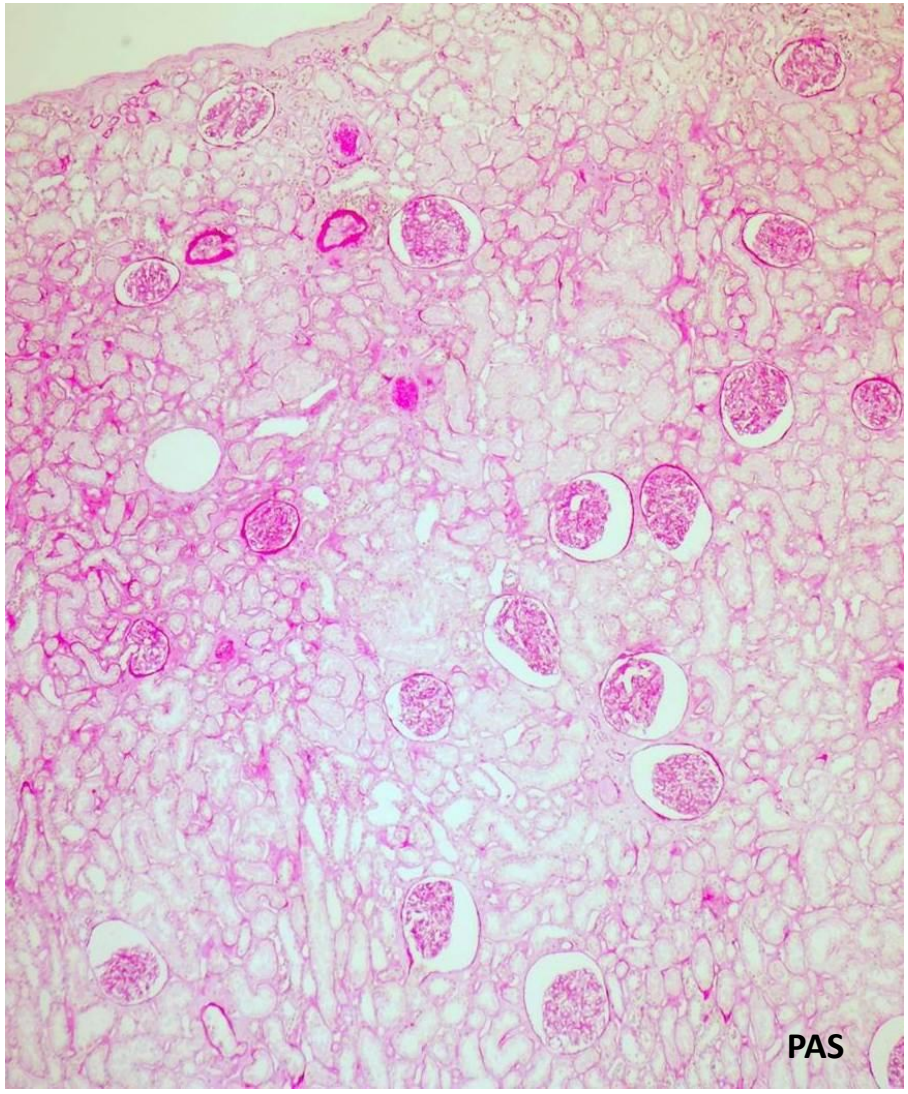
D. Serón[1*], F. Anaya[2], R. Marcén[3], R. García del Moral[4], E. Vázquez Martul[5], A. Alarcón[6], A. Andrés[7], D. Burgos[8], L. Capdevila[9], M. González Molina[8], C. Jiménez[10], J. M. Morales[7], F. Oppenheimer[11], L. Pallardó[12] y A. Sánchez Fructuoso[13]

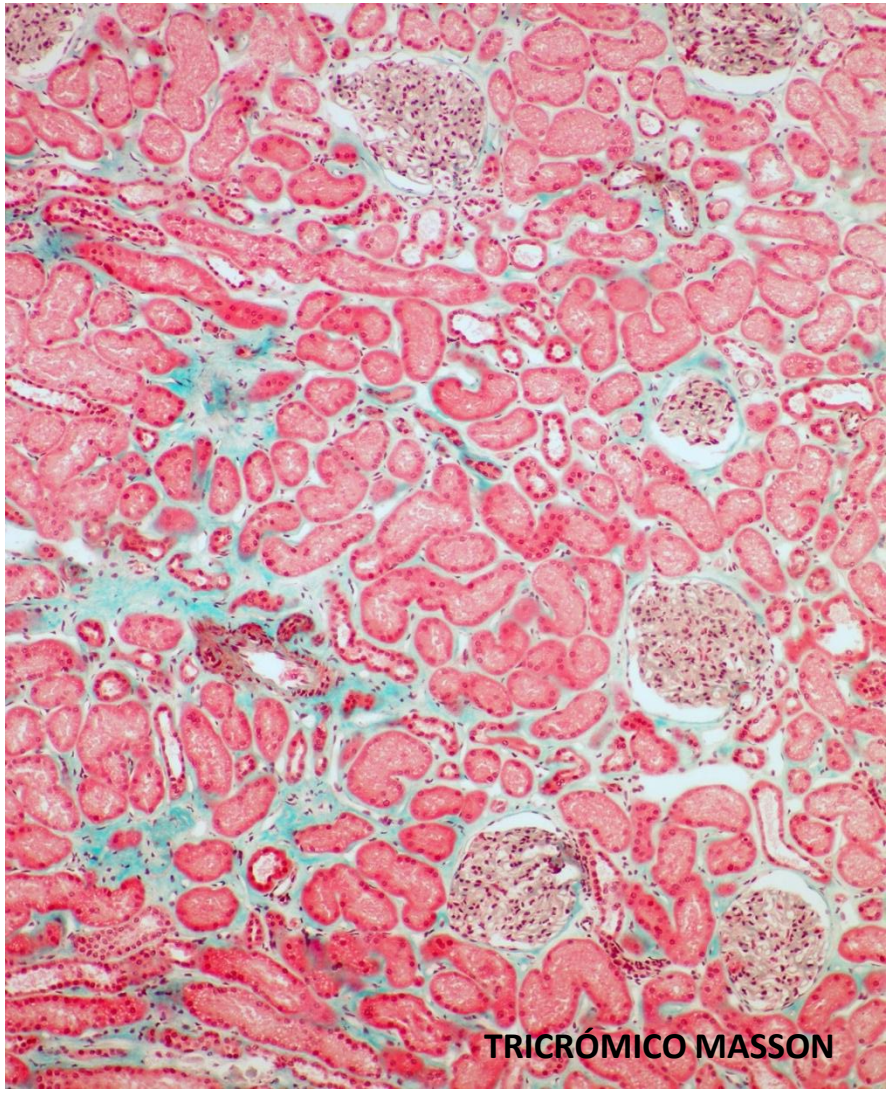
[1]Hospital Universitari de Bellvitge. Barcelona. [2]Hospital Gregorio Marañón. Madrid. [3]Hospital Ramón y Cajal. Madrid. [4]Hospital Universitario de Granada. Granada. [5]Complejo Hospitalario Universitario Juan Canalejo. A Coruña. [6]Hospital Universitario Son Dureta. Palma de Mallorca. [7]Hospital 12 de Octubre. Madrid. [8]Hospital Regional Universitario Carlos Haya. Málaga. [9]Hospital de la Vall d'Hebron. Barcelona. [10]Hospital Universitario La Paz. Madrid. [11]Hospital Clínic. Barcelona. [12]Hospital Doctor Peset. Valencia. [13]Hospital Clínico San Carlos. Madrid.

Nefrología 2008; 28 **(4)** 385-396

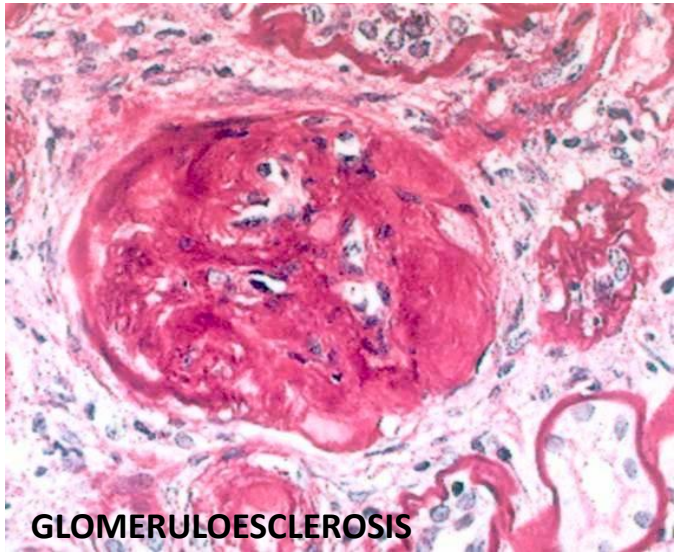
¿TIENE VALOR PREDICTIVO PRONÓSTICO LA BIOPSIA DEL RIÑÓN DEL DONANTE?

BIOPSIA DE RIÑÓN DE DONANTE

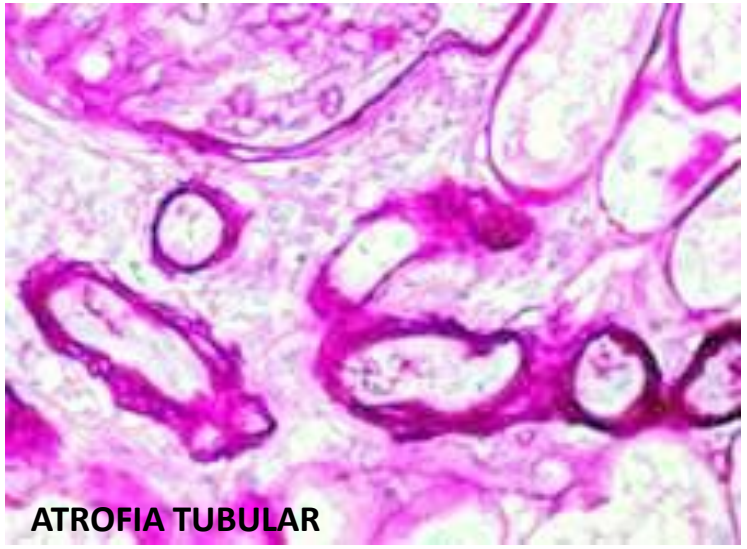




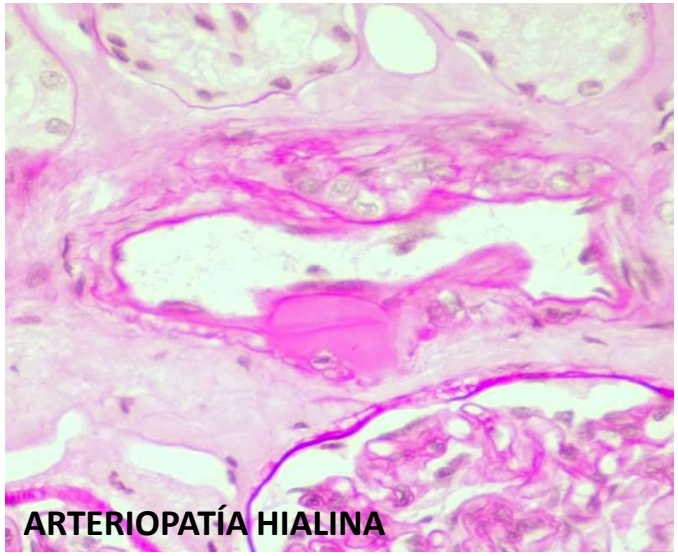
BIOPSIA DE RIÑÓN DE DONANTE



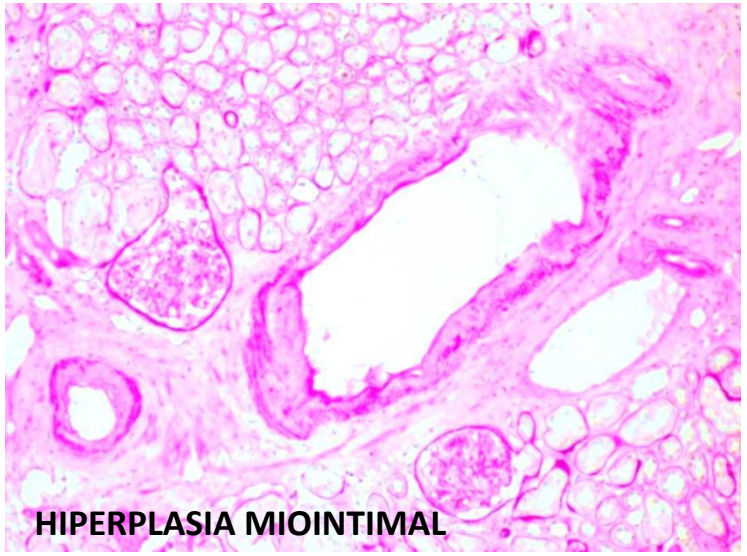
GLOMERULOESCLEROSIS



ATROFIA TUBULAR



ARTERIOPATÍA HIALINA



HIPERPLASIA MIOINTIMAL

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Long-Term Outcome of Renal Transplantation from Older Donors

Giuseppe Remuzzi, M.D., Paolo Cravedi, M.D., Annalisa Perna, Stat.Sci.D., Borislav D. Dimitrov, M.D., M.Sc., Marta Turturro, Biol.Sci.D., Giuseppe Locatelli, M.D., Paolo Rigotti, M.D., Nicola Baldan, M.D., Marco Beatini, M.D., Umberto Valente, M.D., Mario Scalamogna, M.D., and Piero Ruggenenti, M.D., for the Dual Kidney Transplant Group*

N Engl J Med 2006;354:343-52.

Remuzzi et al (2006): *Long-term outcome of renal transplantation from older donors. N Eng J Med. 2006; 35:343-52*

GLOMÉRULOS ESCLEROSADOS:
(0) Ausencia
(1) No definido
(2) No definido
(3) + de 50%

LESIONES VASCULARES:
(0) Ausencia
(1) Leve
(2) Moderada
(3) Intensa (grosor pared≥diam. luz)

ATROFIA TUBULAR:
(0) Ausencia
(1) <25% túbulos corticales
(2) 26-50%
(3) >50%

FIBROSIS INTERSTICIAL:
(0) Ausencia o <5% del área cortical
(1) 6-25%.
(2) (2) 26-50%
(3) >50%

GLOBAL KIDNEY SCORE: 0-12

0-3: TRASPLANTE ÚNICO

4-6: TRASPLANTE DOBLE

7 O MÁS: ÓRGANOS DESCARTADOS

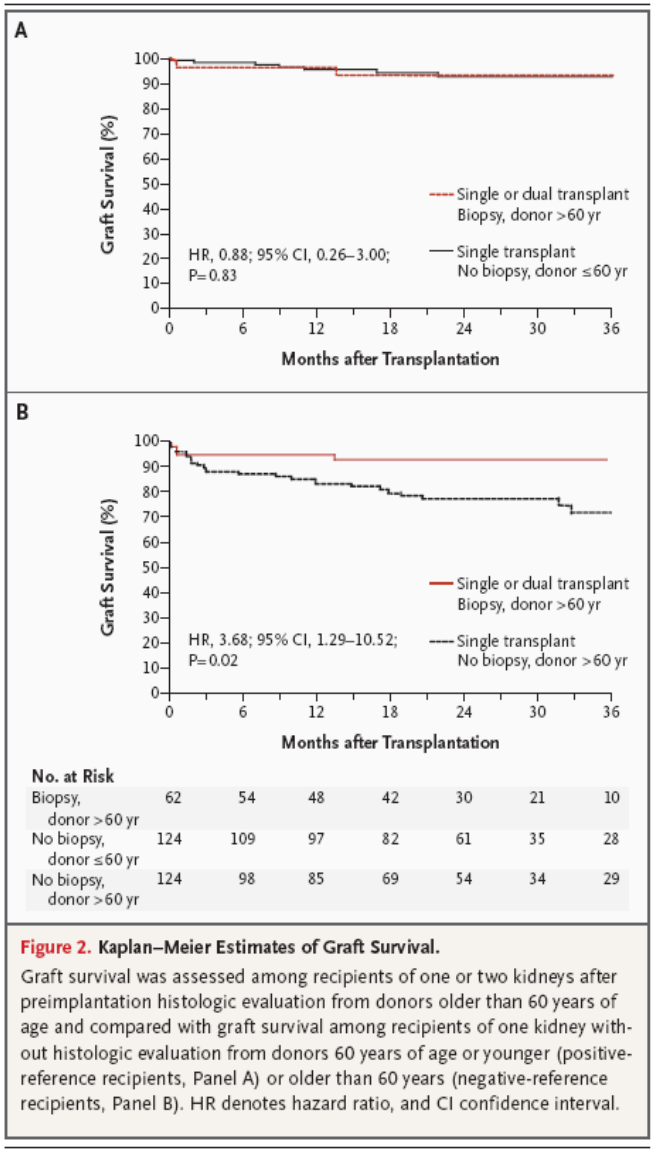


Figure 2. Kaplan–Meier Estimates of Graft Survival.

Graft survival was assessed among recipients of one or two kidneys after preimplantation histologic evaluation from donors older than 60 years of age and compared with graft survival among recipients of one kidney without histologic evaluation from donors 60 years of age or younger (positive-reference recipients, Panel A) or older than 60 years (negative-reference recipients, Panel B). HR denotes hazard ratio, and CI confidence interval.

Remuzzi et al (2006): *Long-term outcome of renal transplantation from older donors. N Eng J Med. 2006; 35:343-52*

ANTES DE REMUZZI ET AL (2006):

1. *Gaber LW, Moore LW, Alloway RR, Amiri MH, Vera SR, Gaber AO. Glomerulosclerosis as a determinant of posttransplant function of older donor renal allografts. Transplantation. 1995 Aug 27;60(4):334-9.*
2. *Remuzzi G, Grinyò J, Ruggenenti P, et al. Early experience with dual kidney transplantation in adults using expanded donor criteria. Double Kidney Transplant Group (DKG). J Am Soc Nephrol. 1999 Dec;10(12):2591-8.*
3. *Pokorná E, Vítko S, Chadimová M, Schück O, Ekberg H. Proportion of glomerulosclerosis in procurement wedge renal biopsy cannot alone discriminate for acceptance of marginal donors. Transplantation. 2000 Jan 15;69(1):36-43.*
4. *Randhawa PS, Minervini MI, Lombardero M, et al. Biopsy of marginal donor kidneys: correlation of histologic findings with graft dysfunction. Transplantation. 2000 Apr 15;69(7):1352-7.*
5. *Protocolo Andaluz de Biopsia Renal de Donante (2003)*

http://www.senefro.org

artículo especial

Recomendaciones para la indicación, obtención, procesamiento y evaluación de biopsias en el trasplante renal

D. Serón[1*], F. Anaya[2], R. Marcén[3], R. García del Moral[4], E. Vázquez Martul[5], A. Alarcón[6], A. Andrés[7], D. Burgos[8], L. Capdevila[9], M. González Molina[8], C. Jiménez[10], J. M. Morales[7], F. Oppenheimer[11], L. Pallardó[12] y A. Sánchez Fructuoso[13]

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Nefrología 2008; 28 **(4)** 385-396

La biopsia del implante renal: tiene valor pronóstico? RGM

Tabla II. Modelo propuesto para el estudio de las biopsias del donante en la Comunidad Autónoma de Andalucía (en revisión)[66]

1. Glomérulos esclerosados o con atrofia total por quistificación

0: Ausencia.
1: 0-10%.
2: 11-20.
3: Más del 20%.

Nota: La afectación subcapsular exclusiva no debe ser considerada como condición excluyente del órgano a no ser que esté asociada a patología relevante vascular, tubular del parénquima subyacente.

2. Arteriolopatía hialina

0: Ausencia de engrosamiento hialino Pas (+) de las paredes arteriolares.
1: De leve a moderado engrosamiento hialino Pas (+) en al menos una arteriola.
2: De moderado a intenso engrosamiento hialino Pas (+) en más de una arteriola.
3: Intenso engrosamiento hialino Pas (+) en la mayoría de las arteriolas.

3. Engrosamiento fibroso de la íntima vascular

0: Ausencia de lesiones vasculares crónicas.
1: Menos del 25% de estrechamiento de la luz vascular por engrosamiento miointimal.
2: Incremento de las lesiones descritas en 1 afectando entre el 26-50% de la luz vascular.
3: Incremento de las lesiones descritas en 2 afectando a más del 50% de la luz vascular.

4. Atrofia tubular

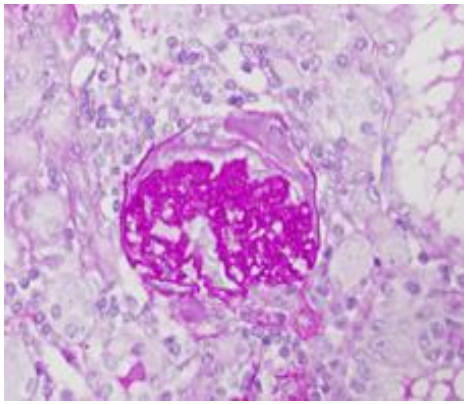
0: Ausencia de atrofia tubular cortical.
1: Menos del 25% de túbulos corticales atróficos.
2: 26%-50% de túbulos corticales atróficos.
3: Más del 50% de túbulos corticales atróficos.

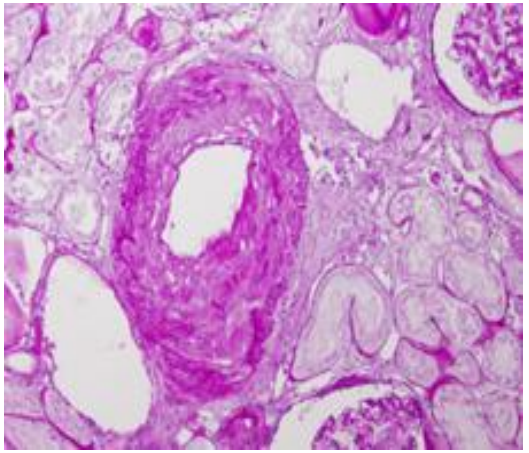
5. Fibrosis intersticial

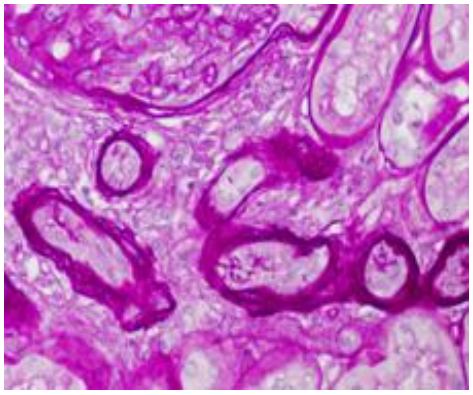
0: 5% o menos del área cortical afectada.
1: 6%-25% del área cortical afectada.
2: 26%-50% del área cortical afectada.
3: Más del 50% del área cortical afectada.

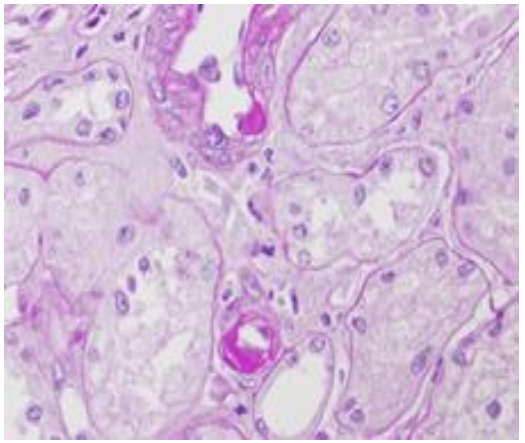
Valoración de la puntuación total:

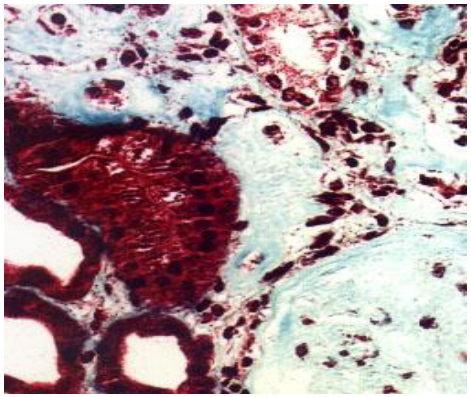
Muestra renal con histología favorable si la puntuación es ≤ 7.



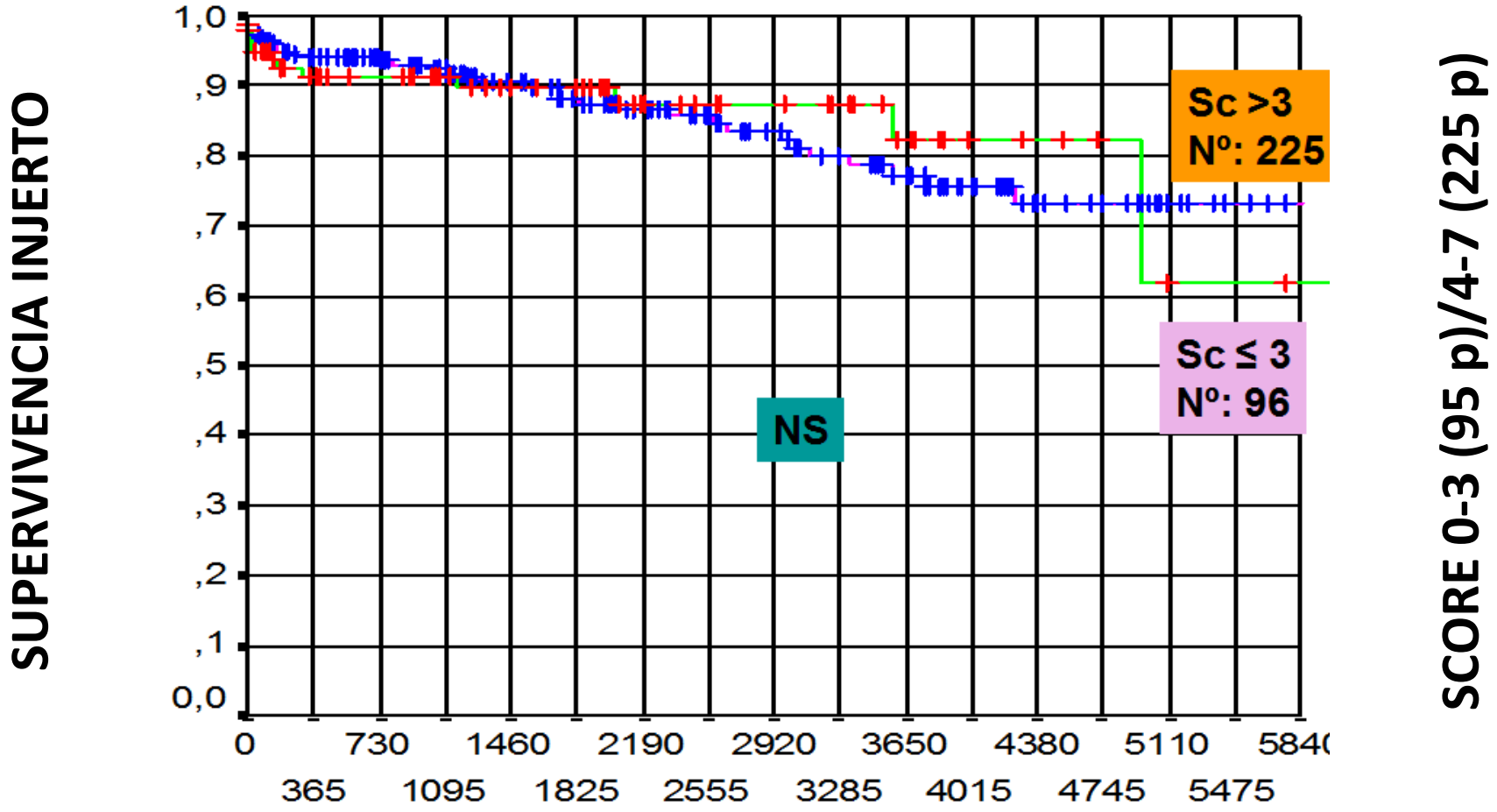








RESULTADOS BIOPSIA DONANTE EN GRANADA 1997-2014 (n = 320 PACIENTES)



RESULTADOS BIOPSIA DONANTE EN GRANADA 1997-2014 (n = 320 PACIENTES)

a. La causa más frecuente de éxitus de donante en esta serie es el ACV.
b. Las lesiones histológicas por orden de frecuencias han sido:
   - ✓ Atrofia tubular: 78,5%
   - ✓ Elastosis intimal: 70,5%
   - ✓ Esclerosis glomerular: 68,5%
   - ✓ Fibrosis intersticial: 66,7%
   - ✓ NTA : 16,8%
c. La biopsia renal no interviene en la evolución a largo plazo del injerto, probablemente por descartar órganos potencialmente válidos para receptores añosos (28,6% de riñones rechazados en Granada frente a 23,3% en el resto de Andalucía).
d. Aquellos órganos que tienen un sc ≤ 3 tienen mejor FG al año.
e. La inexistencia de esclerosis glomerular, atrofia tubular, y arteriolopatía hialina en el donante definen un mejor FG al año.

http://www.kidney-international.org clinical investigation

see commentary on page 1016

The reproducibility and predictive value on outcome of renal biopsies from expanded criteria donors

M. Antonieta Azancot[1], Francesc Moreso[1], Maite Salcedo[2], Carme Cantarell[1], Manel Perello[1], Irina B. Torres[1], Angeles Montero[2], Enric Trilla[3], Joana Sellarés[1], Joan Morote[3] and Daniel Seron[1]

[1]Department of Nephrology, Hospital Universitari Vall d'Hebron, Universitat Autònoma Barcelona, Barcelona, Spain; [2]Department of Pathology, Hospital Universitari Vall d'Hebron, Universitat Autònoma Barcelona, Barcelona, Spain and [3]Department of Urology, Hospital Universitari Vall d'Hebron, Universitat Autònoma Barcelona, Barcelona, Spain

Reproducibility and predictive value on outcome are the main criteria to evaluate the utility of histological scores. Here we analyze the reproducibility of donor biopsy assessment by different on-call pathologists and the retrospective evaluation by a single renal pathologist blinded to clinical outcomes. We also evaluate the predictive value on graft outcome of both evaluations. A biopsy was performed in donors with any of the following: age ⩾55 years, hypertension, diabetes, creatinine >1.5 mg/dl, or stroke. Glomerulosclerosis, interstitial fibrosis, tubular atrophy, intimal thickening, and arteriolar hyalinosis evaluated according to the Banff criteria were added to obtain a chronic score. Biopsies were classified as mild (⩾3), intermediate (4–5), or advanced (6–7) damage, and unacceptable (⩾8) for transplantation of 127 kidneys biopsied. Weighted κ value between both readings was 0.41 (95% CI: 0.28–0.54). Evaluation of biopsies by the renal pathologist was significantly and independently associated with estimated 12-month glomerular filtration rate and a significant composite outcome variable, including death-censored graft survival and time to reach an estimated glomerular filtration rate <30 ml/min per 1.73 m^2. Thus, there was no association between readings of on-call pathologists and outcome. The lack of association between histological scores obtained by the on-call pathologists and graft outcome suggests that a specific training on renal pathology is recommended to optimize the use of kidneys retrieved from expanded criteria donors.

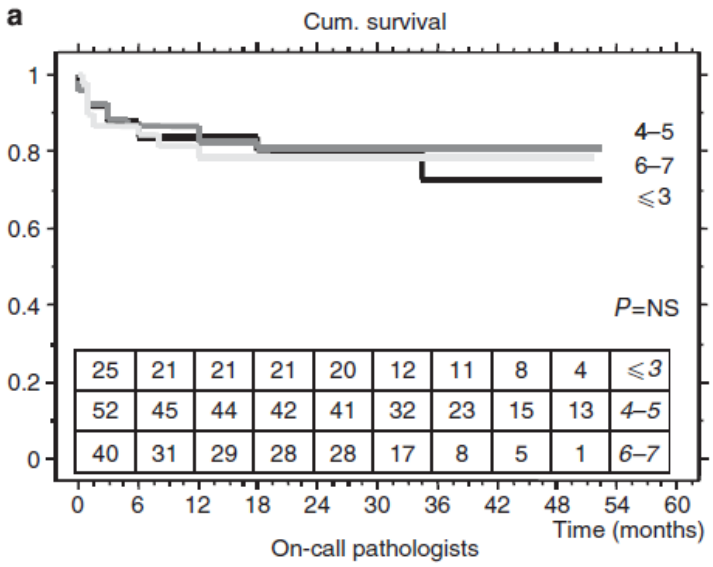
Kidney International (2014) **85,** 1161–1168; doi:10.1038/ki.2013.461; published online 27 November 2013

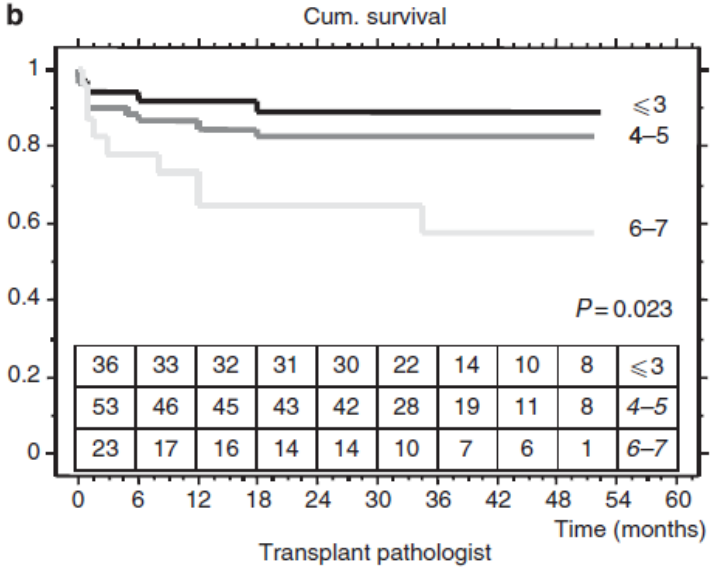
KEYWORDS: donor pre-implantation biopsies; expanded criteria donors; kidney transplantation

Renal transplantation is the best available treatment option for patients with end-stage renal disease as it offers a longer survival and a better quality of life at a lower cost than dialysis.[1,2] Despite the sustained effort to increase the number of kidneys retrieved from deceased and living donors, the number of patients in the waiting list is still growing.[3,4]

A steady increase in donor age has been paralleled by a rising number of discarded kidneys for transplantation.[3,5] Different policies have been proposed to safely transplant kidney from aged donors or donors with comorbidities, the so called expanded criteria donors (ECDs),[6] as they offer a survival benefit in comparison to patients who remain on the waiting list.[7,8] These kidneys are usually offered to aged recipients in order to match kidney and patient survival expectancies according to an old-for-old policy.[9,10] Sophisticated statistical models evaluating donor and recipient characteristics have been proposed to better estimate risk for graft failure based on clinical data, but these proposals have not been widely used.[11–13] Instead, many centers evaluate donor biopsies to assess the risk of graft failure.[14] The consideration of histological information to decide the acceptance of a kidney for transplantation is based on different reports showing that donor histological damage is associated with renal function and graft survival.[15–19] In many centers, the decision to accept or discard a kidney on a daily basis practice relies on the histological evaluation by different on-call pathologists. Interobserver variability in the evaluation of biopsies is an important issue as it may influence grading of histological lesions and consequently affect the final diagnosis and clinical decisions.[20]

At our center, we perform donor biopsies as a standard





LOS PATÓLOGOS DE GUARDIA DE TRASPLANTE Y LOS NEFROPATÓLOGOS ESTÁN: ¿IMPLICADOS O INVOLUCRADOS?

DESPUÉS DE REMUZZI ET AL (2006):

1. ***De Vusser K, Lerut E, Kuypers D, et al. The predictive value of kidney allograft baseline biopsies for long-term graft survival. J Am Soc Nephrol. 2013 Nov;24(11):1913-23.***

2. ***Hofer J, Regele H, Böhmig GA, et al. Pre-implant biopsy predicts outcome of single-kidney transplantation independent of clinical donor variables. Transplantation. 2014 Feb 27;97(4):426-32.***

3. ***Índice MAPI para evaluación de biopsias pretrasplante***

4. ***Protocolo Español de Consenso para Biopsia del Donante (2014)***

5. ***Índice clínico KDPI para donantes con criterios expandidos***

American Journal of Transplantation 2008; 8: 2316–2324
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2008.02370.x

The Maryland Aggregate Pathology Index: A Deceased Donor Kidney Biopsy Scoring System for Predicting Graft Failure

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[a]*Division of Transplantation, Department of Surgery,* [b]*Department of Pathology,* [c]*VA Maryland Health Care System and Department of Epidemiology and Preventive Medicine,* [d]*Division of Nephrology, Department of Medicine,* [e]*Department of Pharmacy, School of Medicine, University of Maryland, Baltimore, MD*
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Introduction

The resulting severe shortage of organs for transplantation has led to continuous efforts to expand the kidney donor pool (1). One strategy has been to incorporate the use of nonideal donor kidneys that may have been considered unusable in earlier times (2–10). Biopsy of deceased donor kidneys before transplantation is commonly practiced, especially in clinical situations where histologic abnormalities are deemed likely. In the United States about 75% of kidneys from expanded criteria donors (ECD) are biopsied and 41% of these ECDs in turn discarded secondary to pathological parameters (11). Biopsy is indicated for assessment of kidneys from elderly, hypertensive or

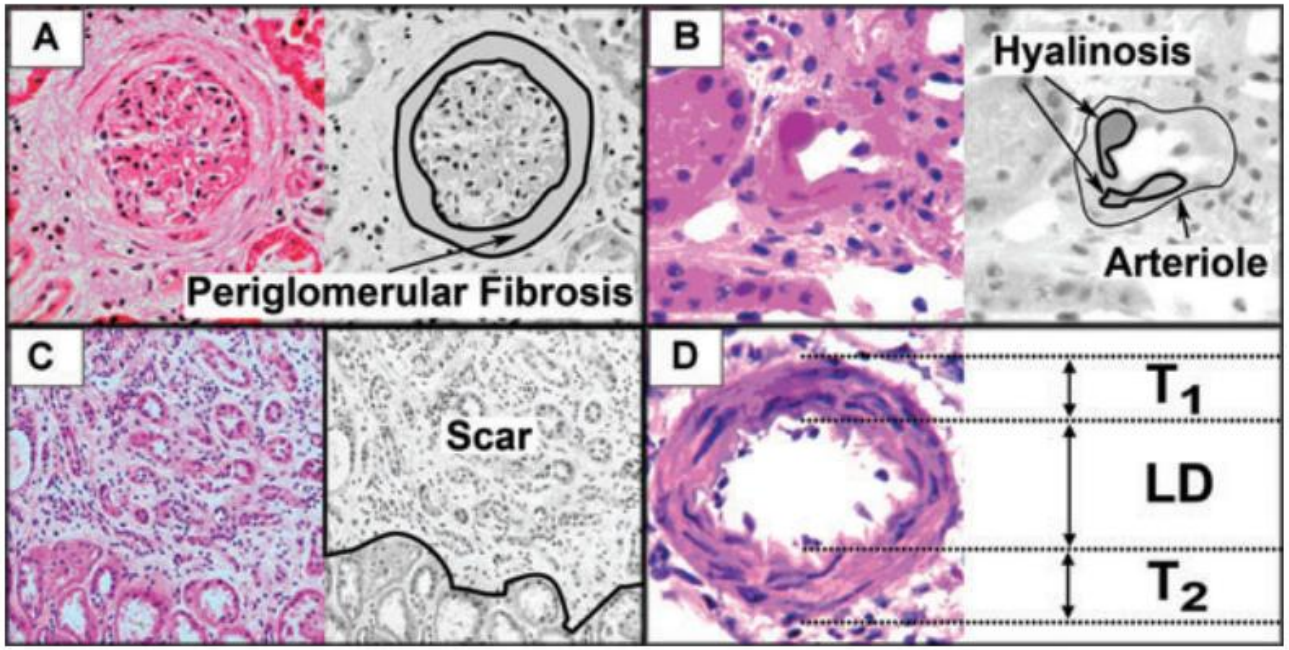
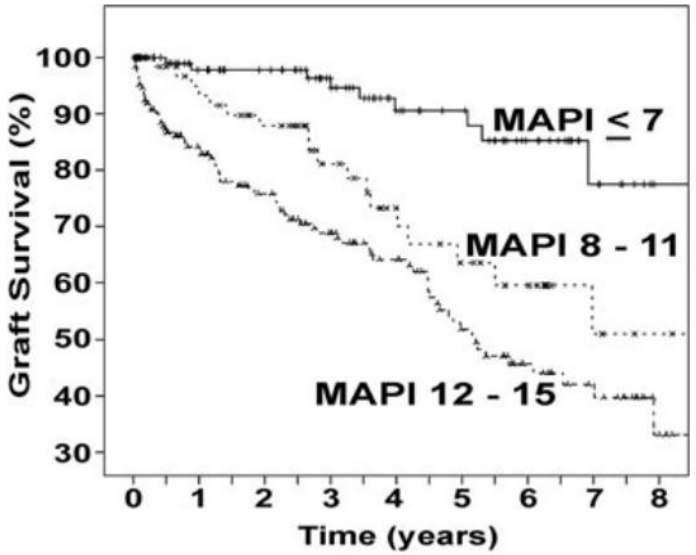


Figure 1: Pathologic features used in MAPI as seen on frozen section preparations. (A) Periglomerular fibrosis, (B) arteriolar hyalinosis, (C) scar including features of interstitial fibrosis, tubular atrophy and glomerulosclerosis, and (D) measurements for arterial wall-to-lumen ratio (WLR) calculation, including the thickness of two opposing walls (T_1 and T_2) and the luminal diameter (LD). $WLR = (T_1 + T_2)/LD$.

Table 1 | MAPI assessment of donor kidney biopsy samples

Contributors to graft loss	Threshold	Points if present
Arteriolar hyalinosis	Any	4
Periglomerular fibrosis	Any	4
Fibrosis, tubular atrophy and/or scar	Affecting ≥10 tubules	3
Glomerulosclerosis	15.0%	2
Interlobular artery wall to lumen ratio	0.5	2

Points for each feature are added together, resulting in a MAPI score of 0–15 points. Abbreviation: MAPI, Maryland aggregate pathology index. Permission obtained from John Wiley and Sons © Munivenkatappa, R. B. *et al. Am. J. Transplant.* **8**, 2316–2324 (2008).



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Article type : Original Article

Spanish consensus document for acceptance and rejection of kidneys from expanded criteria donors.

Lledó-García E[1], Riera L[1], Passas J[1], Paredes D[1], Morales JM[2], Sánchez-Escuredo A[2], Burgos-Revilla FJ[2], de Andrés Belmonte A[3], Oppenheimer F[3], Rodríguez-Ferrero ML[3], Solé M[4], Matesanz R[5], Valentín M[6], Pascual J[3].

Asociación Española de Urología (1)

Sociedad Española de Trasplantes (2)

Sociedad Española de Nefrología (3)

Sociedad Española de Anatomía Patológica (4)

Organización Nacional de Trasplantes (5)

Running head: Consensus in transplantation of kidneys from ECD

Enrique Lledó-García MD PhD

Table 3 : Histologic decision score

Glomerular sclerosis:

0: absence
1:1-10%
2: 11-20%
3: over 20%.

Hialine arteriopathy:

0 No
1 Mild
2 Moderate
3 Severe

Fibrous intimal thickening:

0 No
1 Mild
2 Moderate
3 Severe

Interstitial fibrosis / Tubular atrophy*

0 No
1 Mild
2 Moderate
3 Severe

- ***Consider the joint assessment or the more***
- ***severe of the two parameters***

0-4 – Mild lesions
5-6 – Moderate lesions
>6 – Severe lesions

CLINICAL AND TRANSLATIONAL RESEARCH

A Comprehensive Risk Quantification Score for Deceased Donor Kidneys: The Kidney Donor Risk Index

Panduranga S. Rao,[1,2,7] Douglas E. Schaubel,[2,3] Mary K. Guidinger,[2,4] Kenneth A. Andreoni,[5] Robert A. Wolfe,[2,4] Robert M. Merion,[2,6] Friedrich K. Port,[2,4] and Randall S. Sung[2,6]

Background. We propose a continuous kidney donor risk index (KDRI) for deceased donor kidneys, combining donor and transplant variables to quantify graft failure risk.

Methods. By using national data from 1995 to 2005, we analyzed 69,440 first-time, kidney-only, deceased donor adult transplants. Cox regression was used to model the risk of death or graft loss, based on donor and transplant factors, adjusting for recipient factors. The proposed KDRI includes 14 donor and transplant factors, each found to be independently associated with graft failure or death: donor age, race, history of hypertension, history of diabetes, serum creatinine, cerebrovascular cause of death, height, weight, donation after cardiac death, hepatitis C virus status, human leukocyte antigen-B and DR mismatch, cold ischemia time, and double or en bloc transplant. The KDRI reflects the rate of graft failure relative to that of a healthy 40-year-old donor.

Results. Transplants of kidneys in the highest KDRI quintile (>1.45) had an adjusted 5-year graft survival of 63%, compared with 82% and 79% in the two lowest KDRI quintiles (<0.79 and 0.79–<0.96, respectively). There is a considerable overlap in the KDRI distribution by expanded and nonexpanded criteria donor classification.

Conclusions. The graded impact of KDRI on graft outcome makes it a useful decision-making tool at the time of the deceased donor kidney offer.

Keywords: Deceased donor kidneys, Expanded criteria donors, Risk assessment modeling, Graft failure, Donor evaluation.

(*Transplantation* 2009;88: 231–236)

American Journal of Transplantation 2014; XX: 1–11
Wiley Periodicals Inc.

doi: 10.1111/ajt.12928

The Kidney Donor Profile Index (KDPI) of Marginal Donors Allocated by Standardized Pretransplant Donor Biopsy Assessment: Distribution and Association With Graft Outcomes

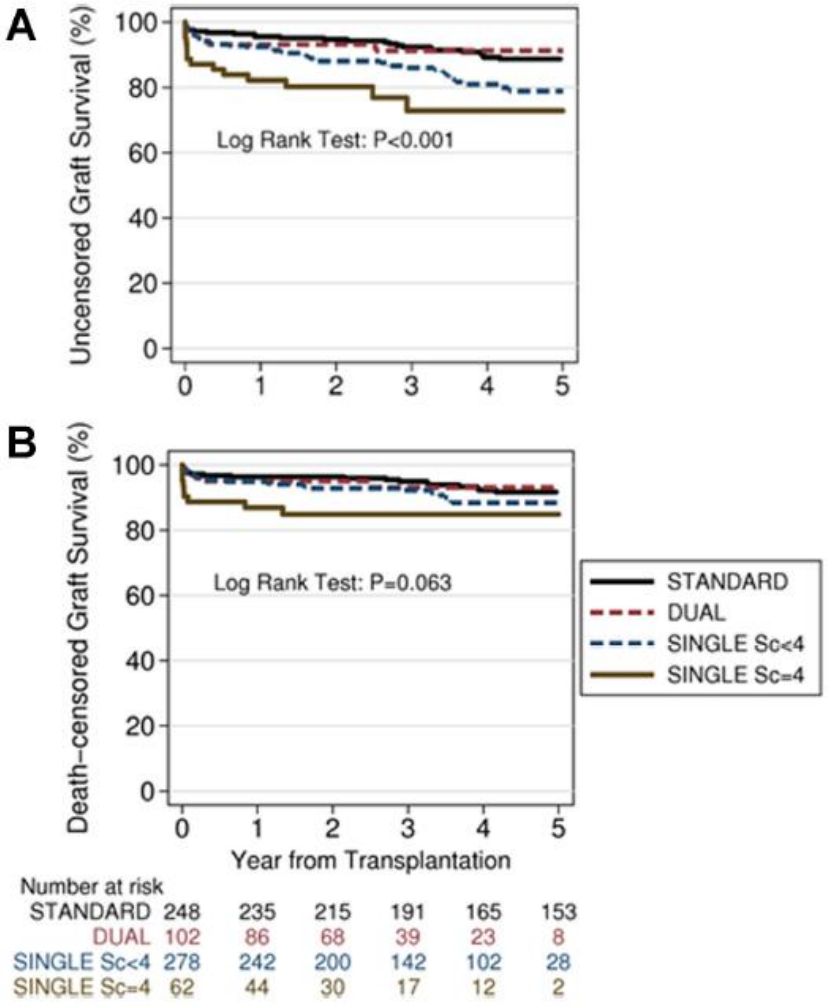
I. Gandolfini[1], C. Buzio[1], P. Zanelli[2], A. Palmisano[1], E. Cremaschi[1], A. Vaglio[1], G. Piotti[1], L. Melfa[1], G. La Manna[3], G. Feliciangeli[3], M. Cappuccilli[3], M. P. Scolari[3], I. Capelli[3], L. Panicali[3], O. Baraldi[3], S. Stefoni[3], A. Buscaroli[4], L. Ridolfi[5], A. D'Errico[6], G. Cappelli[7], D. Bonucchi[7], E. Rubbiani[7], A. Albertazzi[7], A. Mehrotra[8], P. Cravedi[8,†] and U. Maggiore[1,*,†]

led to a limited discard rate of 15% for kidneys with KDPI of 80–90 and of 37% for kidneys with a KDPI of 91–100. Although 1-year estimated GFRs were significantly lower in recipients of marginal kidneys (−9.3, −17.9 and −18.8 mL/min, for dual transplants, single kidneys with PTDB score <4 and =4, respectively; $p < 0.001$), graft survival (median follow-up 3.3 years) was similar between marginal and standard kidney transplants (hazard ratio: 1.20 [95% confidence interval: 0.80–1.79; $p = 0.38$]). In conclusion, PTDB-based allocation allows the safe transplantation of kidneys with KDPI in the highest range that may otherwise be discarded.

Table 1: Donor characteristics

			Marginal			
	All	STANDARD (no PTDB)	DUAL	SINGLE Sc. < 4	SINGLE Sc. = 4	p-Value
N	690	248	102	278	62	
Age, years	56.1 (16.7)	39.3 (13.0)	68.7(8.4)	64.0 (10.6)	65.8 (9.6)	<0.001[1,2,3,4]
Male gender, %	65.7	61.3	70.6	67.6	71.0	0.23
Diabetes, %	8.1	1.2	10.8	12.9	11.3	<0.001[1,2,3]
Hypertension, %	39.7	9.3	53.9	55.8	62.9	<0.001[1,2,3]
eCrCl, mL/min	89.1 (35.4)	112.4 (4.4)	71.9 (21.4)	78.0 (25.1)	73.9 (21.4)	<0.001[1,2,3]
eCrCL 30–59, %	16.6	3.2	28.3	22.8	22.9	<0.001[1,2,3]
eCrCL<30, %	0.4	1.2	0.0	0.0	0.0	0.27
eGFR, mL/min/1.73 m^2	95.4 (35.7)	107.0 (40.3)	87.4 (26.6)	89.9 (33.0)	85.1 (25.8)	<0.001[1,2,3]
eGFR 30–59, %	10.4	3.2	14.0	13.8	16.4	<0.001[1,2,3]
eGFR<30, %	1.0	1.6	0.0	1.1	0.0	0.71
CV death, %	63.5	43.6	79.2	73.7	61.3	<0.001[1,2]
Weight, kg	74.0 (13.4)	73.0 (15.1)	73.7 (13.3)	74.7 (12.5)	76.3 (11.3)	0.28
Height, cm	169.2 (9.0)	171.0 (10.1)	167.7 (8.0)	168.4 (8.3)	168.9 (8.5)	0.002[1,2]
BMI, kg/m^2	25.8 (4.1)	24.9 (4.5)	26.2 (4.0)	26.3 (3.8)	26.8 (3.5)	<0.001[1,2,3]
Obesity, %	9.0	7.7	9.0	11.1	6.6	0.52
CIT, hours	16.4 (5.5)	14.8 (6.4)	17.8 (4.1)	17.2 (5.0)	17.9 (5.0)	<0.001[1,2,3]
ECD donor, %	52.2	0.0	85.0	78.0	88.5	<0.001[1,2,3]
KDRI	1.32 (0.44)	0.86 (0.18)	1.70 (0.31)	1.53 (0.32)	1.57 (0.34)	<0.001[1,2,3,4]
KDPI	66.6 (29.6)	35.0 (19.2)	89.3 (9.9)	82.6 (15.1)	83.9 (15.2)	<0.001[1,2,3,4]
KDPI 80–90, %	16.5	0.0	10.6	25.7	32.8	<0.001[1,2,3]
KDPI 91–100, %	29.7	0.0	66.0	41.8	39.3	<0.001[1,2,3,4,5]

CIT, cold ischemia time; CV death, cerebrovascular death; DUAL, dual kidney transplant; ECD, expanded criteria donor; eGFR, estimated GFR (MDRD formula); eCrCl, estimated creatinine clearance (Cockroft-Gault); KDPI, Kidney Donor Profile Index (see text); KDRI, Kidney Donor Risk Index (see text); PTDB, pretransplant donor biopsy; SINGLE Sc. < 4, single kidney transplant with PTDB yielding a score < 4; SINGLE Sc. = 4, single kidney transplant with PTDB yielding a score = 4; STANDARD, standard criteria donor kidney transplant. Continuous data are reported as mean (standard deviation), categorical data as percentages.



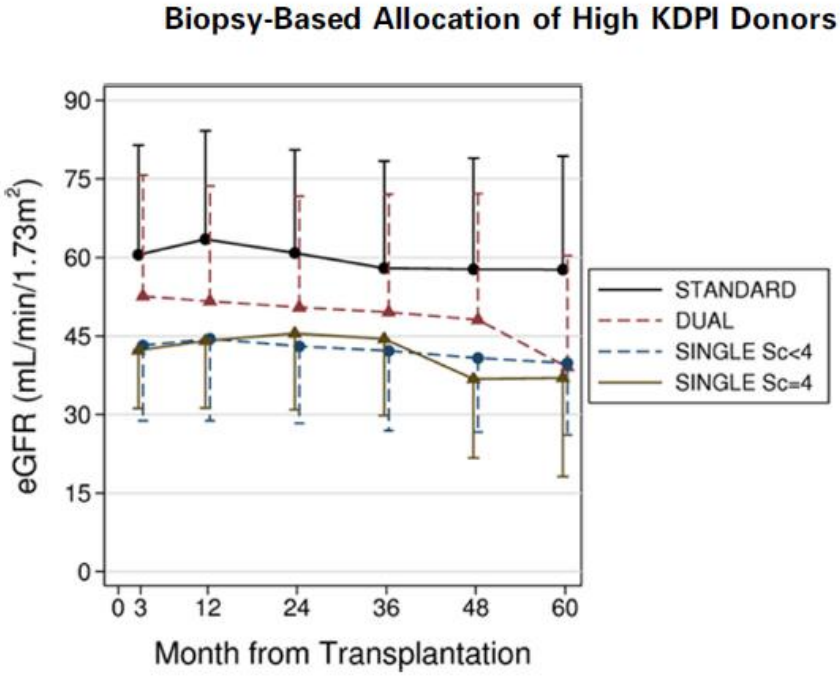


Figure 4: eGFR changes over follow-up period. Crude marginal means (dots) and standard deviation (bars) of the eGFR in the four groups among grafts surviving beyond month 3 posttransplantation. DUAL, dual kidney transplant; eGFR, estimated GFR; SINGLE Sc. < 4, single kidney transplant with pretransplant donor biopsy score < 4; SINGLE Sc. = 4, single kidney transplant with pretransplant donor biopsy score = 4; STANDARD, standard criteria donor kidney transplant.

CONCLUSIÓN DE LA EVIDENCIA DISPONIBLE:

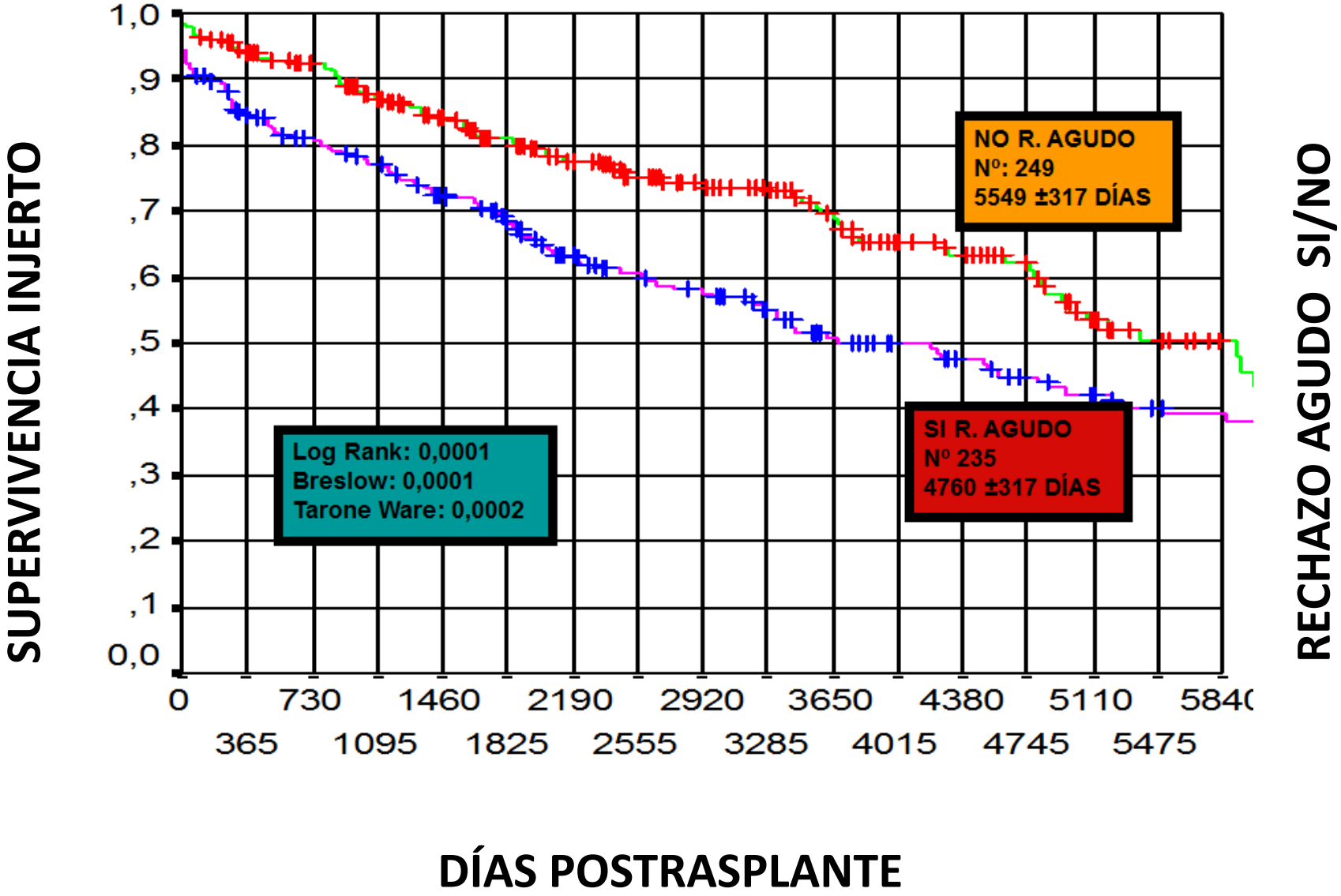
AUNQUE EXISTEN ESTUDIOS RETROSPECTIVOS SOBRE BIOPSIAS DE PROTOCOLO DE QUE LAS LESIONES GLOMERULARES Y VASCULARES DEL RIÑÓN DEL DONANTE TIENEN INFLUENCIA EN EL PRONÓSTICO A DEL INJERTO RENAL, ESTE HECHO DEBE SER TOMADO CON MUCHAS RESERVAS CUANDO LA BIOPSIA DEL DONANTE ES PREVIAMENTE EMPLEADA PARA SELECCIONAR LA IDONEIDAD DEL ÓRGANO

CONCLUSIONES BIOPSIA DEL DONANTE:

1. La biopsia preimplantacional del injerto es capaz de descartar la gran mayoría de los riñones inadecuados para trasplante.
2. Es posible que la biopsia también rechace un número indeterminado de riñones viables para receptores añosos.
3. Es necesario un ensayo clínico del máximo nivel de evidencia que, contraponiendo los criterios clínicos KDPI con biopsia de protocolo frente a los proporcionados por la biopsia tradicional preimplantacional en parafina, permita establecer de una forma fidedigna el valor de esta práctica.
4. Entre tanto, la biopsia preimplantacional en parafina sigue siendo el mejor estándar para definir la validez de los órganos a trasplantar.

INDICADORES HISTOLÓGICOS DE VALOR PRONÓSTICO EN LA BIOPSIA RENAL POR DISFUNCIÓN AGUDA O CRÓNICA DEL INJERTO

CLÁSICAMENTE, EL VALOR PRONÓSTICO DE LAS LESIONES ELEMENTALES EN LA BIOPSIA DEL INJERTO RENAL SIEMPRE SE HA CONSIDERADO SUBROGADO A LA CAPACIDAD DE LA BIOPSIA PARA ESTABLECER EL DIAGNÓSTICO MORFOLÓGICO DEL PACIENTE


SUPERVIVENCIA INJERTO
RECHAZO AGUDO SI/NO
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4380
5110
365
1095
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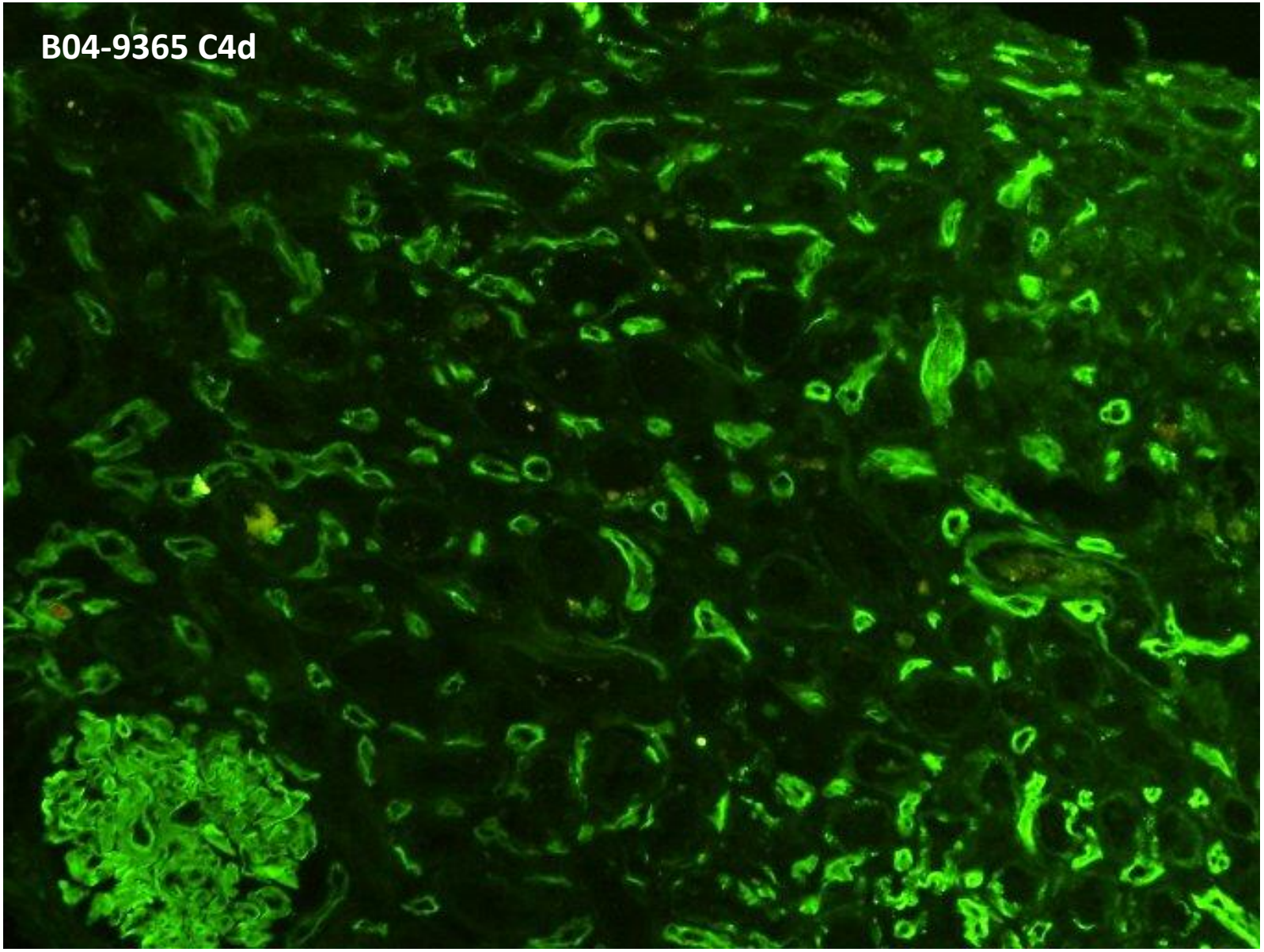
2555
3285
4015
4745
5475
NO R. AGUDO
Nº: 249
5549 ±317 DÍAS
SI R. AGUDO
Nº 235
4760 ±317 DÍAS
Log Rank: 0,0001
Breslow: 0,0001
Tarone Ware: 0,0002
DÍAS POSTRASPLANTE

LA PREGUNTA DEL MILLÓN EN LA BIOPSIA RENAL DEL TRASPLANTE ES: ¿EXISTEN LESIONES MORFOLÓGICAS ELEMENTALES QUE POR SÍ MISMAS SEAN INDICATIVAS DE MAL PRONÓSTICO?


B04-9365 C4d

American Journal of Transplantation 2014; 14: 272–283
Wiley Periodicals Inc.

doi: 10.1111/ajt.12590

Meeting Report

Banff 2013 Meeting Report: Inclusion of C4d-Negative Antibody-Mediated Rejection and Antibody-Associated Arterial Lesions

M. Haas[1,*], B. Sis[2], L. C. Racusen[3], K. Solez[2], D. Glotz[4], R. B. Colvin[5], M. C. R. Castro[6], D. S. R. David[7], E. David-Neto[6], S. M. Bagnasco[3], L. C. Cendales[8], L. D. Cornell[9], A. J. Demetris[10], C. B. Drachenberg[11], C. F. Farver[12], A. B. Farris III[13], I. W. Gibson[14], E. Kraus[15], H. Liapis[16], A. Loupy[17], V. Nickeleit[18], P. Randhawa[10], E. R. Rodriguez[12], D. Rush[19], R. N. Smith[5], C. D. Tan[12], W. D. Wallace[20] and M. Mengel[2] as the Banff meeting report writing committee

[18]Department of Pathology and Laboratory Medicine, Division of Nephropathology, University of North Carolina at Chapel Hill, Chapel Hill, NC
[19]Department of Internal Medicine, University of Manitoba Health Sciences Centre, Winnipeg, Manitoba, Canada
[20]Department of Laboratory Medicine and Pathology, University of California, Los Angeles, CA
**Corresponding author: Mark Haas, mark.haas@cshs.org*

The 12th Banff Conference on Allograft Pathology was held in Comandatuba, Brazil, from August 19–23, 2013, and was preceded by a 2-day Latin American

JUNTA DE ANDALUCIA

Unidad de Anatomía Patológica
Avenida Doctor Olóriz 16
18012 - GRANADA (Teléfono: 958 02 31 99)

B14-02931
HUSSAIN SHAH, MUNAZZAM

Informe de Anatomía Patológica

Entregar en:GRANADA-VIRGEN DE LAS NIEVES HOSP. UNIV. - NEFROLOGIA

NUHSA: AN1229138742
Paciente: HUSSAIN SHAH, MUNAZZAM
Edad: 38 años
Sexo: Hombre
NSS: 231043132057
NTS: 231043132057
Domicilio: CALLE VIRGEN DEL ROSARIO ,Num. 23 ,, Mengíbar (TEL. 632895775) - 23620,
Centro peticionario: GRANADA-VIRGEN DE LAS NIEVES HOSP. UNIV.
Servicio remitente: NEFROLOGIA
Facultativo OSORIO MORATALLA, JM
Tipo de paciente:
Solicitado: 12/03/2014 Hora: 11:42:37 Registrado por: GARRIDO BELTRAN, JOSE

Datos Clínicos

Motivo de la consulta: Paciente de 38 años de edad, afecto de ERC de etiología no filiada, trasplantado renal de donante cadáver en Julio 2008, que presentó un rechazo agudo en 2011, coincidiendo con un viaje a su país. (FIAT II, R. agudo mediado por células T tipo 1B. Capilaritis peritubular ptc 2). Tratado con metil prednisona y timoglobulina, mejoró hasta creat sérica de 2 mg% aprox. Hace unos meses incremento de proteinuria, actualmente de rango nefrótico sin sd. necrótico. Creat de 2.46. Sospecha de rechazo crónico humoral o recidiva enfermedad (??, no filiada). Informe: 30/1/2014 12:06. Se incluye en LE para BP del injerto.

Muestra Tipo de Estudio: BIOPSIA INCISIONAL

Fecha E. macroscópico: 12/03/2014 Patólogo: Caba Molina, Mercedes Técnico: SÁEZ LÓPEZ, FRANCISCA

Descripción macroscópica:
Se reciben 2 clindros renales de 2,5 cm y de 1,9 de longitud respectivamente. Tras su observación con lupa estereoscópica se selecciona material para microscopía electrónica, inmunofluorescencia y procesamiento en parafina. Bloques de parafina finales:1. Se incluye todo el material remitido.

Descripción microscópica:

DIAGNÓSTICO ANATOMOPATOLÓGICO:

RIÑÓN TRANSPLANTADO (BIOPSIA INCISIONAL): RECHAZO CRÓNICO HUMORAL.

CÓDIGOS SNOMED DE LA MUESTRA: T71000,M44107

Residente Dr/Dra.: VIZOSO PEREZ, MARIA LUISA
Pat.Consultor/es: Dr/Dra: Mercedes GOMEZ

Fecha de salida : 21/03/2014
Fecha de validación: 24/03/2014

H.U. SAN CECILIO DE GRANADA
Anatomía Patológica
Avda. Dr. Oloriz,16
GRANADA
GRANADA

B08-08681
MIRANDA ROJAS, MANUEL

Informe Servicio de Anatomía Patológica

ıtregar en: NEFROLOGIA (VN). C. TRASPLANTES

Nº Historia: 434277
Paciente: **MIRANDA ROJAS, MANUEL**
Edad: 67 años
Domicilio: AVE MARIA 4 SALAR 18310 GRANADA (TEL. 958316022)
Sexo: Masculino
Servicio Remitente: NEFROLOGIA (VN)
NSS: 180037186170
Médico Remitente, Dr/a. BRAVO SOTO, J.
Tipo de Paciente: EXTERNO
Solicitado: 16/09/2008 Recibido: 16/09/2008
DNI: 023593216

Datos y diagnóstico clínico:

MOTIVO PETICIÓN BIOPSIA RENAL: DETERIORO DEL FG (Cr = 2 mg%) CONPROTEINURIA DE 1,17 g/24 h DESDE EL 4º AÑO POST-TRR.
SITUACIÓN ACUTAL: TRASPLANTE RENAL REALIZADO EL 17-10-2003. DONANTE DE 67 AÑOS, FALLECIDO DE ACV. SE HIZO BIOPSIA Y EL SC = 5. ISQUEMIA FRIA: 16 H. PROTOCOLO DE TTº INMUNOSUPRESOR: ZENAPAX + FK + MMF + PREDNISONA. NORMALIZA FR AL 6º DIA POST TRR. NECESITA HIPOTENSORES PARA EL CONTROL TENSIONAL. NO EPISODIOS DE R. AGUDO NI INFECCION POR CMV. ALGUNOS EPISODIOS DIARREICOS. ESTEATOSIS HEPATICA. VIRUS B Y C: NEGATIVOS.

Muestra RIÑON (NEOM) Estudio: BIOPSIA DIAGNOSTICA T71000

DESCRIPCION MACROSCOPICA:
DOS CILINDROS DE 2 Y 0.6 CM. Y 3 FRAGMENTOS IRREGULARES DE TEJIDO, EL MAYOR DE 0.7X0.1 CM. DE D.M. CORRESPONDIENTES A TEJIDO ADIPOSO Y MUSCULAR. EL CILINDRO MENOR SE TOMA PARA CONGELACIÓN.

DIAGNOSTICO ANATOMOPATOLOGICO:

RIÑÓN TRASPLANTADO:
.CAMBIOS "BORDERLINE", SOSPECHOSOS DE RECHAZO AGUDO MEDIADO POR CÉLULAS T.
.FIBROSIS INTERSTICIAL Y ATROFIA TUBULAR DE INTENSIDAD MODERADA (GRADO II BANFF 2007).
.GLOMERULOPATÍA DEL TRASPLANTE (cg2)
.LESIONES VASCULARES CRÓNICAS CONSISTENTES EN ENGROSAMIENTO INTIMAL (cv2) Y ARTERIOLOPATÍA HIALINA (ah2).
.SIGNOS DE ISQUEMIA TUBULAR.

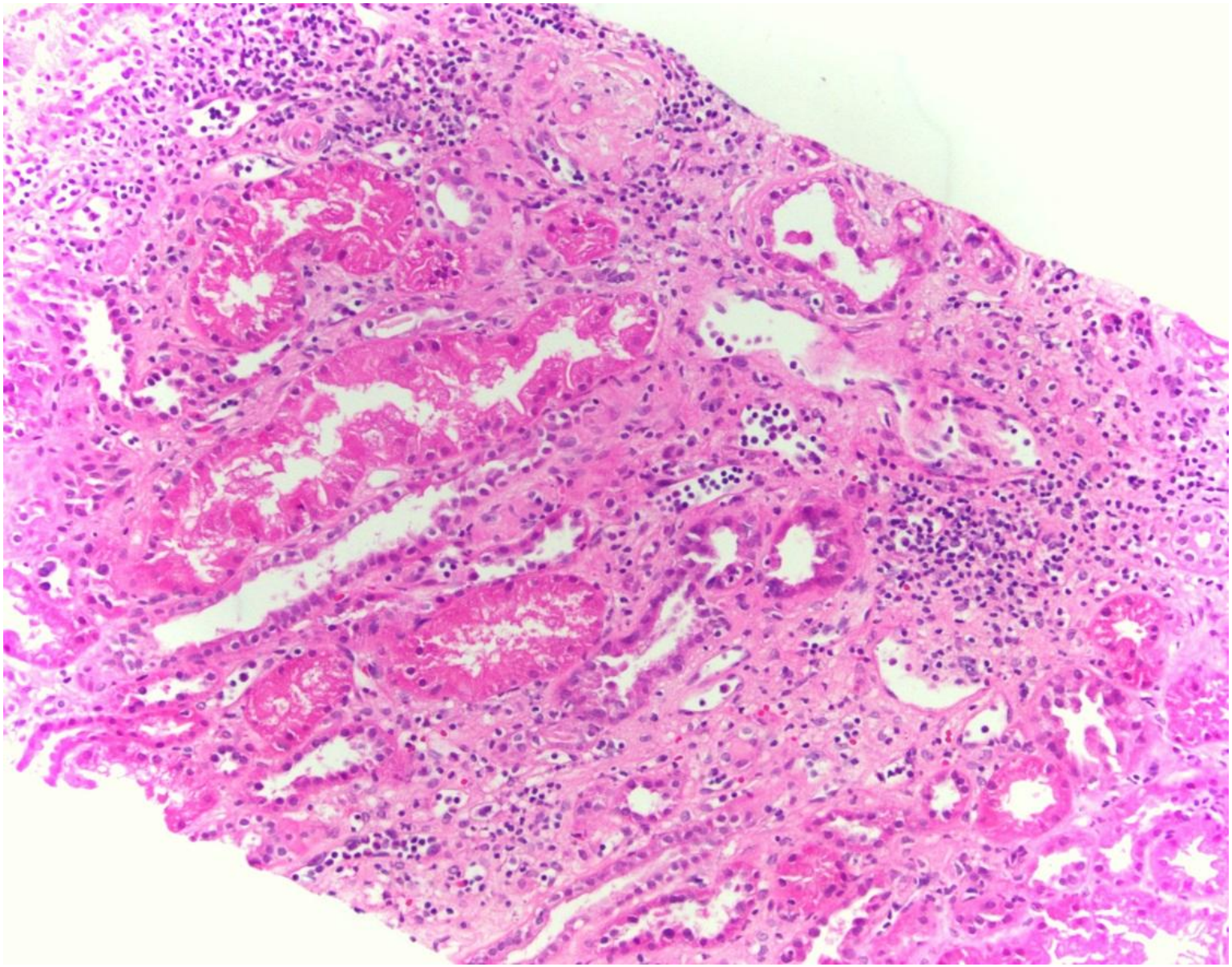
Patólogo: Dr/Dra.: GOMEZ MORALES, Mercedes

Informado: 25/09/2008
Fecha de salida: 25/09/2008

ALCACHOFAS AL PEDRO XIMÉNEZ

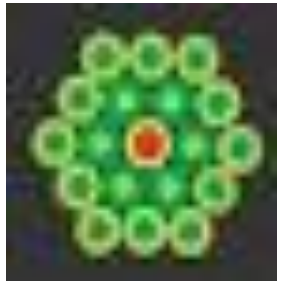
ALCACHOFAS CON PAPADA DE CERDO AL OLOROSO

La biopsia del implante renal: tiene valor pronóstico? RGM

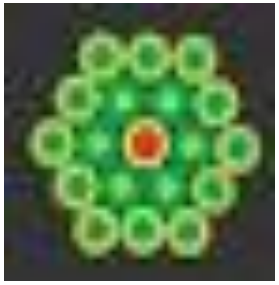


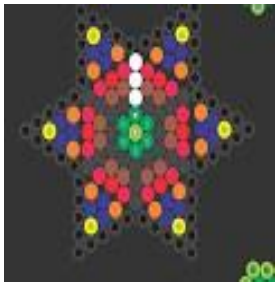
CONOCIMIENTO IMPLÍCITO

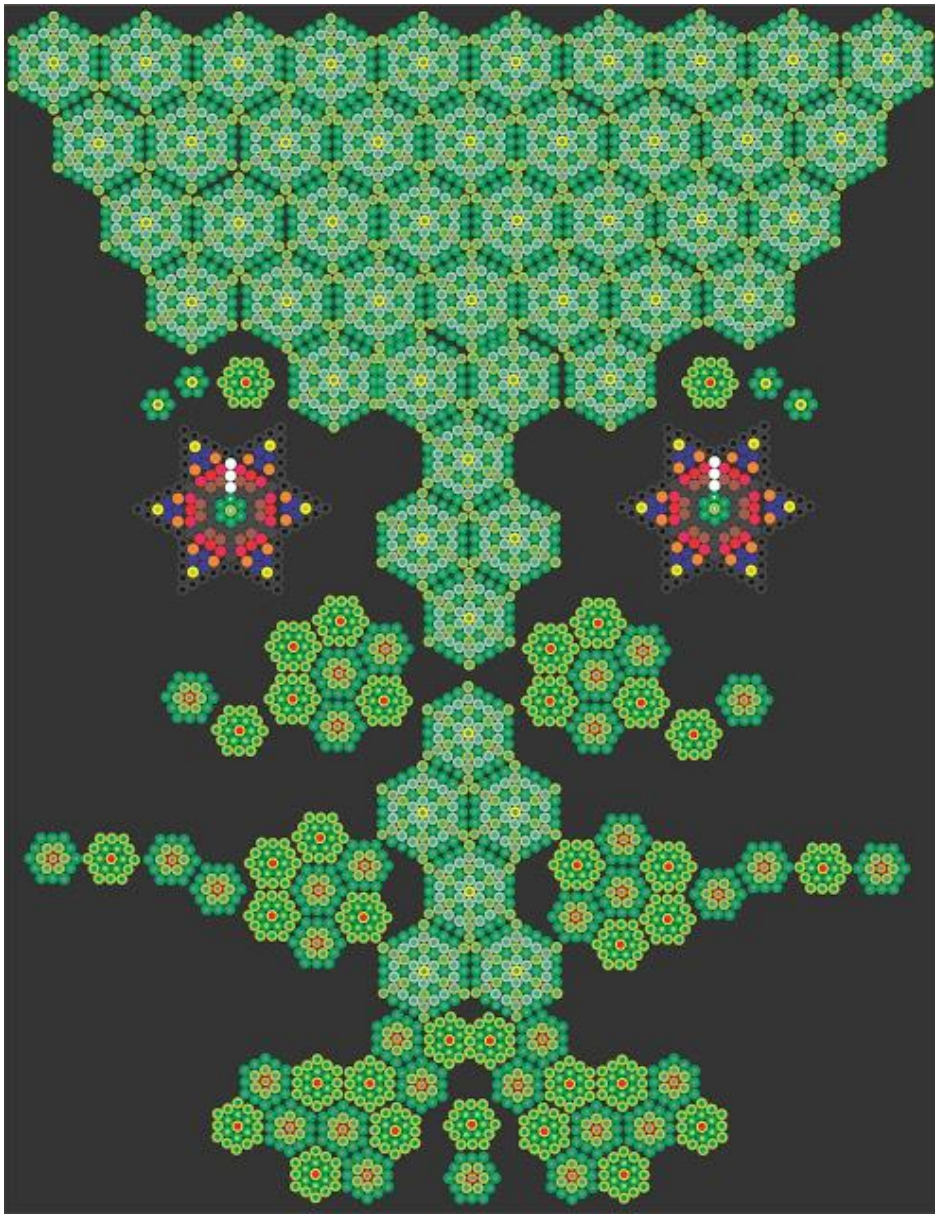
GESTALTISMO ANATOMOPATOLÓGICO:
El todo es más que la suma de las partes



La biopsia del implante renal: tiene valor pronóstico? RGM



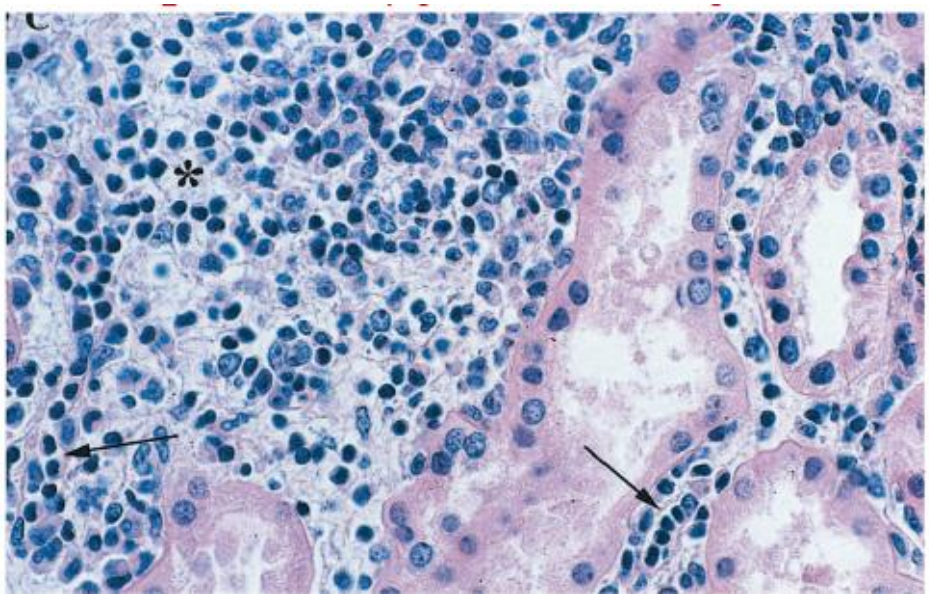


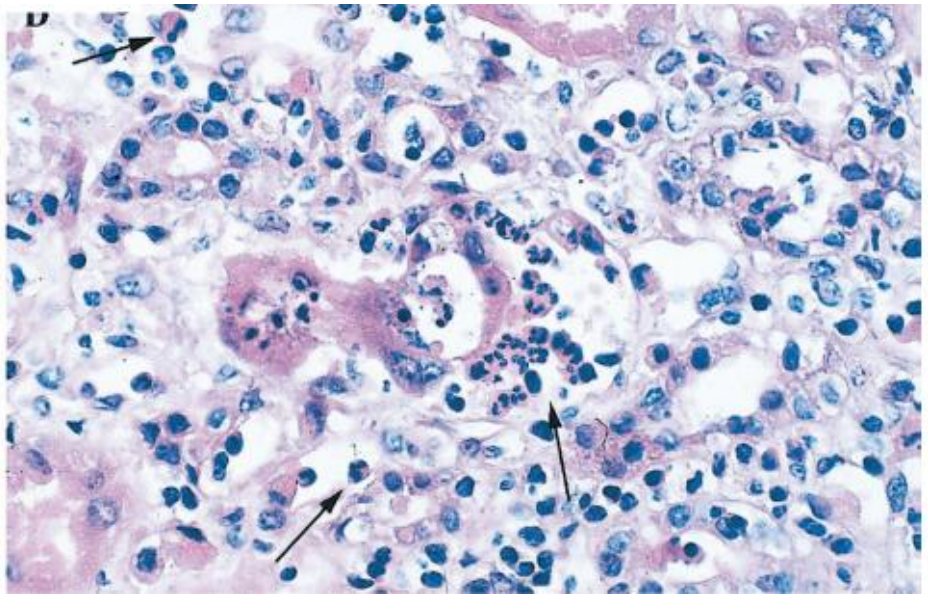


LESIONES ELEMENTALES MÁS FRECUENTES EN EL TRASPLANTE RENAL:

1. Infiltrado inflamatorio intersticial: linfocitario (i) vs granulocítico
2. Tubulitis linfocitaria (t)
3. Arteritis intimal (v)
4. Lesión inflamatoria microcapilar (glomerulitis y/o capilaritis peritubular)
5. Fibrosis intersticial/atrofia tubular (IF/TA)
6. Fibrosis miointimal arterial
7. Cambios por nefrotoxicidad
8. Necrosis tubular aguda
9. Glomerulopatía del trasplante
10. Otras lesiones de valor pronóstico como infecciones virales, marcadores moleculares, etc.

INFILTRADO INTERSTICIAL GRANULOCÍTICO A PARTIR DE 1 MES TRAS INJERTO



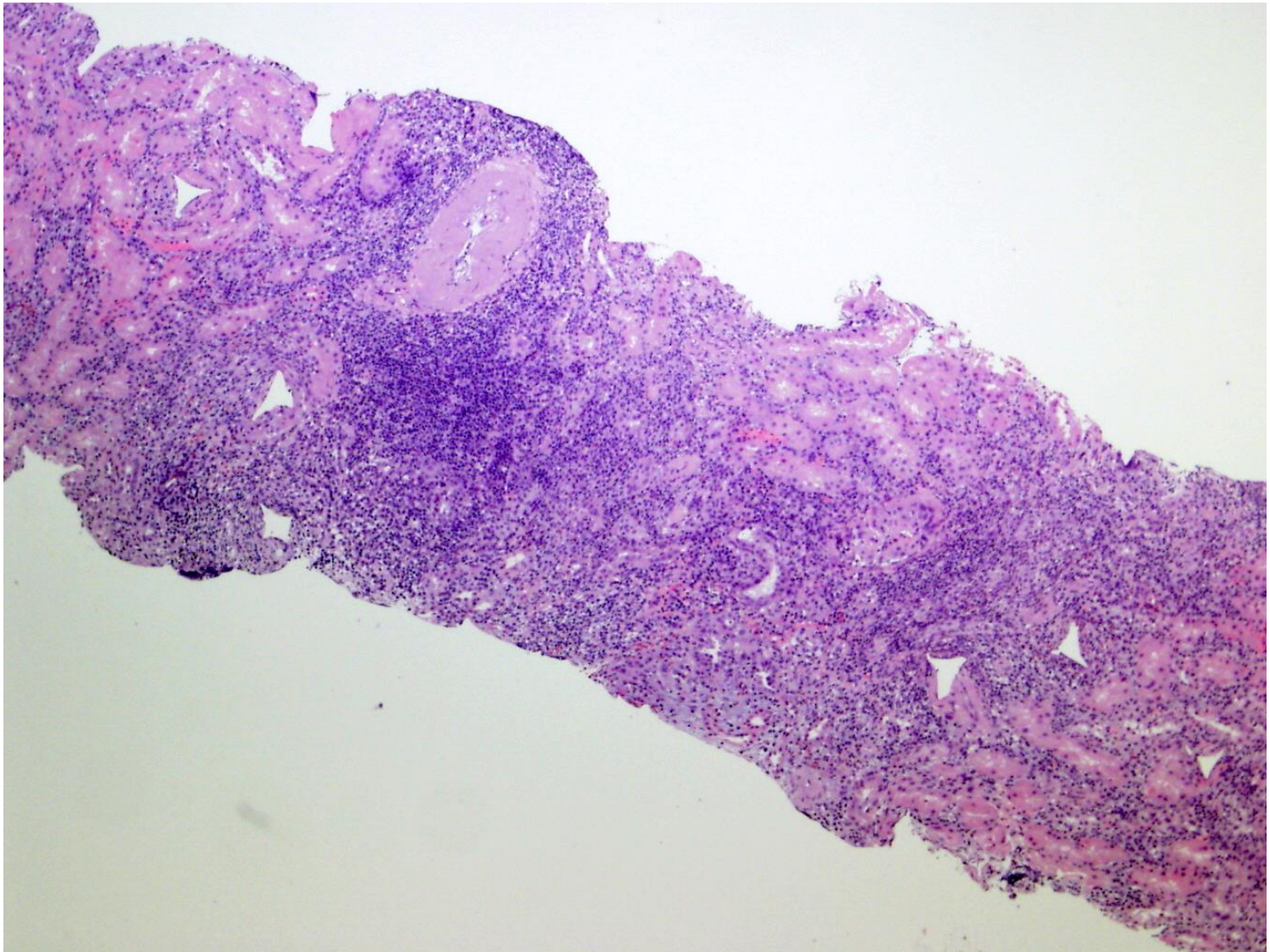


J Am Soc Nephrol 13: 779–787, 2002

Acute Humoral Rejection in Kidney Transplantation: II. Morphology, Immunopathology, and Pathologic Classification

SHAMILA MAUIYYEDI,*† MARTA CRESPO,‡§ A. BERNARD COLLINS,*†
EVELINE E. SCHNEEBERGER,* MANUEL A. PASCUAL,‡§ SUSAN L. SAIDMAN,*‡
NINA E. TOLKOFF-RUBIN,‡§ WINFRED W. WILLIAMS,‡§
FRANCIS L. DELMONICO,‡¶ A. BENEDICT COSIMI,‡¶ and ROBERT B. COLVIN*
**Pathology Service, †Immunopathology Unit, ‡Transplantation Unit, §Medical Service, and ¶Surgical Service, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts.*

INFILTRADO INFLAMATORIO INTERSTICIAL LINFOCITARIO Y TUBULITIS



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Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2010.03415.x

Inflammation Lesions in Kidney Transplant Biopsies: Association with Survival Is Due to the Underlying Diseases

J. Sellarés[a,b], D. G. de Freitas[a,b], M. Mengel[a,c], B. Sis[a,c], L. G. Hidalgo[a,b], A. J. Matas[d], B. Kaplan[e] and P. F. Halloran[a,b,*]

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[b] *Department of Medicine, Division of Nephrology and Transplant Immunology, University of Alberta, Edmonton, AB, Canada*
[c] *Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB, Canada*
[d] *Department of Surgery, University of Minnesota, Minneapolis, MN*
[e] *Department of Medicine (Division of Nephrology), University of Arizona, Tucson, AZ*
* *Corresponding author: Philip F. Halloran, Phil.halloran@ualberta.ca*

Abbreviations: ABMR, antibody-mediated rejection; ATN, acute tubular necrosis; BFC, biopsy for clinical indications; GN, glomerulonephritis; IFTA, interstitial fibrosis and tubular atrophy; TCMR, T-cell-mediated rejection.

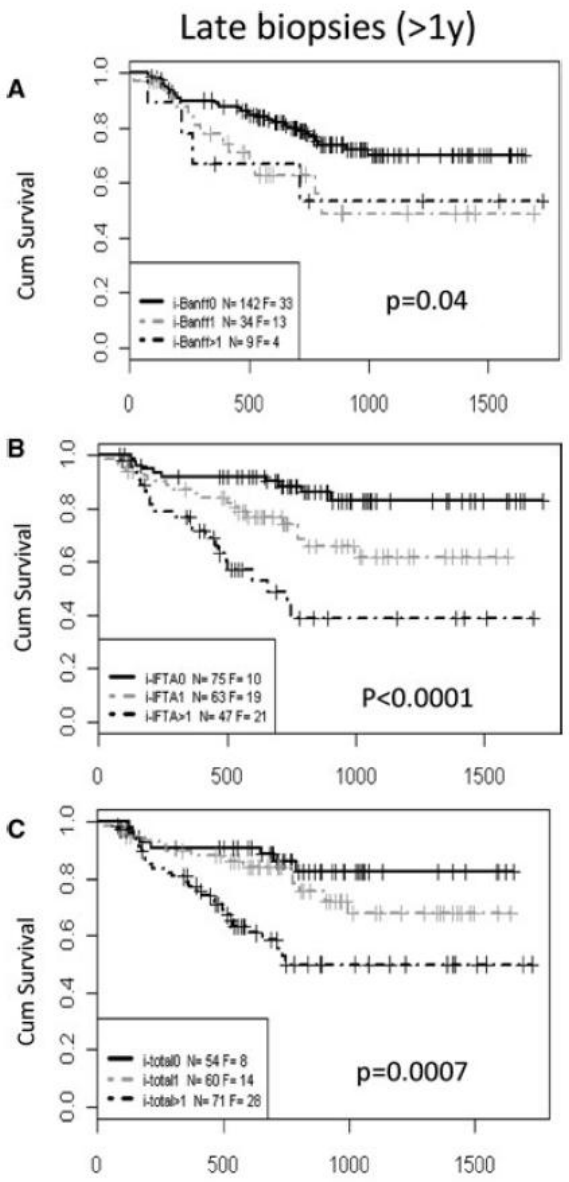
Received 24 September 2010, revised 10 December 2010 and accepted for publication 10 December 2010

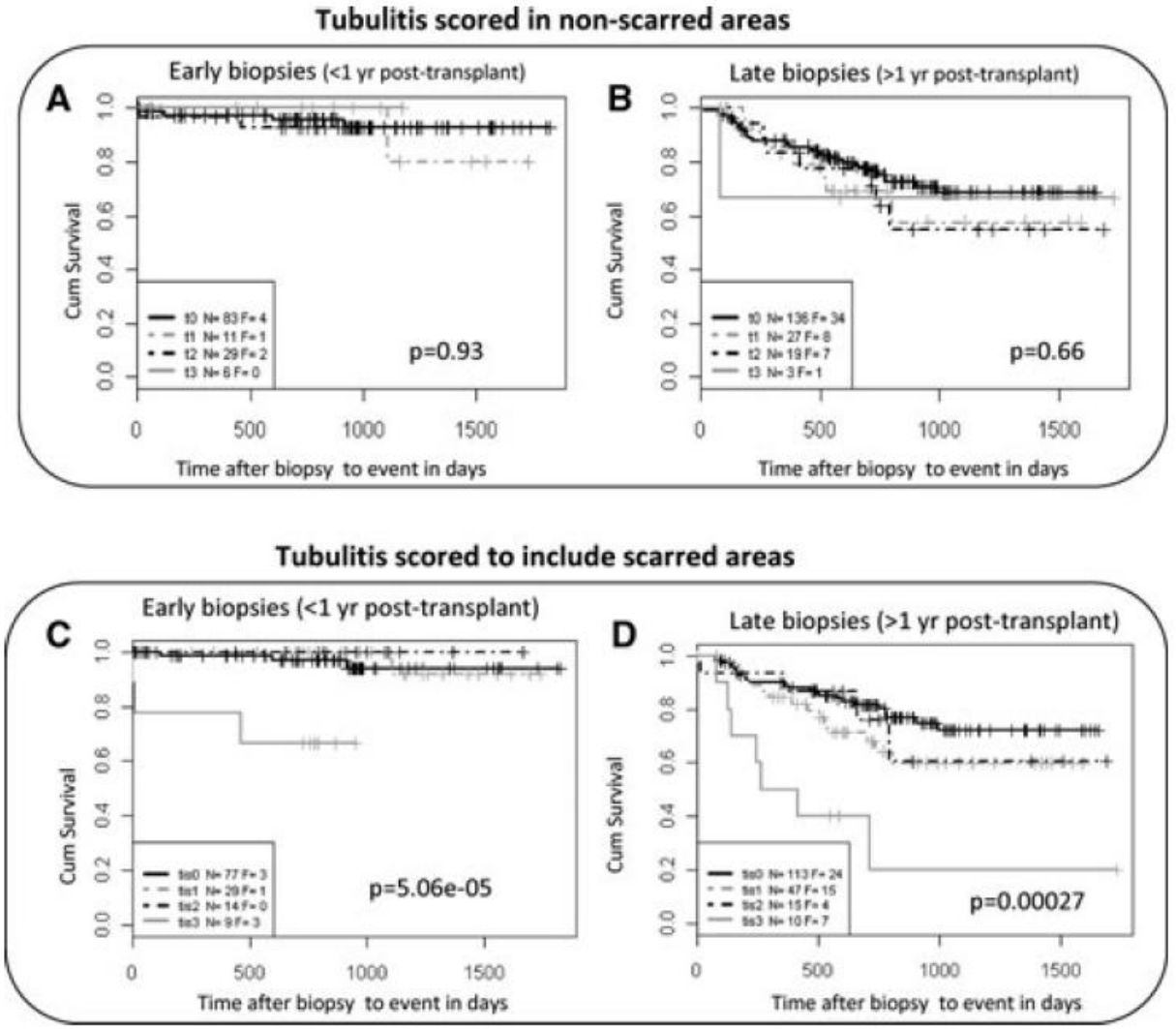
Introduction

Assessment of biopsies of troubled kidney transplants relies heavily on inflammatory lesions, which are the basis of diagnosing rejection and have implications for prognosis. The lesions used by the current criteria (1) for the diagnosis of T-cell-mediated rejection (TCMR) are interstitial in-

La biopsia del implante renal: tiene valor pronóstico? RGM

Sellarés et al.





Sellarés J, de Freitas DG, Mengel M, et al. Am J Transplant. 2011 Mar;11(3):489-99.

Clin Transplant 2014: 28: 410–418 DOI: 10.1111/ctr.12333

Clinical Transplantation

Acute cellular rejection with isolated v-lesions is not associated with more favorable outcomes than vascular rejection with more tubulointerstitial inflammations

Wu KY, Budde K, Schmidt D, Neumayer HH, Rudolph B. Acute cellular rejection with isolated v-lesions is not associated with more favorable outcomes than vascular rejection with more tubulointerstitial inflammations.

Abstract: Background: The impact of isolated v-lesions on clinical outcome in biopsies with acute cellular rejection (ACR) is unclear. Methods: Two hundred and sixty-five biopsies showing the highest ACR severity for each patient were recruited and classified into four groups: (i) acute interstitial rejection (AIR) I with minimal tubulointerstitial inflammation (TI), (ii) AIR II with intensive TI, (iii) acute vascular rejection (AVR) I with minimal TI, and (iv) AVR II with intensive TI. Results: The complete reversal rates of AIR I and AIR II groups were marginally higher than AVR I and AVR II groups (p = 0.16). At eight yr of transplantation, the death-censored graft survival (DCGS) rate of AIR I group (93.3%) was significantly higher compared with the AVR I (72.7%) or AVR II (72.9%) group. AVR I group had a similar DCGS rate with AVR II group (72.7% vs. 74.1%), whereas AVR with v1-lesion showed significantly higher graft survival (GS) rate than those with v2-lesion (70.2% vs. 45.5%). The t-lesion of AIR and v-lesion of AVR group were associated with graft loss.
Conclusion: The extent of TI is non-specifically associated with graft loss in biopsies with AVR; the higher grade v-lesion predicts the lower complete reversal rate and poorer long-term graft survival.

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Key words: acute cellular rejection – graft outcome – isolated v-lesions – kidney transplantation – tubulointerstitial inflammation

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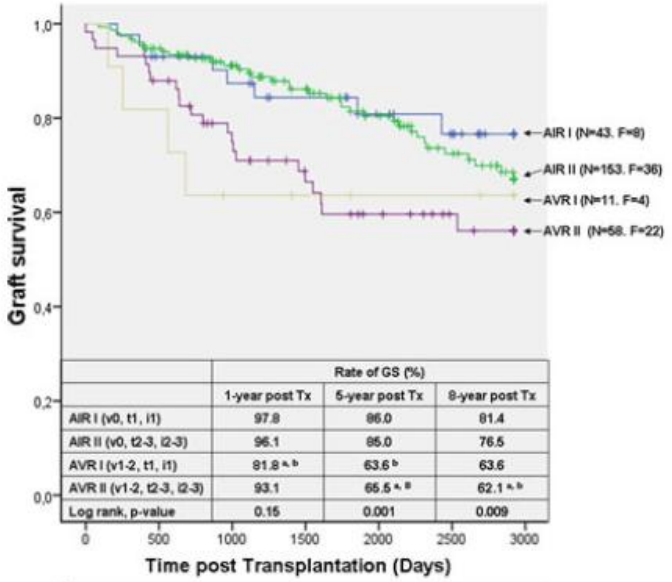
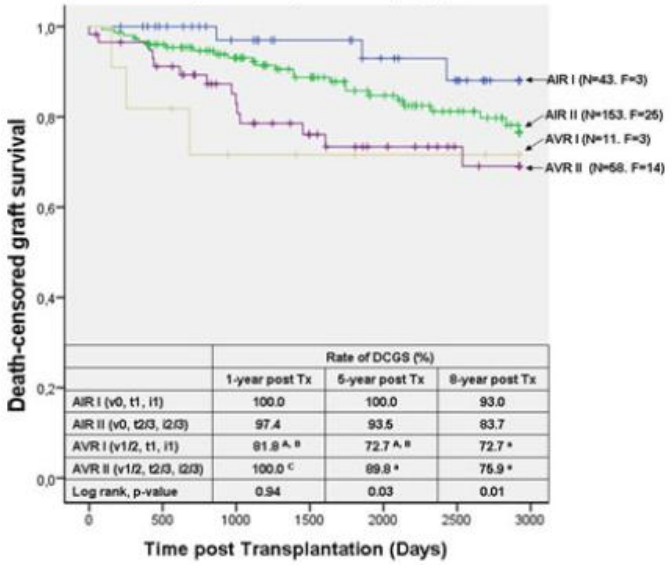
Conflict of interest: None of the authors has declared any competing financial conflict of interest.

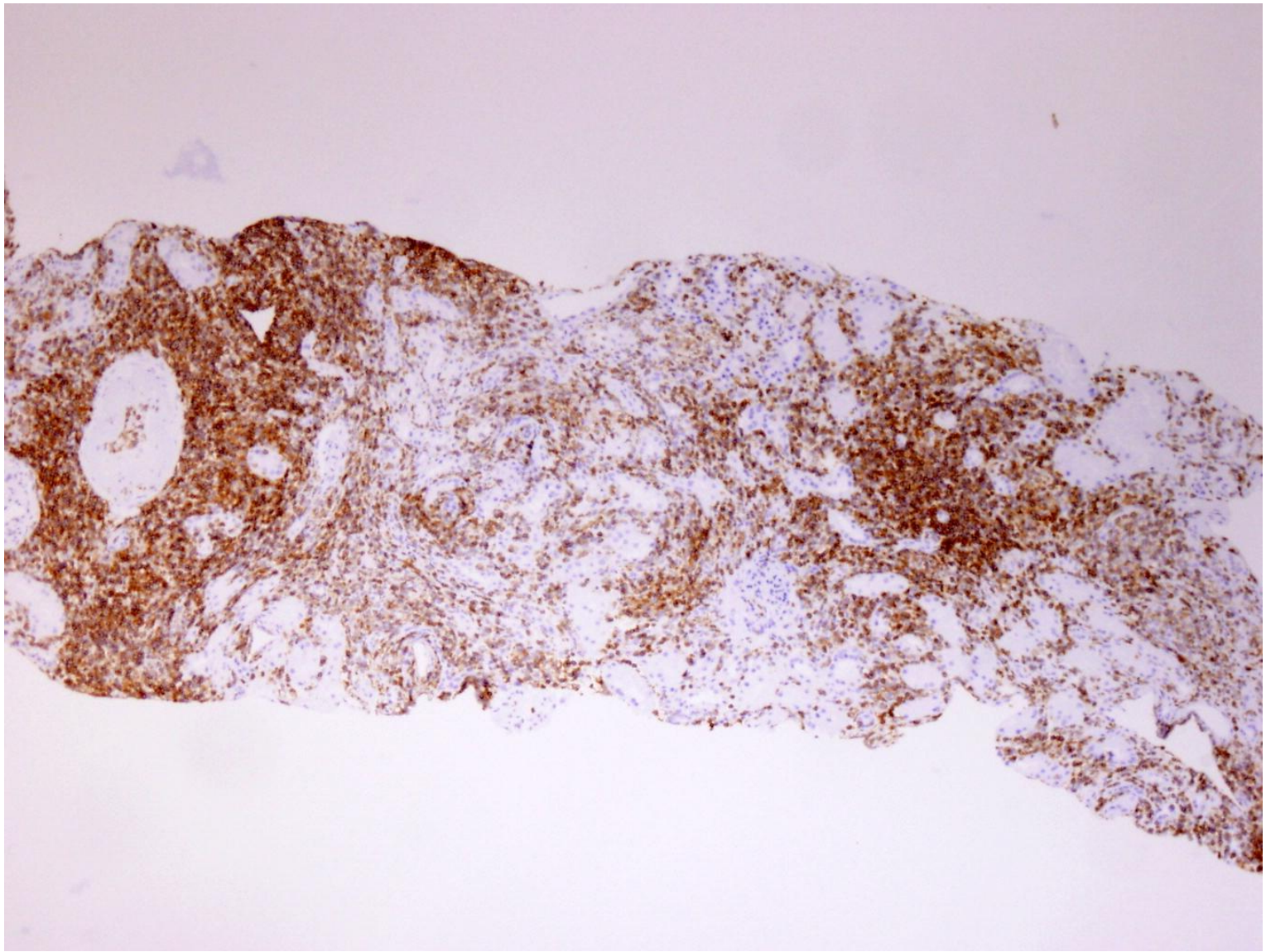


	Rate of GS (%)		
	1-year post Tx	5-year post Tx	8-year post Tx
AIR I (v0, t1, i1)	97.8	86.0	81.4
AIR II (v0, t2-3, i2-3)	96.1	85.0	76.5
AVR I (v1-2, t1, i1)	91.8 a, b	63.6 b	63.6
AVR II (v1-2, t2-3, i2-3)	93.1	65.5 a, B	62.1 a, b
Log rank, p-value	0.15	0.001	0.009



	Rate of DCGS (%)		
	1-year post Tx	5-year post Tx	8-year post Tx
AIR I (v0, t1, i1)	100.0	100.0	93.0
AIR II (v0, t2/3, i2/3)	97.4	93.5	83.7
AVR I (v1/2, t1, i1)	91.8 A, B	72.7 A, B	72.7 a
AVR II (v1/2, t2/3, i2/3)	100.0 C	89.8 a	75.9 a
Log rank, p-value	0.94	0.03	0.01

INFILTRADO INFLAMATORIO INTERSTICIAL LINFOCITARIO Y TUBULITIS



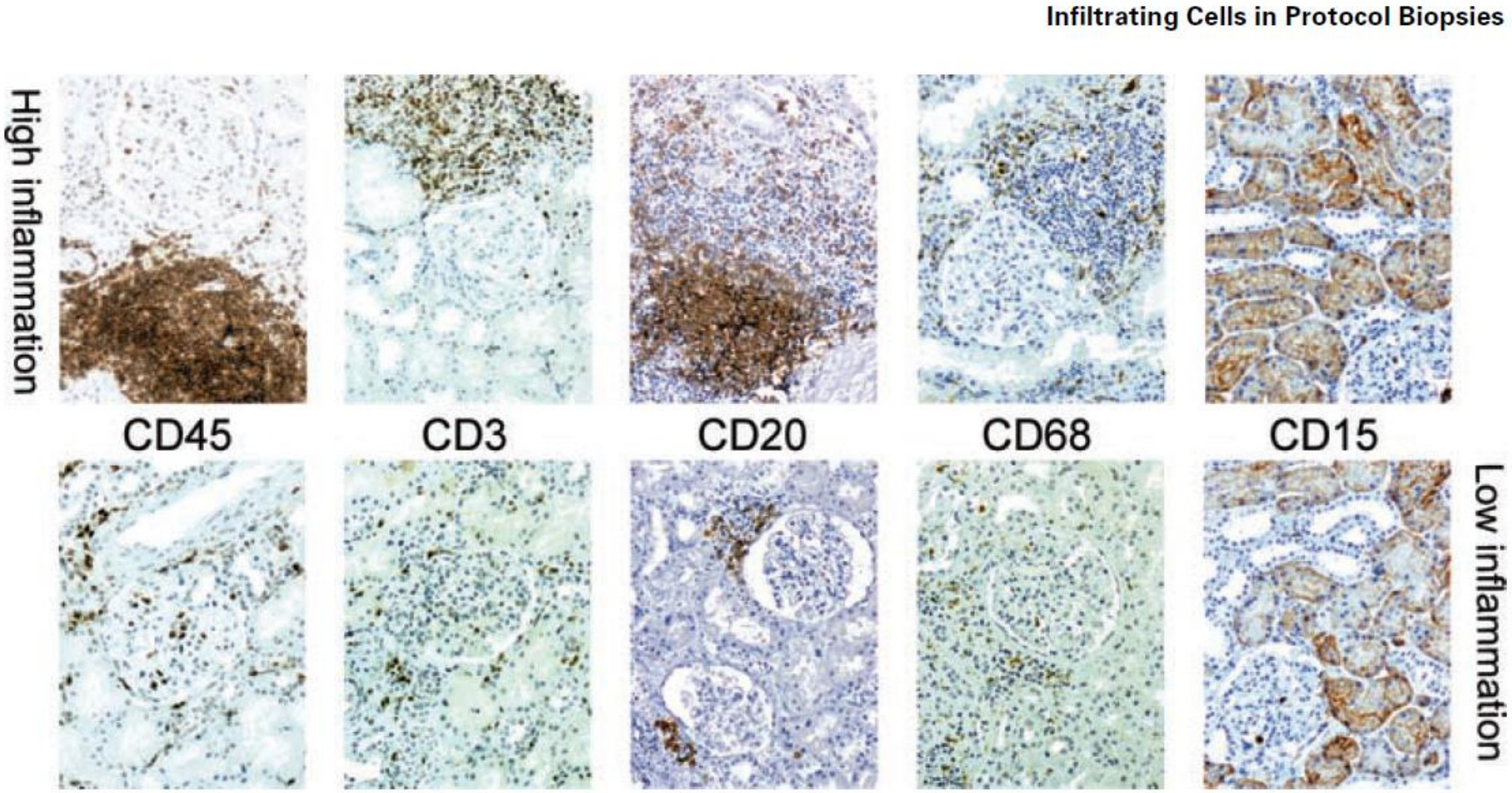


Figure 4: Examples of low and high interstitial inflammation for each cell immunophenotype in the protocol biopsies.

Tomada de: Moreso F, Seron D, O'Valle F, Ibernon M, Gomà M, Hueso M, Cruzado JM, Bestard O, Duarte V, del Moral RG, Grinyó JM. Immunephenotype of glomerular and interstitial infiltrating cells in protocol renal allograft biopsies and histological diagnosis. Am J Transplant. 2007 Dec;7(12):2739-47.

American Journal of Transplantation 2007; 7: 2739–2747
Blackwell Munksgaard

doi: 10.1111/j.1600-6143.2007.02013.x

Immunephenotype of Glomerular and Interstitial Infiltrating Cells in Protocol Renal Allograft Biopsies and Histological Diagnosis

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Patients with a protocol renal allograft biopsy simultaneously displaying interstitial fibrosis/tubular atrophy (IF/TA) and subclinical rejection (SCR) have a shortened graft survival than patients with a normal biopsy, or with a biopsy only displaying IF/TA or SCR. The poor outcome of these patients could be related with a more severe inflammation. We evaluate the immunophenotype of infiltrating cells in these diagnostic categories.

Introduction

In protocol renal allograft biopsies, the presence of chronic allograft nephropathy (1,2), that is, interstitial fibrosis and tubular atrophy (IF/TA), is associated with a poorer allograft survival (3–5). In studies of serial protocol biopsies, it has been observed that the presence of subclinical rejection (SCR), that is, tubulitis and interstitial infiltration, in a first biopsy is associated with a higher risk for the progression of IF/TA in the second one, suggesting that early graft inflammation is a risk factor for the progression of chronic lesions (6–8). This notion is further reinforced by the observation that 10-year graft survival is reduced in patients with SCR on a 2-week protocol biopsy (9).

Recently, in studies performed at different centers, it has been observed that graft survival is especially shortened in patients displaying simultaneously SCR and IF/TA in pro-

was not different among groups. The upper tertile of CD20 positive interstitial cells was associated with a decreased death-censored graft survival (relative risk: 3.01, 95% confidence interval: 1.23–7.35; p = 0.015). These data suggest that B-cell interstitial infiltrates are associated with histological damage and outcome, but do not distinguish whether these infiltrates were the cause or the consequence of chronic tubulo-interstitial damage.

Human Pathol 2001, 32:205-15

The Clinical and Pathologic Implications of Plasmacytic Infiltrates in Percutaneous Renal Allograft Biopsies

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Plasmacytic infiltrates in renal allograft biopsies are uncommon and morphologically distinctive lesions that may represent variants of acute rejection. This study sought significant clinical and pathologic determinants that might have influenced development of these lesions and assessed their prognostic significance. Renal allograft biopsies ($n = 19$), from 19 patients, with tubulointerstitial inflammatory infiltrates containing abundant plasma cells, composing 32 ± 8% of the infiltrating mononuclear cells, were classified using Banff '97 criteria. Clonality of the infiltrates was determined by immunoperoxidase staining for kappa and lambda light chains and polymerase chain reaction for immunoglobulin heavy-chain gene rearrangements, using V_H gene framework 3 and JH consensus primers. In situ hybridization for Epstein-Barr virus encoded RNA (EBER) was performed in 17 cases. The clinical features, histology, and outcome of these cases were compared with kidney allograft biopsies ($n = 17$) matched for time posttransplantation and type of rejection by Banff '97 criteria, with few plasma cells (7 ± 5%). Sixteen of 19 biopsies (84%) with plasmacytic infiltrates had EBER-negative (in 14 cases tested) polyclonal plasma cell infiltrates that were classifiable as acute rejection (types 1A [4], 1B [10], and 2A [2]). These biopsies were obtained between 10 and 112 months posttransplantation. Graft loss from acute and/or chronic rejection was 50% at 1 year and 63% at 3 years, and the median time to graft failure was 4.5 months after biopsy. There was no significant difference in overall survival or time to graft failure compared with the controls. Three of 19 biopsies (16%) had EBER-negative polyclonal plasmacytic hyperplasia, mixed monoclonal and polyclonal polymorphous B cell hyperplasia, and monoclonal plasmacytoma-like posttransplantation lymphoproliferative disease (PTLD) and were obtained at 17 months, 12 weeks, and 7 years after transplantation, respectively. Graft nephrectomies were performed at 1, 19, and 5 months after biopsy, respectively. Plasmacytic infiltrates in renal allografts comprise a spectrum of lesions from acute rejection to PTLD, with a generally poor prognosis for long-term graft survival. HUM PATHOL 32:205-215.

Key words: **plasma cells, acute rejection, kidney, allograft, posttransplantation lymphoproliferative disease.**

Abbreviations: **AR, acute rejection; PCR, polymerase chain reaction; EBV, Epstein-Barr virus; FITC, fluorescein isothiocyanate; EBER, Epstein-Barr virus encoded RNA; PTLD, posttransplantation lymphoproliferative disease; HLA, human leukocyte antigen; ISH, in situ hybridization; Ig, immunoglobulin.**

NEPHROLOGY

Nephrology **16** (2011) 777–783

Original Article

Plasma cell infiltrates and renal allograft outcomes in indigenous and non-indigenous people of the Northern Territory of Australia

NATASHA M ROGERS,[1,2] PAUL D LAWTON[3] and MATTHEW D JOSE[4]

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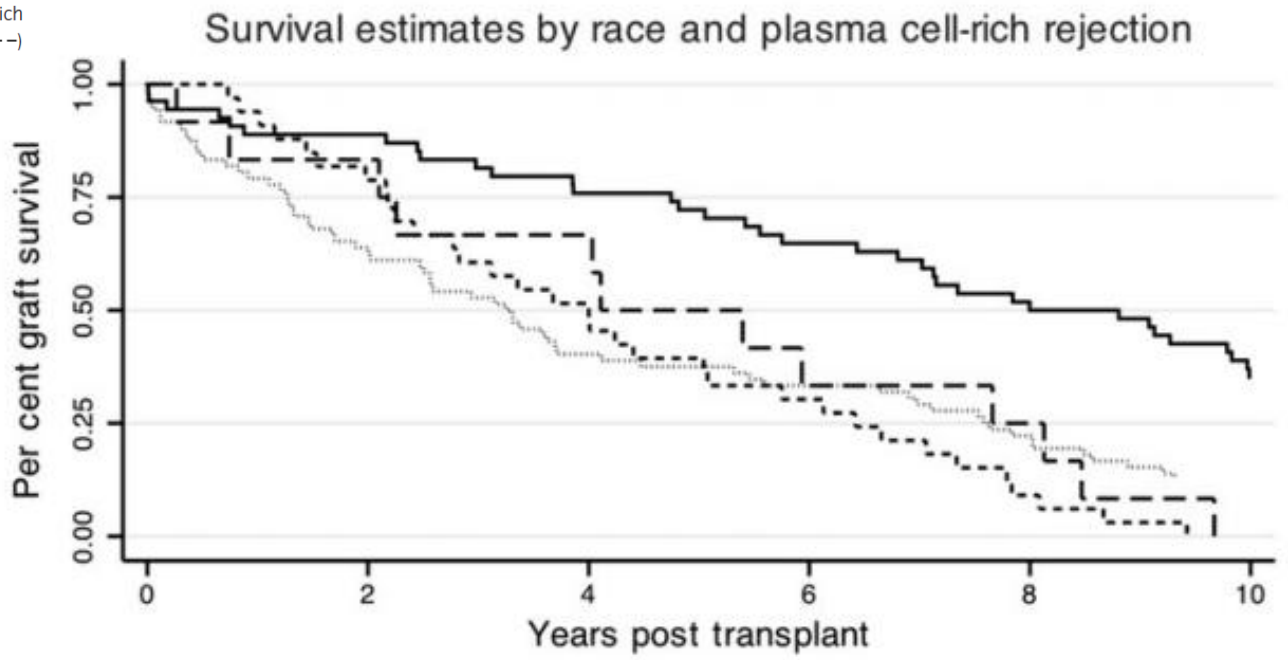
La biopsia del implante renal: tiene valor pronóstico? RGM

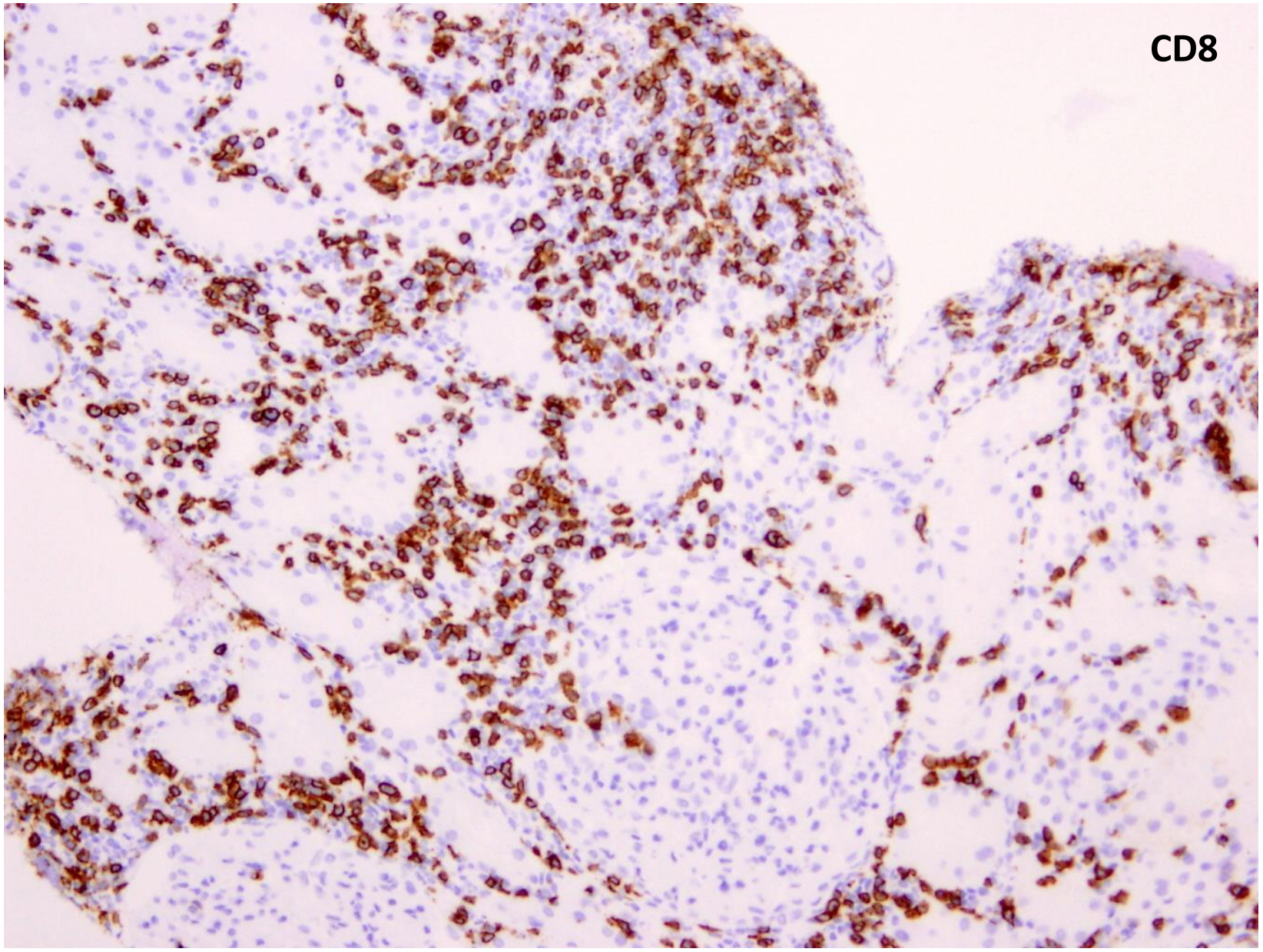
plasma cell-rich rejection. (·····) ATSI/no plasma cell-rich rejection (rej), (·---·) ATSI/plasma cell-rich rej, (——) NI/no plasma cell-rich rej, (– –) NI/plasma cell-rich rej.



Number at risk

ATSI/no plasma cell-rich rej	72	46	29	24	16	9
ATSI/plasma cell-rich rej	33	26	17	10	3	0
NI/no plasma cell-rich rej	54	48	41	35	27	19
NI/plasma cell-rich rej	12	10	8	4	3	0

Rogers NM, Lawton PD, Jose MD. Plasma cell infiltrates and renal allograft outcomes in indigenous and non indigenous people of the Northern Territory of Australia. Nephrology (Carlton). 2011; 16(8):777-83.


CD8

American Journal of Transplantation 2014; 14: 39–48
Wiley Periodicals Inc.

doi: 10.1111/ajt.12515

Natural CD8+CD122+ T Cells Are More Potent in Suppression of Allograft Rejection Than CD4+CD25+ Regulatory T Cells

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Introduction

Emerging evidence has shown that naturally occurring CD8+CD122+ T cells are also regulatory T cells (Tregs) that maintain T cell homeostasis, suppress aggressive T cell responses (1–6) and antitumor immunity (7), and control autoimmunity (8,9). We have also found that CD8+CD122+ T cells are memory-like Tregs (10). Therefore, CD8+ CD122+ Tregs well correspond to CD4+CD25+ Treg counterparts given that CD122 is the β subunit of IL-2 receptor on T cells while CD25 is the α subunit of the same

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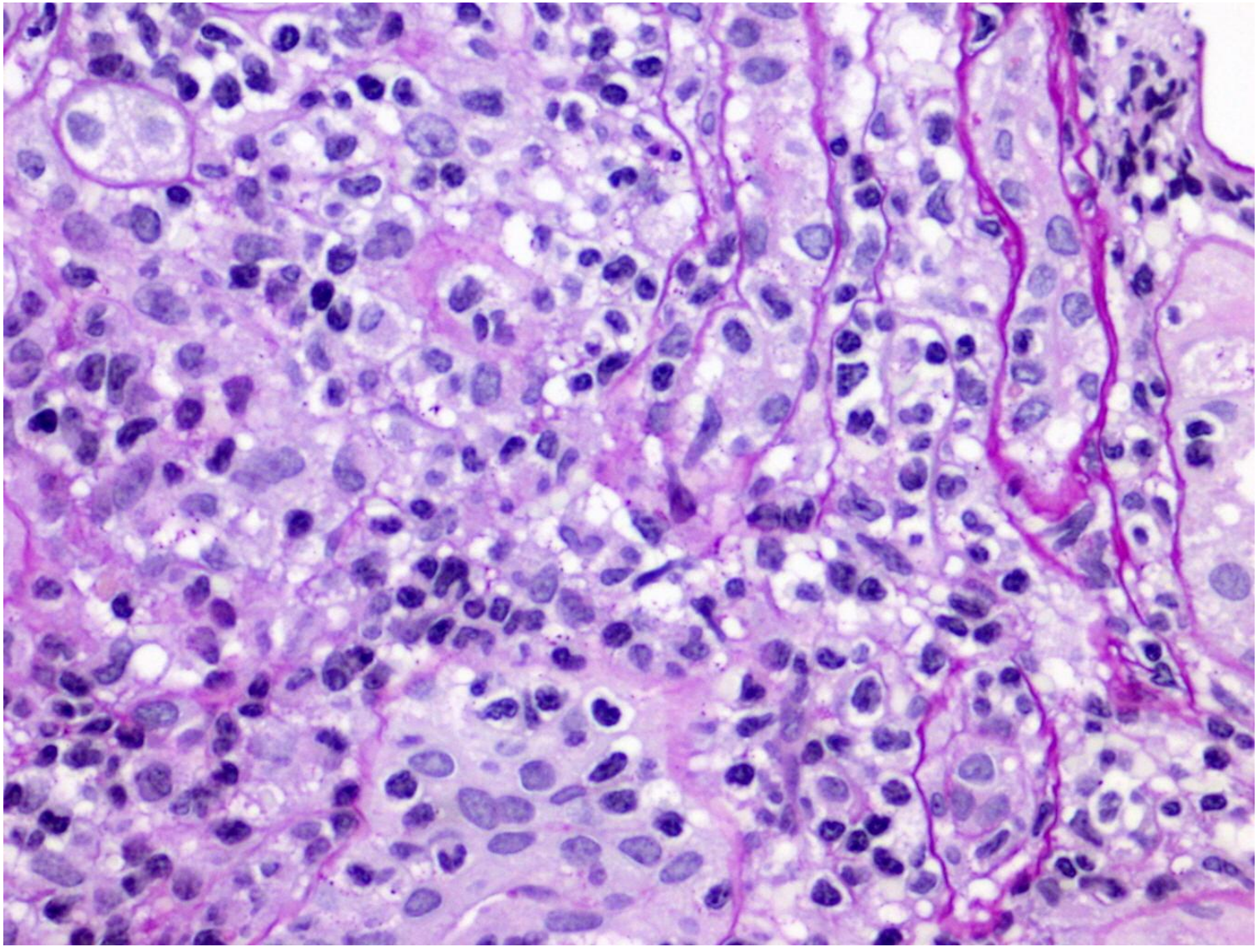

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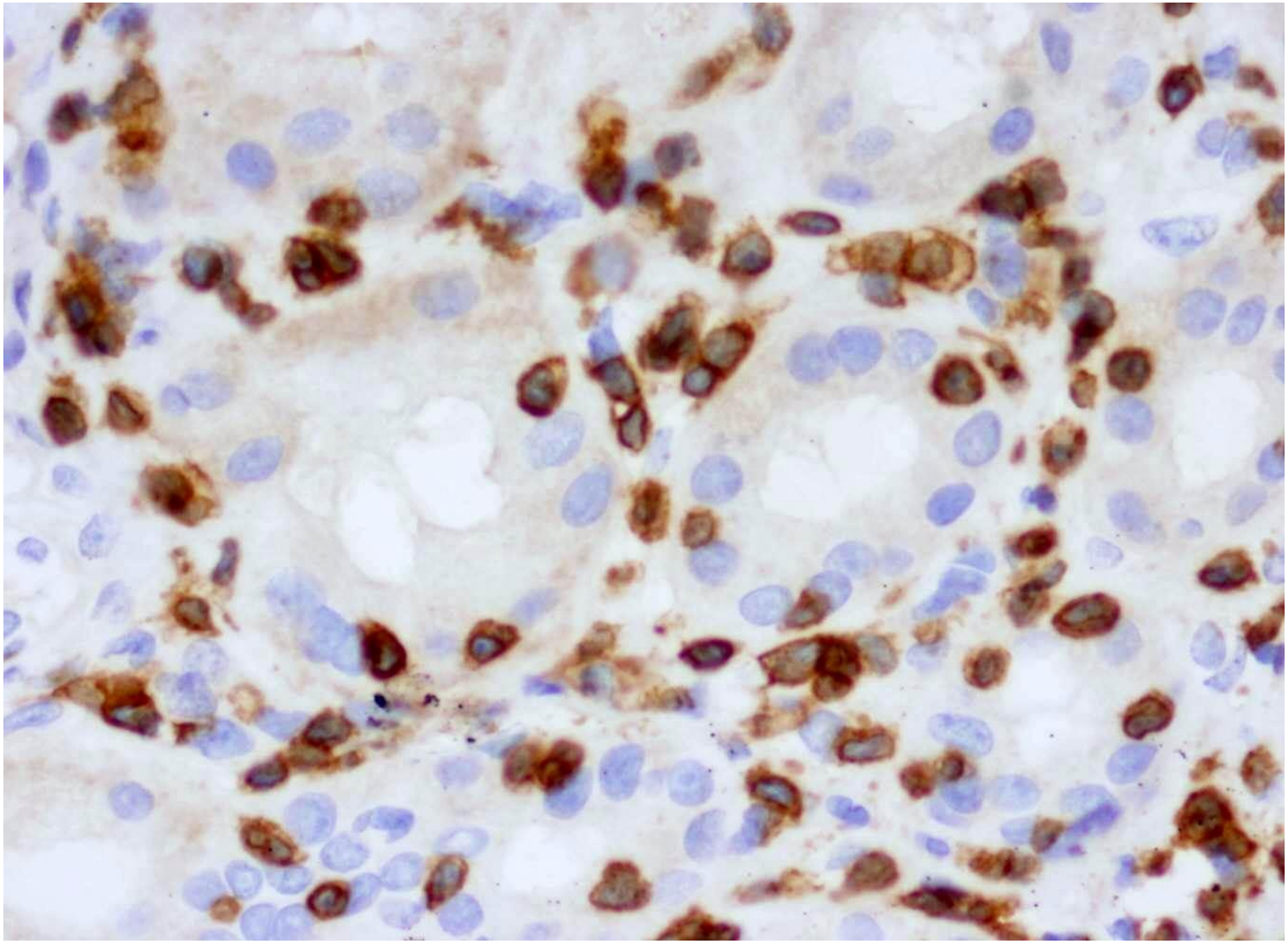

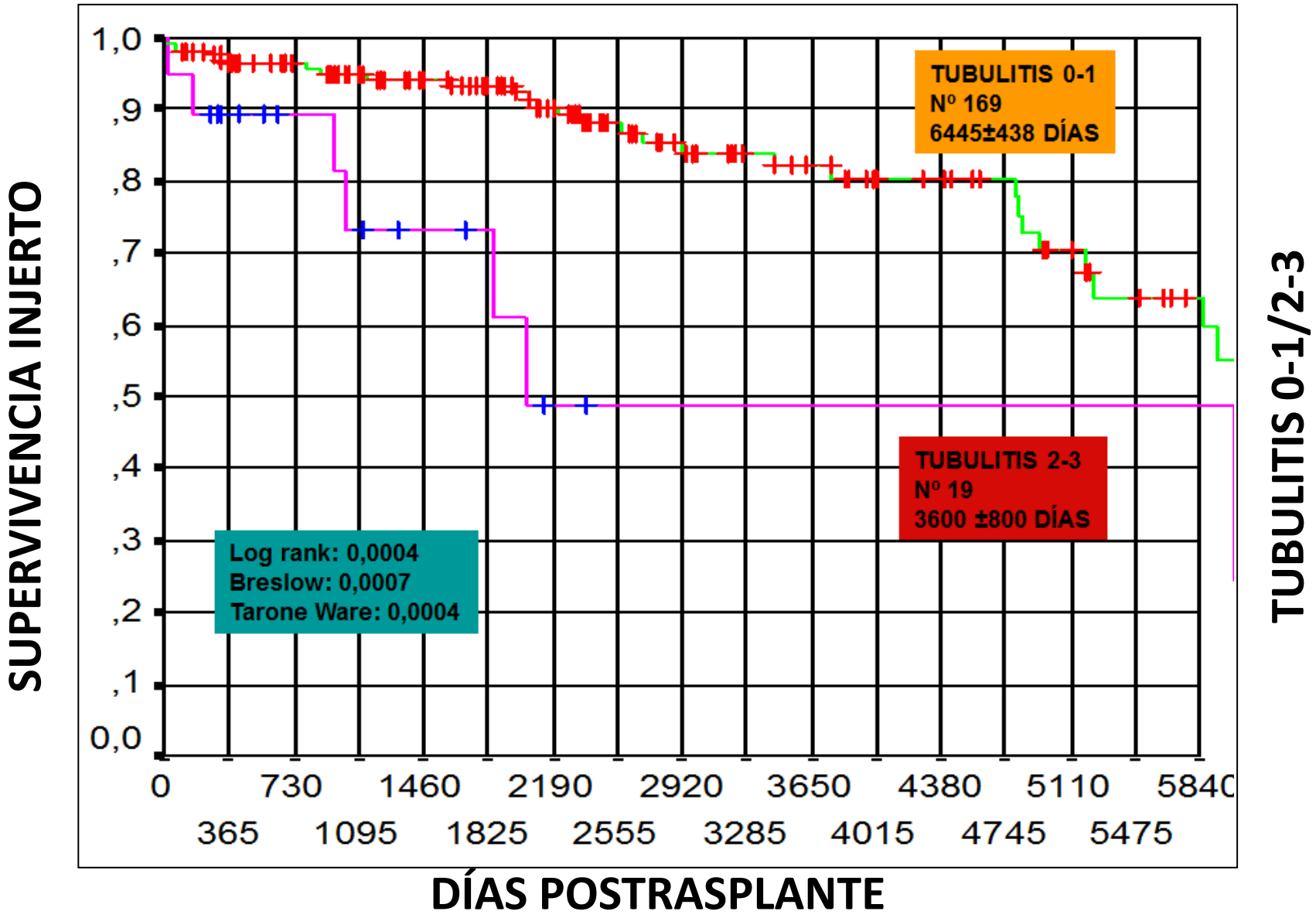
SUPERVIVENCIA INJERTO
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0,0
TUBULITIS 0-1
Nº 169
6445±438 DÍAS
TUBULITIS 2-3
Nº 19
3600 ±800 DÍAS
Log rank: 0,0004
Breslow: 0,0007
Tarone Ware: 0,0004
0
730
1460
2190
2920
3650
4380
5110
5840
365
1095
1825
2555
3285
4015
4745
5475
DÍAS POSTRASPLANTE
TUBULITIS 0-1/2-3

CLINICAL AND TRANSLATIONAL RESEARCH

The Severity of Acute Cellular Rejection Defined by Banff Classification Is Associated With Kidney Allograft Outcomes

Kaiyin Wu,[1] Klemens Budde,[1] Huber Lu,[1] Danilo Schmidt,[1] Lutz Liefeldt,[1] Petra Glander,[1] Hans Helmut Neumayer,[1] and Birgit Rudolph[2,3]

Background. It is unclear if the severity or the timing of acute cellular rejection (ACR) defined by Banff classification 2009 is associated with graft survival.

Methods. Borderline changes, TCMR I (interstitial rejection), and TCMR II/III (vascular rejection) were defined as low, moderate, and high ACR severity, respectively. Approximately 270 patients who had at least one episode of ACR were enrolled, 270 biopsies were chosen which showed the highest ACR severity of each patient and were negative for donor-specific antibodies (DSA), C4d, and microcirculation changes (MC). Six months were used as the cutoff to define early and late ACR; 370 patients without biopsy posttransplantation were recruited in the control group.

Results. Up to 8-year posttransplantation, death-censored graft survival (DCGS) rates of control, borderline, TCMR I, and TCMR II/III groups were 97.6%, 93.3%, 79.6%, and 73.6% (log rank test, $P<0.001$); the control group had significantly higher DCGS rate than the three ACR groups (each pairwise comparison yields $P<0.05$). The DCGS rate of late ACR was significantly lower compared with early ACR (63.6% vs. 87.4%, $P<0.001$). Intimal arteritis (Banff v-lesion) was an independent histologic risk factor correlated with long-term graft loss regardless of the timing of ACR. The v-lesions with minimal or high-grade tubulitis displayed similar graft survival (72.7% vs. 72.9%, $P=0.96$).

Conclusion. All types of ACR affect long-term graft survival. Vascular or late ACR predict poorer graft survival; the extent of tubulointerstitial inflammation (TI) is of no prognostic significance for vascular rejection.

Keywords: Kidney transplantation, Acute cellular rejection, Banff classification, Graft outcome.

(*Transplantation* 2014;97: 1146–1154)

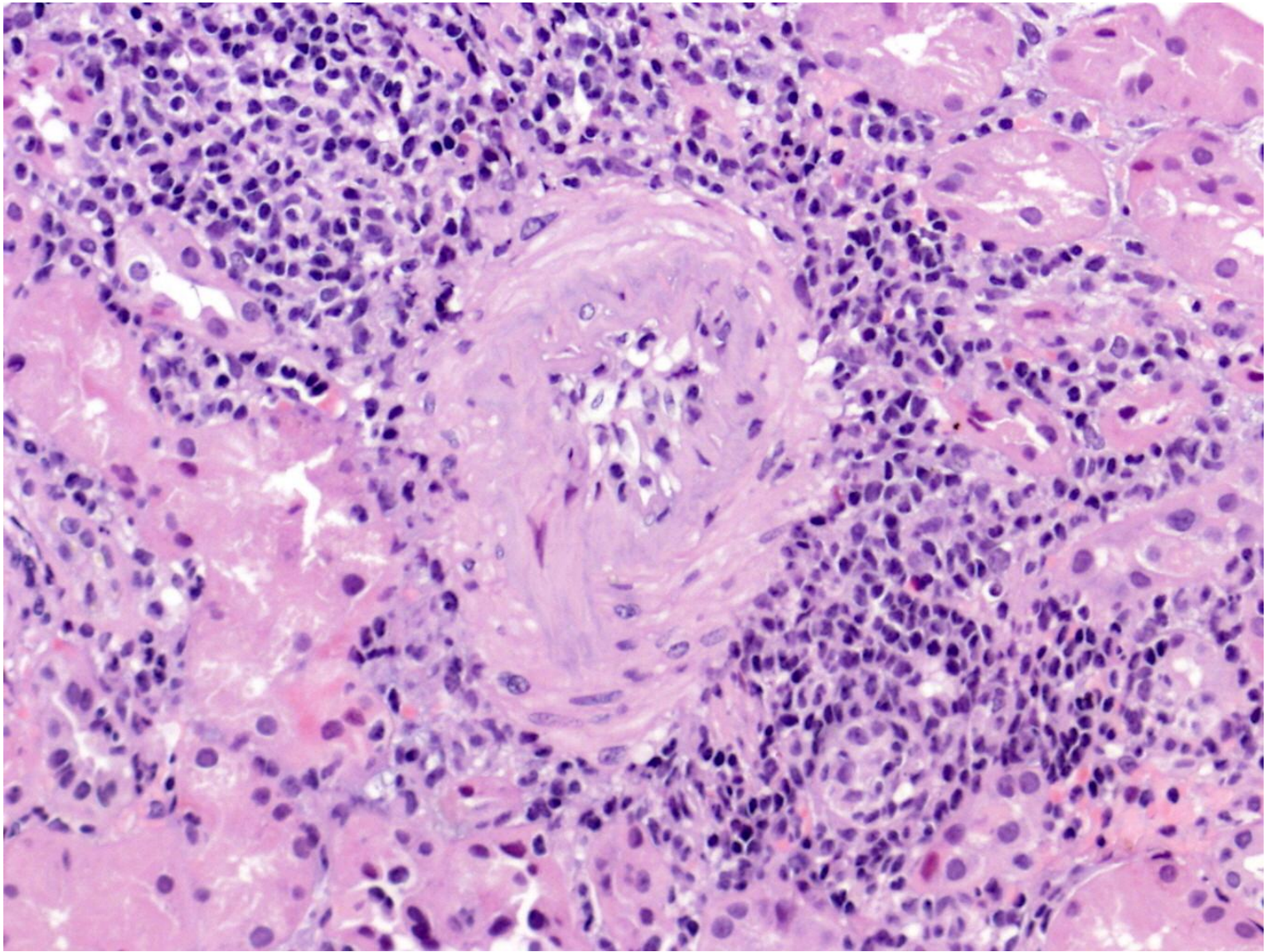
Part B: Comparison between early and late ACR in three groups

	Scores of lesions (mean±SD)							
	Overall		Borderline		TCMR I		TCMR II/III	
	Early (n=215)	Late (n=55)	Early (n=76)	Late (n=14)	Early (n=77)	Late (n=31)	Early (n=62)	Late (n=10)
mm (0–3)	0.1±0.3	0.2±0.4$^{\Delta}$	0.1±0.3	0.1±0.3	0.1±0.4	0.2±0.4	0.0±0.2	0.2±0.4$^{\Delta}$
v (0–3)	0.4±0.7	0.3±0.7	0.0±0.0	0.0±0.0	0.0±0.0	0.0±0.0	1.3±0.5$^{B, C}$	1.5±0.7$^{D, E}$
ah (0–3)	0.7±0.9	1.3±1.0$^{\#}$	0.7±0.9	1.1±0.8	0.8±0.9	1.4±1.1$^{\#}$	0.7±0.9	1.6±1.1$^{\#}$
cv (0–3)	1.0±1.0	1.4±1.0$^{\Delta}$	1.0±0.9	1.2±1.1	0.9±0.9	1.2±1.0	1.2±1.0	2.2±0.6$^{\#, d, E}$
i (0–3)	1.9±0.6	2.1±0.6$^{\#}$	1.5±0.5	1.5±0.5	2.2±0.5^{B}	2.3±0.4^{D}	2.0±0.6^{B}	2.4±0.5^{D}
t (0–3)	1.7±0.7	2.1±0.8$^{\#}$	1.0±0.1	1.0±0.2	2.3±0.5^{B}	2.4±0.5^{D}	1.8±0.8$^{B, C}$	2.4±0.5$^{\Delta, D}$
ci/ct (0–3)	0.1±0.4	1.1±0.9$^{\#}$	0.1±0.2	0.6±0.6$^{\#}$	0.2±0.4	1.1±1.0$^{\#}$	0.2±0.4	1.8±0.8$^{\#, D}$

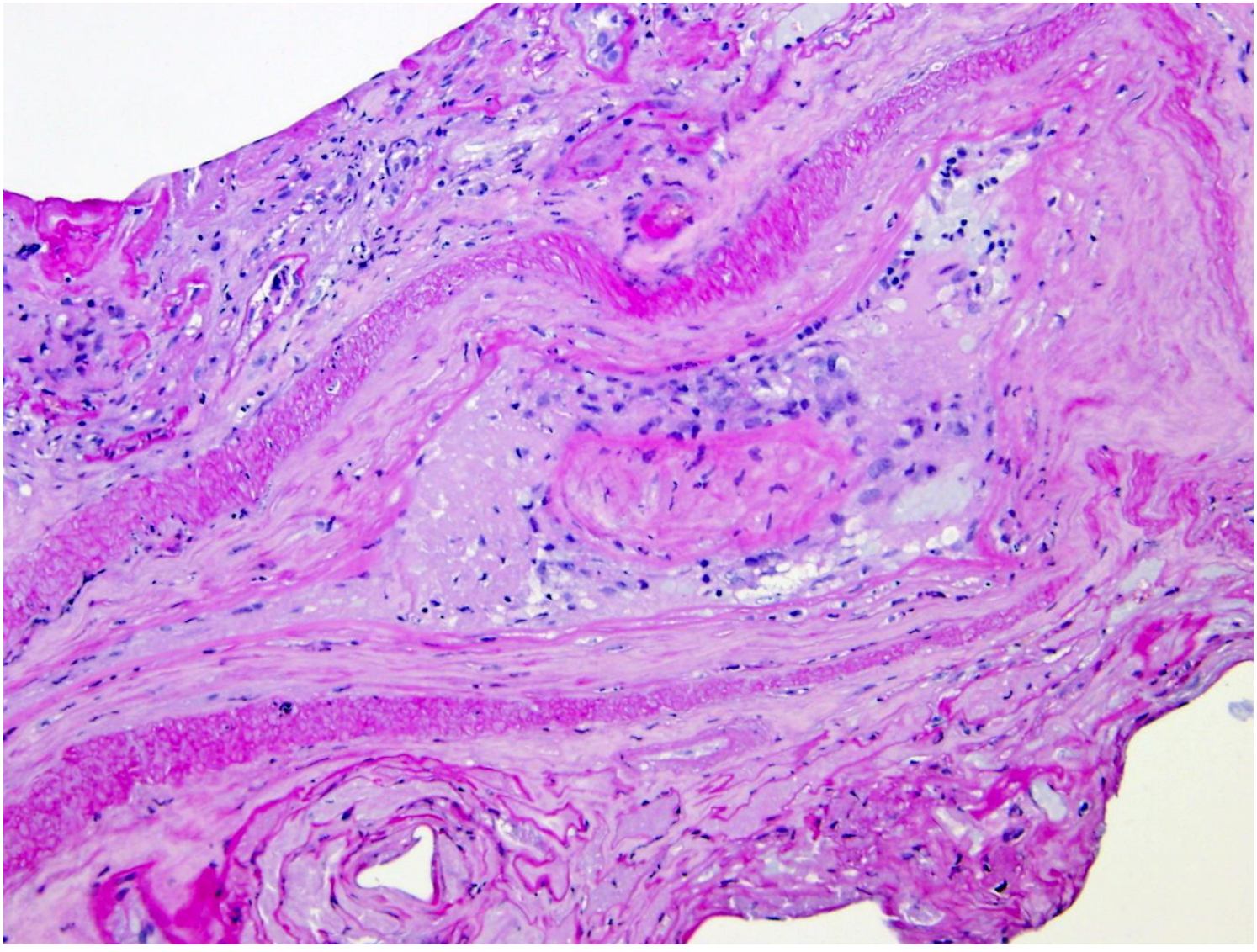
CONCLUSIÓN:

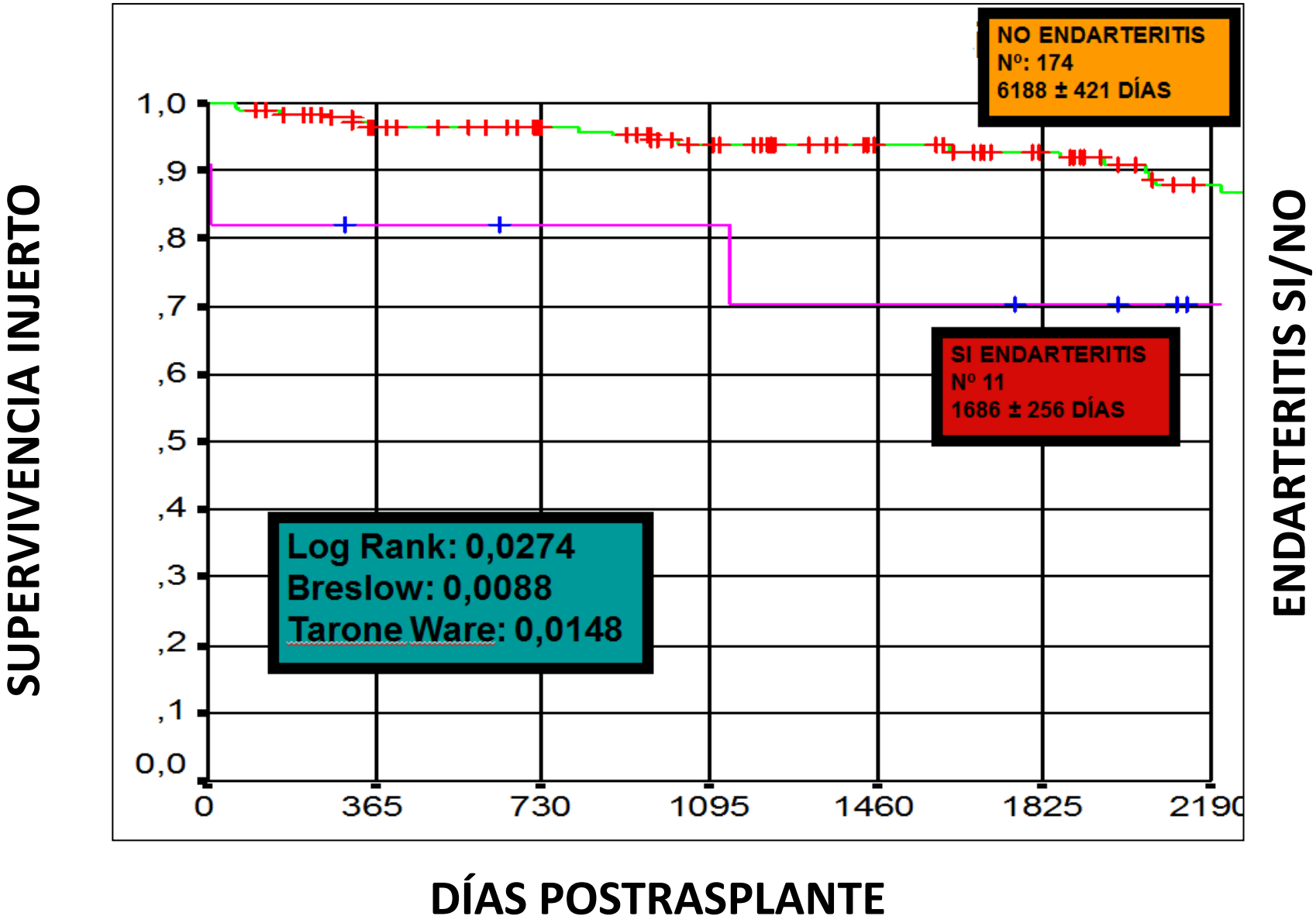
1. ***NO EXISTEN EVIDENCIAS SUFICIENTES PARA AFIRMAR QUE LA INTENSIDAD DEL INFILTRADO INFLAMATORIO TENGA INFLUENCIA EN EL PRONÓSTICO A LARGO PLAZO DEL INJERTO RENAL.***
2. ***RESPECTO A LA TUBULITIS, AUNQUE EXISTE RELACIÓN, PROBABLEMENTE ESTÁ SUBROGADA A LA INTENSIDAD DEL RECHAZO AGUDO CONCOMITANTE.***

ARTERITIS INTIMAL



ARTERITIS INTIMAL




NO ENDARTERITIS
Nº: 174
6188 ± 421 DÍAS
SI ENDARTERITIS
Nº 11
1686 ± 256 DÍAS
Log Rank: 0,0274
Breslow: 0,0088
Tarone Ware: 0,0148
1,0
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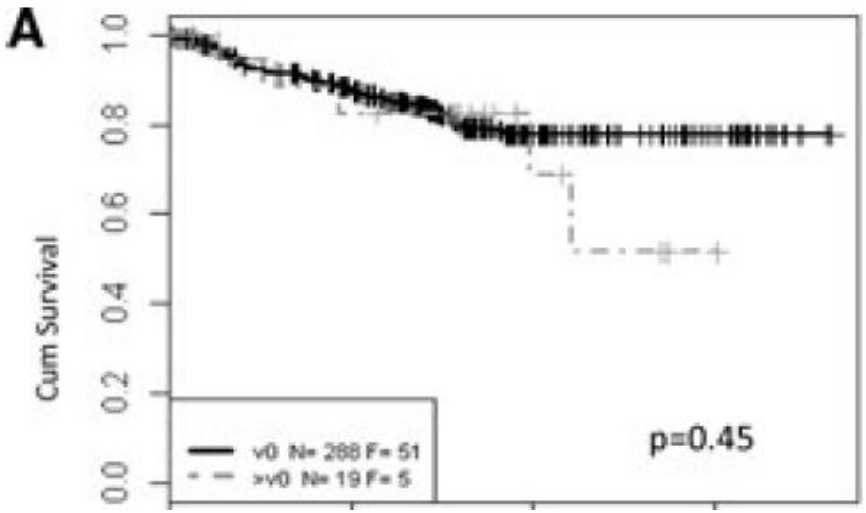
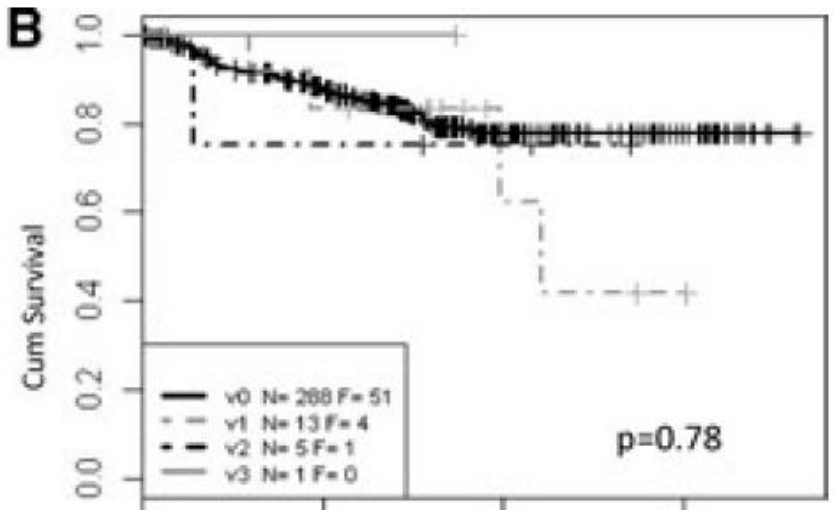
DÍAS POSTRASPLANTE





American Journal of Transplantation 2011; 11: 489–499
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2010.03415.x

Inflammation Lesions in Kidney Transplant Biopsies: Association with Survival Is Due to the Underlying Diseases

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Abbreviations: ABMR, antibody-mediated rejection; ATN, acute tubular necrosis; BFC, biopsy for clinical indications; GN, glomerulonephritis; IFTA, interstitial fibrosis and tubular atrophy; TCMR, T-cell-mediated

CLINICAL AND TRANSLATIONAL RESEARCH

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Results. Up to 8-year posttransplantation, death-censored graft survival (DCGS) rates of control, borderline, TCMR I, and TCMR II/III groups were 97.6%, 93.3%, 79.6%, and 73.6% (log rank test, $P<0.001$); the control group had significantly higher DCGS rate than the three ACR groups (each pairwise comparison yields $P<0.05$). The DCGS rate of late ACR was significantly lower compared with early ACR (63.6% vs. 87.4%, $P<0.001$). Intimal arteritis (Banff v-lesion) was an independent histologic risk factor correlated with long-term graft loss regardless of the timing of ACR. The v-lesions with minimal or high-grade tubulitis displayed similar graft survival (72.7% vs. 72.9%, $P=0.96$).

Conclusion. All types of ACR affect long-term graft survival. Vascular or late ACR predict poorer graft survival; the extent of tubulointerstitial inflammation (TI) is of no prognostic significance for vascular rejection.

Keywords: Kidney transplantation, Acute cellular rejection, Banff classification, Graft outcome.

(*Transplantation* 2014;97: 1146–1154)

TABLE 4. The Banff lesions associated with graft failure at 8-year posttransplantation based on Cox proportional hazard analysis

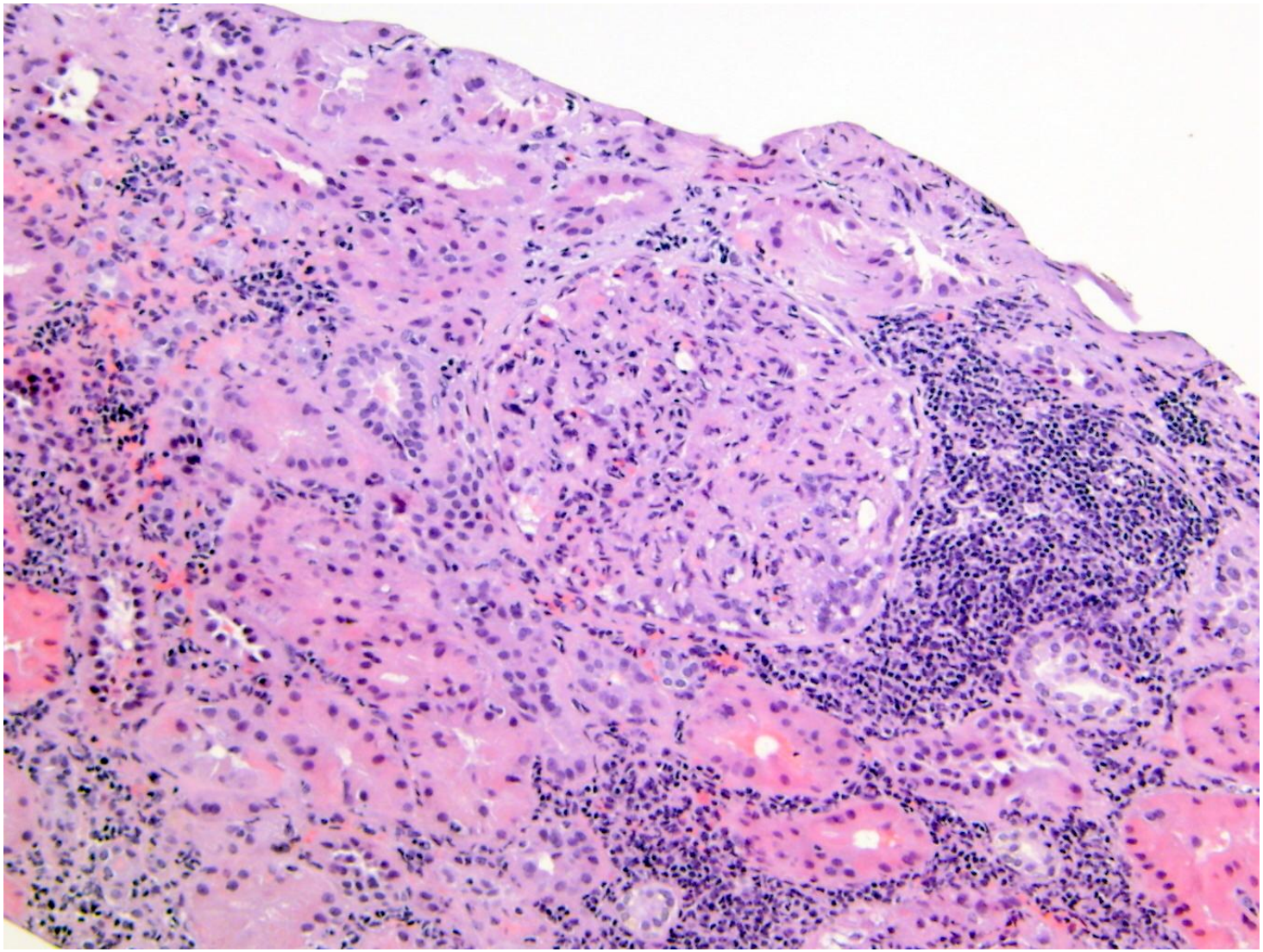
Univariate analysis (all ACR n=270)					Univariate analysis (early ACR n=215)					Univariate analysis (late ACR n=55)				
Lesions (0–3)	HR	95% CI		*P*	Lesions (0–3)	HR	95% CI		*P*	Lesions (0–3)	HR	95% CI		*P*
v	1.7	1.3	2.3	<0.001	v	1.7	1.3	2.4	0.001	v	2.1	1.3	3.2	0.001
ci/ct	1.6	1.2	2.0	**0.001**	t	1.7	1.2	2.6	**0.005**	cv	1.9	1.1	3.2	**0.03**
t	1.7	1.3	2.4	**0.001**	ci/ct	2.0	1.2	3.3	**0.009**	t	1.4	0.8	2.5	0.23
mm	2.0	1.2	3.4	**0.008**	mm	1.8	0.9	3.5	0.07	mm	1.8	0.8	4.5	0.23
ah	1.3	1.1	1.6	**0.01**	ah	1.3	1.0	1.7	0.08	i	1.5	0.7	3.3	0.26
cv	1.3	1.0	1.7	**0.02**	i	1.2	0.8	2.1	0.38	ci/ct	1.2	0.8	1.9	0.38
i	1.4	0.9	2.1	0.09	cv	1.0	0.8	1.4	0.77	ah	1.1	0.7	1.7	0.59
Multivariate analysis (all ACR n=270)					**Multivariate analysis (early ACR n=215)**					**Multivariate analysis (late ACR n=55)**				
Lesions (0–3)	HR	95% CI		P-Value	Lesions (0–3)	HR	95% CI		P-Value	Lesions (0–3)	HR	95% CI		P-Value
v	1.7	1.3	2.4	<0.001	v	1.7	1.2	2.4	0.004	v	2.0	1.2	3.1	0.004
t	1.5	1.1	2.1	0.009	t	1.7	1.1	2.4	**0.009**	cv	1.4	0.8	2.5	0.24
mm	1.7	0.9	3.0	0.08	ci/ct	1.8	1.1	3.0	**0.03**					
ci/ct	1.2	0.9	1.6	0.23										
ah	1.1	0.9	1.5	0.30										
cv	1.1	0.9	1.5	0.44										

Wu K, Budde K, Lu H, Schmidt D, Liefeldt L, Glander P, Neumayer HH, Rudolph B. The severity of acute cellular rejection defined by Banff classification is associated with kidney allograft outcomes. Transplantation. 2014 15;97:1146-54

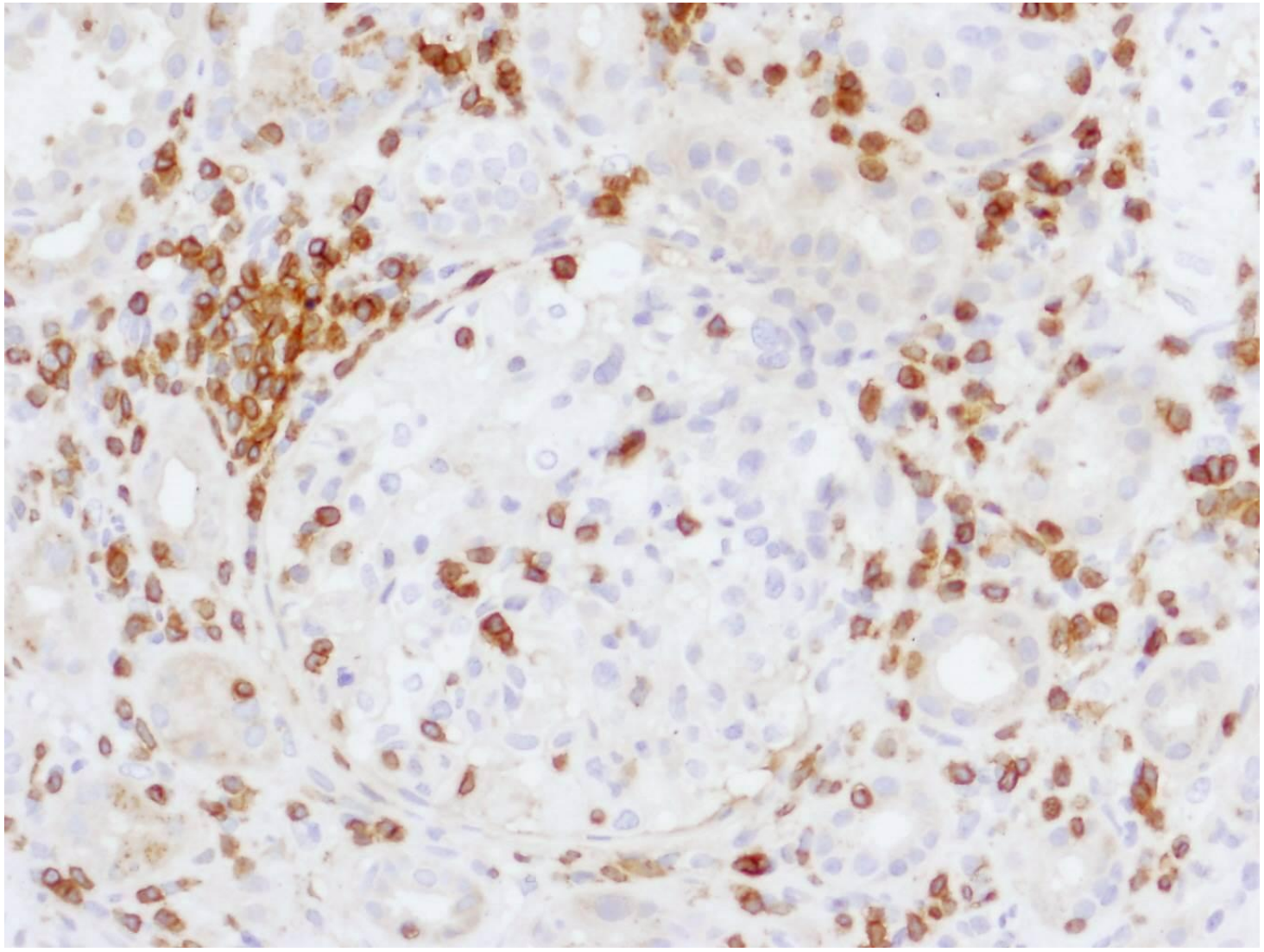
CONCLUSIÓN:

EXISTEN ALGUNAS EVIDENCIAS, AUNQUE AÚN CONTRADICTORIAS, DE QUE LA PRESENCIA DE ARTERITIS INTIMAL TIENE INFLUENCIA EN EL PRONÓSTICO A LARGO PLAZO DEL INJERTO RENAL

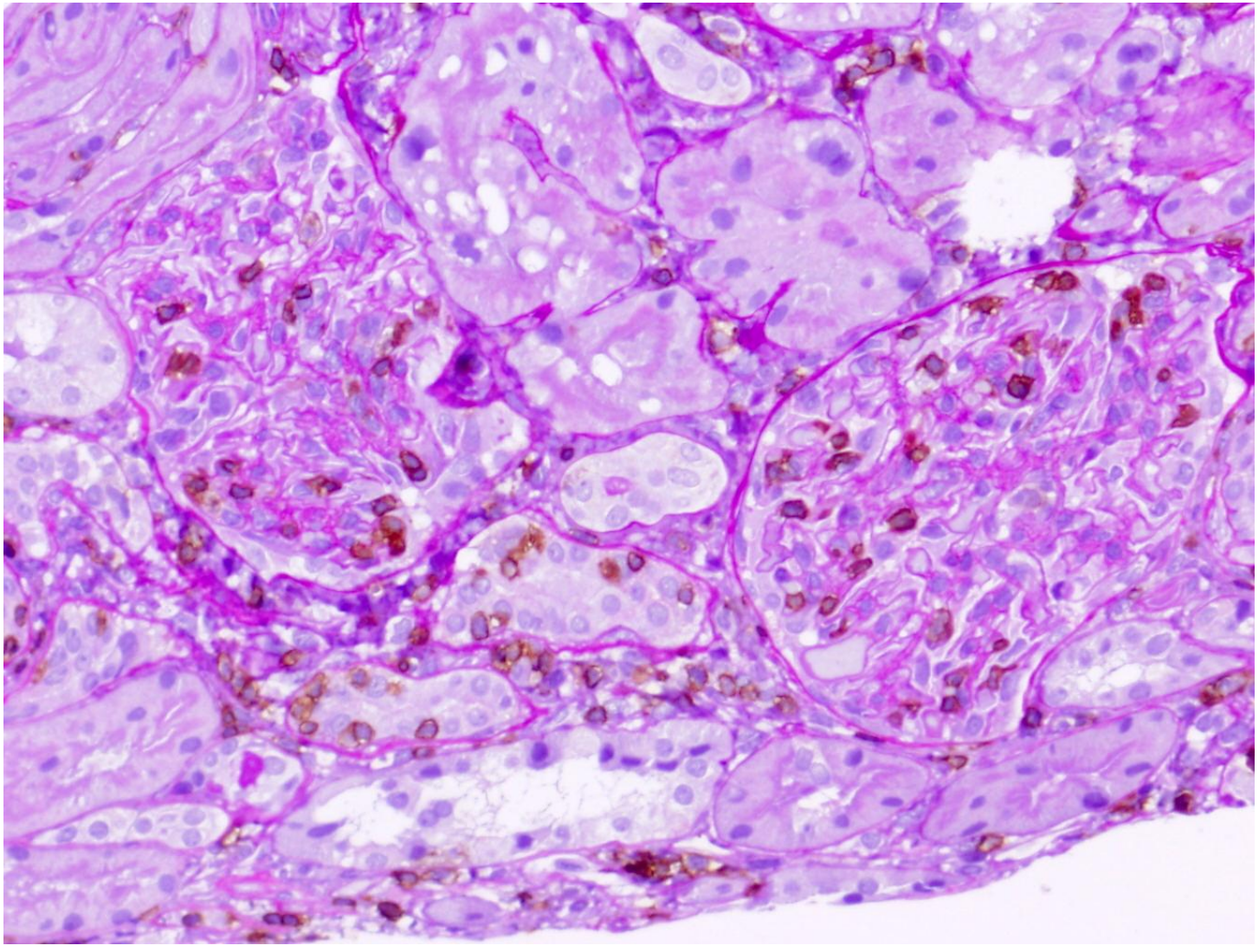
LA LESIÓN INFLAMATORIA MICROCAPILAR: GLOMERULITIS



LA LESIÓN INFLAMATORIA MICROCAPILAR: GLOMERULITIS POR IHQ



LA LESIÓN INFLAMATORIA MICROCAPILAR: GLOMERULITIS POR IHQ + PAS



ELSEVIER

Immunohistochemical Quantification of Leukocyte Subsets in the Long-Term Prognosis of Kidney Transplants

E. Vergara, M. Gómez-Morales, A. Osuna, F. O'Valle, D. Aguilar, M. Masseroli, T. Martínez, M. Higueras, J. Bravo, C. Asensio, and R.G. Del Moral

SINCE 1993 the Banff schema (BS) for acute kidney graft rejection have gained acceptance,[1] but their usefulness in predicting the long-term course of the graft is still unclear, and further revision of the assessment criteria has proved necessary.[2-5] The occurrence of acute rejection episodes is the most powerful predictive factor for the later development of chronic rejection, and many authors advocate strategies to detect and revert acute rejection episodes as early as possible.[6] Procedures to diagnose renal allograft depend on the detection of graft dysfunction and the presence of a mononuclear leukocytic infiltrate; an unequivocal identification of lymphocytes in tubulitis, glomerulitis, and intimal arteritis lesions is often difficult.[2] Moreover, the presence of modest cellular infiltrate is often not conclusive and can be detected in the nonrejecting graft.[6] For these reasons the accurate quantification of the inflammatory infiltrate may be an important complementary diagnostic parameter.

MATERIALS AND METHODS

Sixty renal transplant biopsies from patients with acute dysfunction (mean age 44.23 ± 11.68 years, 41.66% females and 58.33% males). The clinical parameters analyzed were creatinine (CR), creatinine clearance (CRC), and serum levels of cyclosporin A (CsA). Rejection type was classified using the modified Sanfilippo Classical System (SCS): glomerulo-interstitial rejection (GIR = 15 cases), interstitial rejection (IR = 27 cases), vasculo-interstitial rejection (VIR = 16 cases), and undetermined (2 cases).[7] The severity by BS[1] was borderline in 8 cases, grade I in 12, grade II in 18, and grade III in 15, and 7 biopsies were inadequate for diagnosis. The leukocyte subsets CD3, CD4, CD8, CD16, CD25 (Dakopatts, Glostrup, Denmark), CD45, CD20, CD57, and CD68 (Master Diagnóstica, Granada, Spain) were quantified in 4 μm cryostat sections using the streptavidin-biotin-alkaline-phosphatase method (Master Diagnóstica). Separate evaluations were done of the subsets present in the glomeruli (mean of cells/glomerulus) and of the infiltrates in interstitium (mean of cells/mm^2). Statistical analysis used standard tests; the log-rank test (LR) was used for survival curves.

RESULTS AND DISCUSSION

The severity of the rejection as graded by the SCS or BS systems did not correlate with clinical or analytical parameters. In contrast, the SCS-graded severity of the rejection correlated with the number of inflammatory cells in the glomerulus that were positive for CD45, CD4, CD3 ($P < .001$); CD8, CD68 ($P < .01$); CD16 ($P < .05$) (Table 1). In the interstitium, however, severity only correlated with CD20+ cells ($P < .05$) (Table 1).

Interestingly, when we used BS to grade the acute rejection, there was only correlation with the number of CD45+ cells in the interstitium ($P < .05$)(Table 1). These results show that the phenotyping and quantifying of the inflammatory infiltrate in acute rejection may complement the evaluation of renal allograft biopsies by BS because they allow easier recognition and characterization of the presence of tubulitis, assess glomerulitis, and provide more reproducible results. In this context, Solez et al[8] reported that for difficult and equivocal cases it would be useful to have additional techniques, including immunostaining for CD45.

In relation to the prognosis of the renal graft, the most relevant clinical data were serum levels of CsA >200 and <200 ng/mL (LR, $P < .05$). Of significant utility (LR, $P < .01$) in the long-term prognosis of the renal allograft were the following glomerular leukocyte populations classified in three categories (Fig 1): CD4$^+$, CD3$^+$, CD57$^+$, CD68$^+$, and CD16$^+$. The only infiltrating leukocyte populations in the interstitium that showed significance were the CD57$^+$ ($P < .01$) and CD16$^+$ cells (LR, $P < .05$) (Fig 1).

In diagnosing early acute rejection, the BS system shows greater reproducibility than a conventional approach but does not produce more correct diagnoses because the BS concentrates on tubulitis and arteritis and ignores other features of possible benefit.[9] In summary, the BS is highly useful to grade the severity of acute rejection lesions, but

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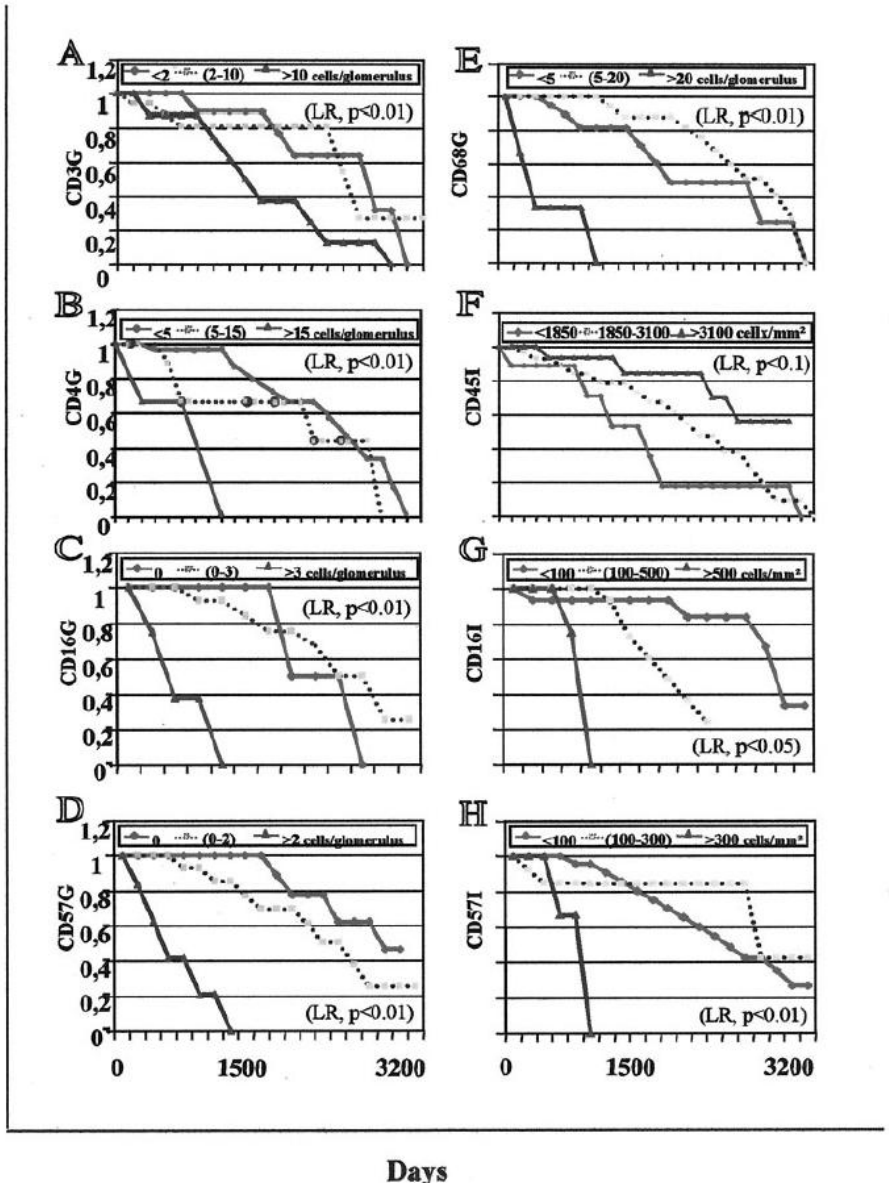
Address reprint requests to Dr Raimundo G. del Moral, Department of Pathology, School of Medicine, Avda de Madrid 11 E-18012, Granada, Spain.

0041-1345/98/$19.00
PII S0041-1345(98)00661-7



CLINICAL AND TRANSLATIONAL RESEARCH

Glomerular Inflammation in Renal Allografts Biopsies After the First Year: Cell Types and Relationship With Antibody-Mediated Rejection and Graft Outcome

John C. Papadimitriou,[1,4] Cinthia B. Drachenberg,[1] Raghava Munivenkatappa,[2] Emilio Ramos,[3] Joseph Nogueira,[3] Charles Sailey,[1] David K. Klassen,[3] and Abdolreza Haririan[3]

Background. Antibody-mediated rejection manifests with glomerular and peritubular capillary inflammation and transplant glomerulopathy (TG). The role of glomerular inflammation (GI) components in the development of TG and their impact on outcome are incompletely understood.

Methods. GI was quantified on hematoxylin-eosin, CD3, CD20, and CD68 stains on biopsies from 240 patients with grafts functioning more than or equal to 1 year.

Results. A predominance of $CD68^+$ cells followed by less numerous $CD3^+$ cells was found in TG and glomerulitis. $CD68^+$ cells more than 12 in the most inflamed glomerulus were strongly associated with TG, donor-specific antibody (DSA), and C4d staining. Glomerular $CD68^+$ cells correlated with peritubular capillary multilamellation, and similarly, the Banff g score correlated with light and electron microscopic indexes of chronic microvascular damage. Overall, GI components correlated with the g score, DSA, and peritubular capillary $C4d^+$. The Banff cg 1, 2, and 3 scores showed high levels of GI composed mostly of $CD68^+$ cells, similar to but not higher than cases of g2 and g3 glomerulitis. Glomerular T cells and neutrophils followed similar trends as the predominant macrophages. T-cell–mediated rejection in this cohort did not significantly affect the composition of GI. Prognostically, all types of pronounced GI, g scores, DSA^+, $C4d^+$, and capillaropathy were associated with worse prognosis; however, only high level of macrophages was an independent predictor of graft failure.

Conclusions. GI in more than or equal to 1 year grafts is mostly antibody-mediated rejection related, correlates with chronic microvascular damage, and consists predominantly of macrophages. The latter seem to represent a pivotal pathogenetic, diagnostic, and prognostic factor in this setting.

Keywords: Glomerulitis, Macrophages, CD68, Transplant glomerulopathy, Graft failure, Glomerulonephritis, Diabetes mellitus, Thrombotic microangiopathy, Hepatitis C, Ischemia.

(*Transplantation* 2010;90: 1478–1485)

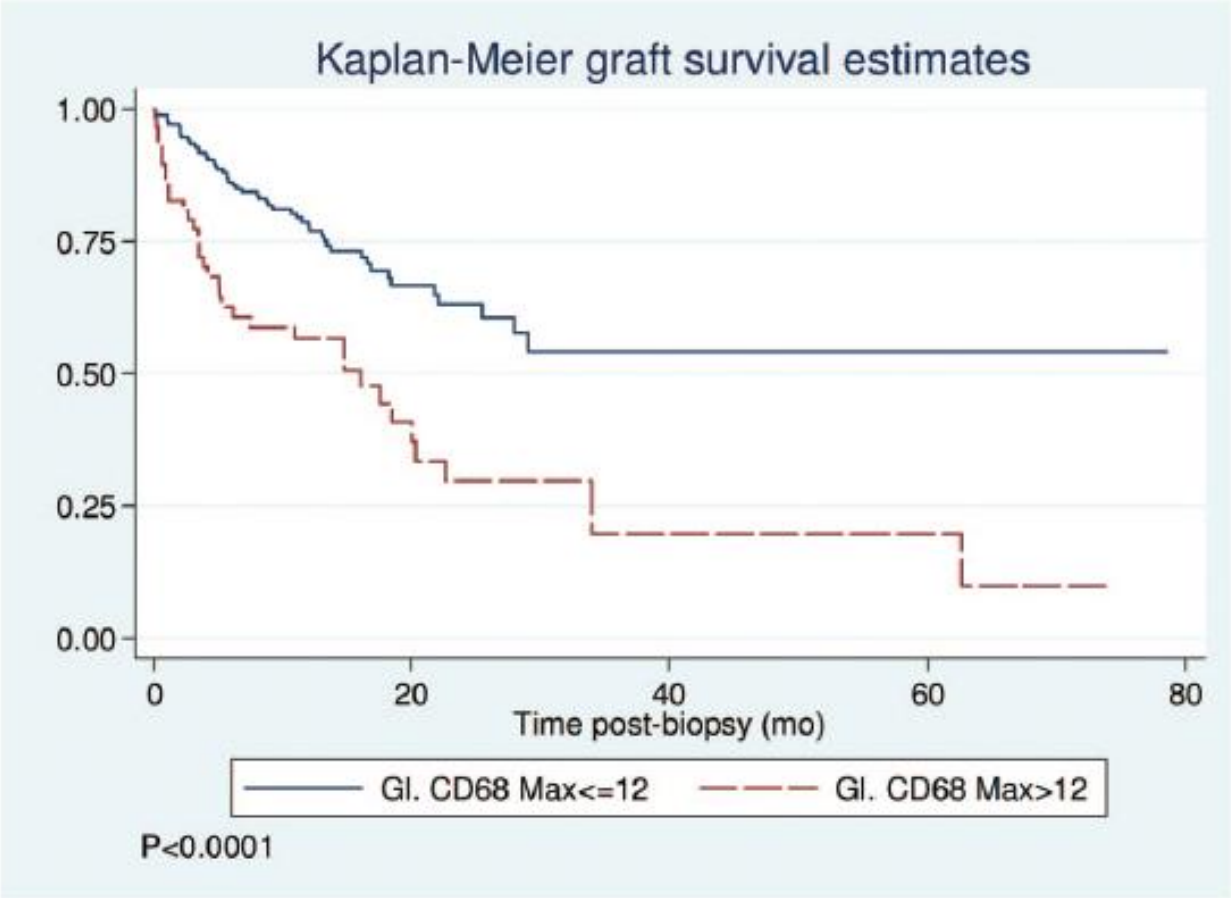
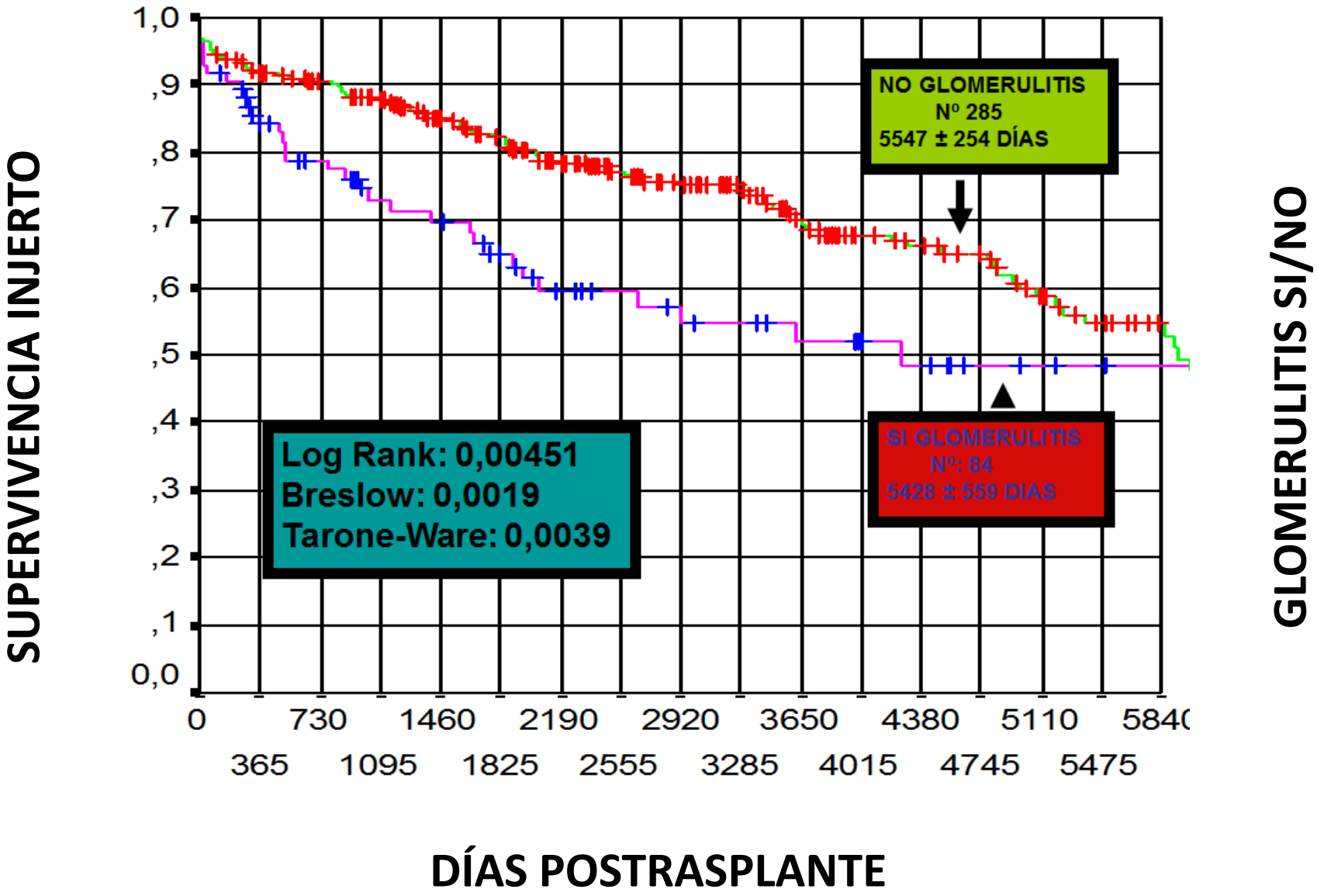


FIGURE 3. Graft survival estimates postbiopsy by presence or absence of $CD68_{Max}$ more than 12. GI, glomerular inflammation.

Papadimitriou et al. Transplantation, 2010, 90: 1478-85


SUPERVIVENCIA INJERTO
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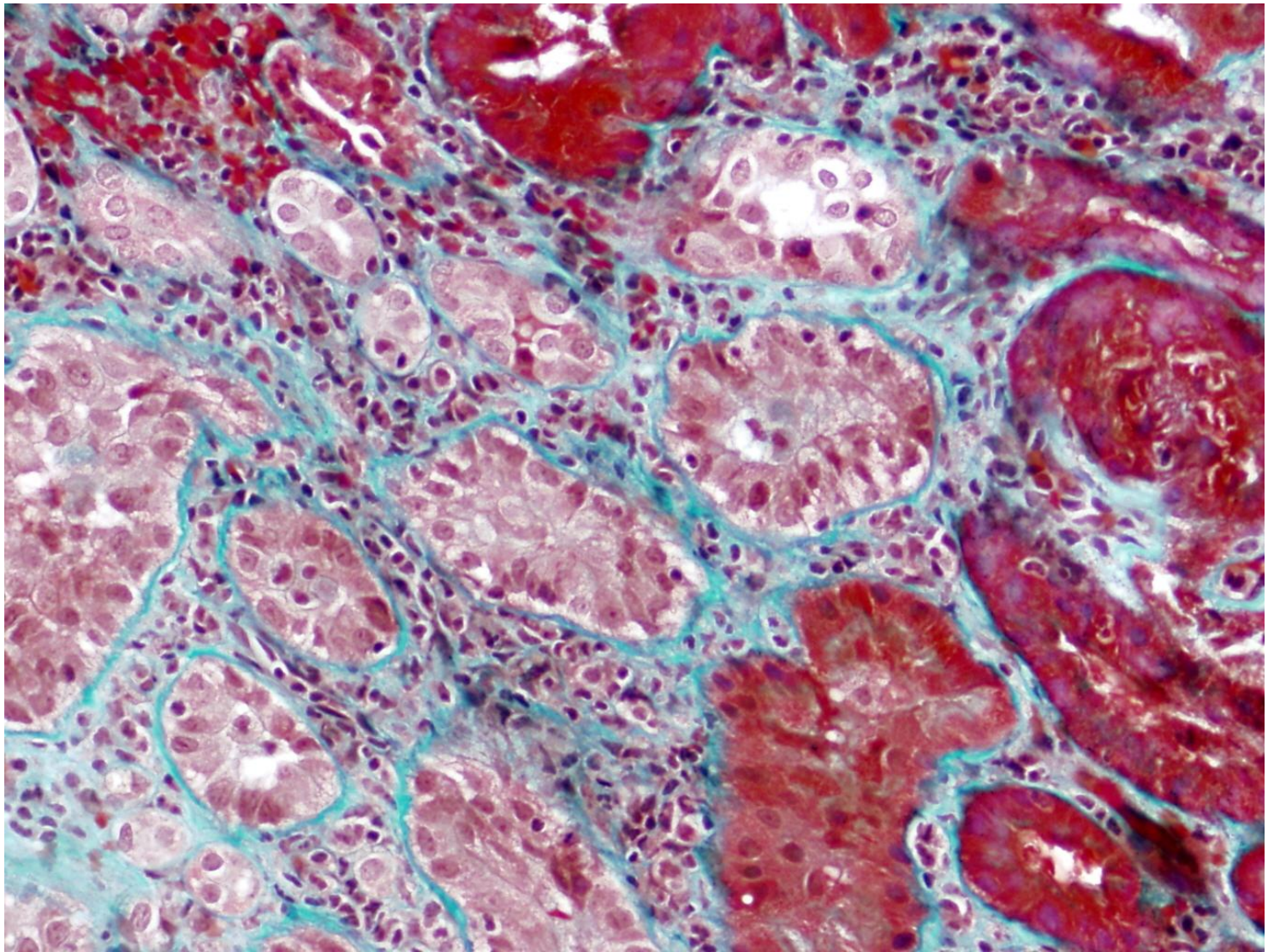
NO GLOMERULITIS
Nº 285
5547 ± 254 DÍAS
SI GLOMERULITIS
Nº: 84
5428 ± 559 DIAS
Log Rank: 0,00451
Breslow: 0,0019
Tarone-Ware: 0,0039
0
730
1460
2190
2920
3650
4380
5110
365
1095
1825
2555
3285
4015
4745
5475
GLOMERULITIS SI/NO
DÍAS POSTRASPLANTE

CONCLUSIÓN:

EXISTEN EVIDENCIAS DE QUE LA PRESENCIA DE GLOMERULITIS, ESENCIALMENTE POR CÉLULAS CON FENOTIPO CD68+, TIENE MUY FUERTE INFLUENCIA EN EL PRONÓSTICO A LARGO PLAZO DEL INJERTO RENAL

LA LESIÓN INFLAMATORIA MICROCAPILAR: CAPILARITIS PERITUBULAR



American Journal of Transplantation 2008; 8: 819–825
Blackwell Munksgaard

doi: 10.1111/j.1600-6143.2007.02137.x

Peritubular Capillaritis in Renal Allografts: Prevalence, Scoring System, Reproducibility and Clinicopathological Correlates

I. W. Gibson[a,*], W. Gwinner[b], V. Brőcker[c], B. Sis[d,e], J. Riopel[d], I.S.D. Roberts[f], I. Scheffner[b], G. S. Jhangri[g] and M. Mengel[c,e]

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[b]*Department of Nephrology, Medizinische Hochschule Hannover, Hannover, Germany*
[c]*Medizinische Hochschule Hannover, Institute for Pathology, Hannover, Germany*
[d]*Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Canada*
[e]*Division of Nephrology & Immunology, Department of Medicine, Alberta Transplant Applied Genomics Centre, University of Alberta, Edmonton, Canada*
[f]*Department of Cellular Pathology, John Radcliffe Hospital, Oxford, United Kingdom*
[g]*Department of Public Health Sciences, School of Public Health, University of Alberta, Edmonton, Canada*
**Corresponding author: Ian Gibson, IGibson@exchange.hsc.mb.ca*

observed in TCMR cases. Thus, scoring of peritubular capillaritis is feasible and can provide prognostic and diagnostic information in renal allograft biopsies.

Key words: Peritubular capillary, rejection, renal transplantation

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Introduction

The primary target of circulating antidonor HLA antibodies in the setting of antibody-mediated rejection (ABMR) is the endothelium of the allograft microcirculation i.e. in renal transplants, the glomerular and peritubular capillaries (PTC) (1). Luminal accumulation of inflammatory cells in PTC, i.e. peritubular capillaritis, is a lesion that has been previously associated with ABMR in renal allografts (2–4). Numerous studies have shown that peritubular cap-

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Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2011.03931.x

A New Diagnostic Algorithm for Antibody-Mediated Microcirculation Inflammation in Kidney Transplants

B. Sis[a,b,*], G. S. Jhangri[c], J. Riopel[a], J. Chang[b,d], D. G. de Freitas[b,d], L. Hidalgo[a,b], M. Mengel[a,b], A. Matas[e] and P. F. Halloran[b,d]

[a]*Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Alberta, Canada*
[b]*Alberta Transplant Applied Genomics Centre, University of Alberta, Edmonton, Alberta, Canada*
[c]*School of Public Health, University of Alberta, Edmonton, Alberta, Canada*
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antigen; TCMR, T-cell-mediated rejection; TG, transplant glomerulopathy.

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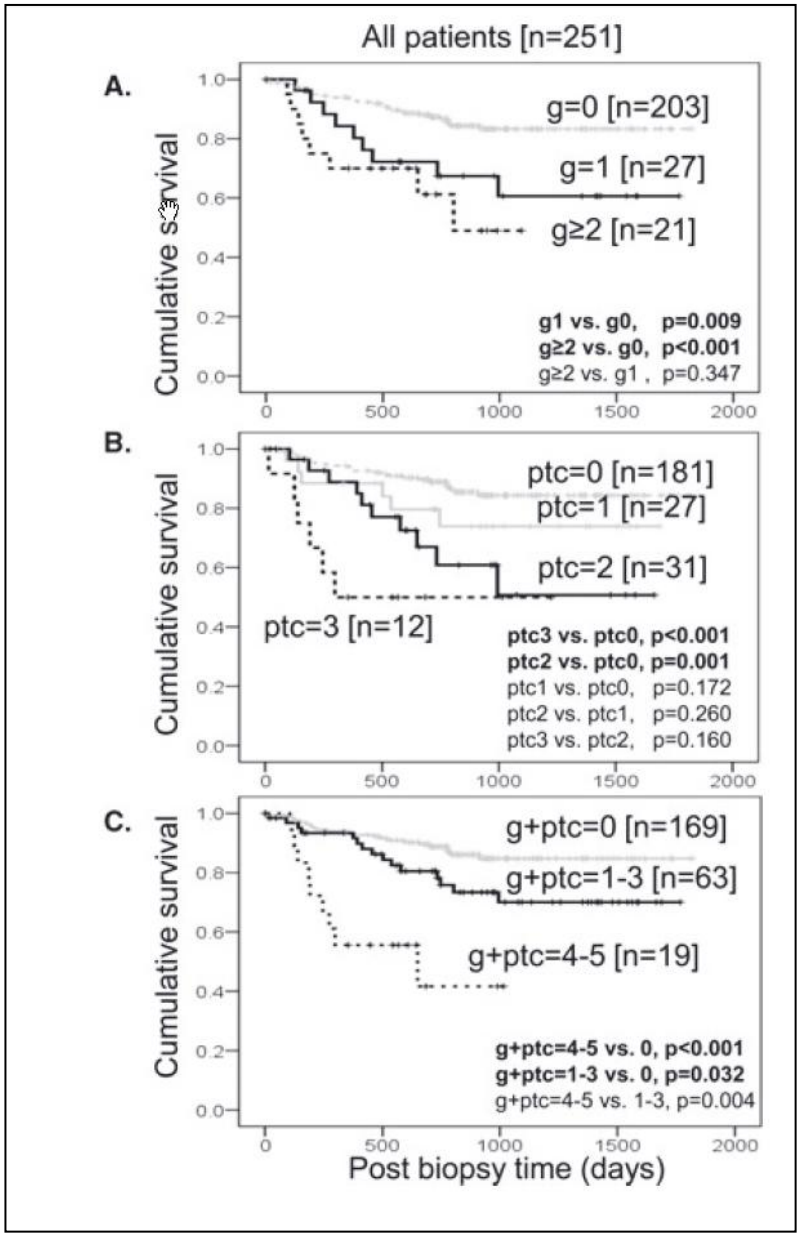
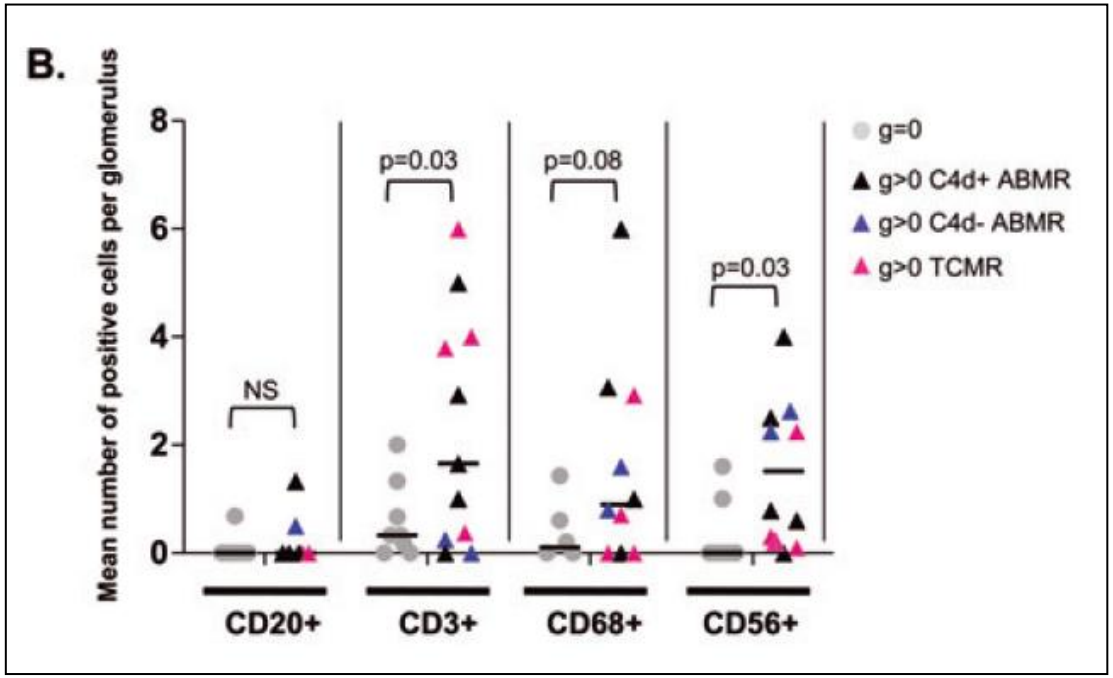
Introduction

Microcirculation inflammation (glomerulitis [g], peritubular capillaritis [ptc]) in kidney transplants is defined as intraluminal accumulation of inflammatory cells in glomerular or peritubular capillaries (1–3). Microcirculation inflammation was the first histological feature used to diagnose delayed acute antibody-mediated rejection (ABMR; 4,5), followed by the discovery of C4d staining (6–8). Accord-

La biopsia del implante renal: tiene valor pronóstico? RGM

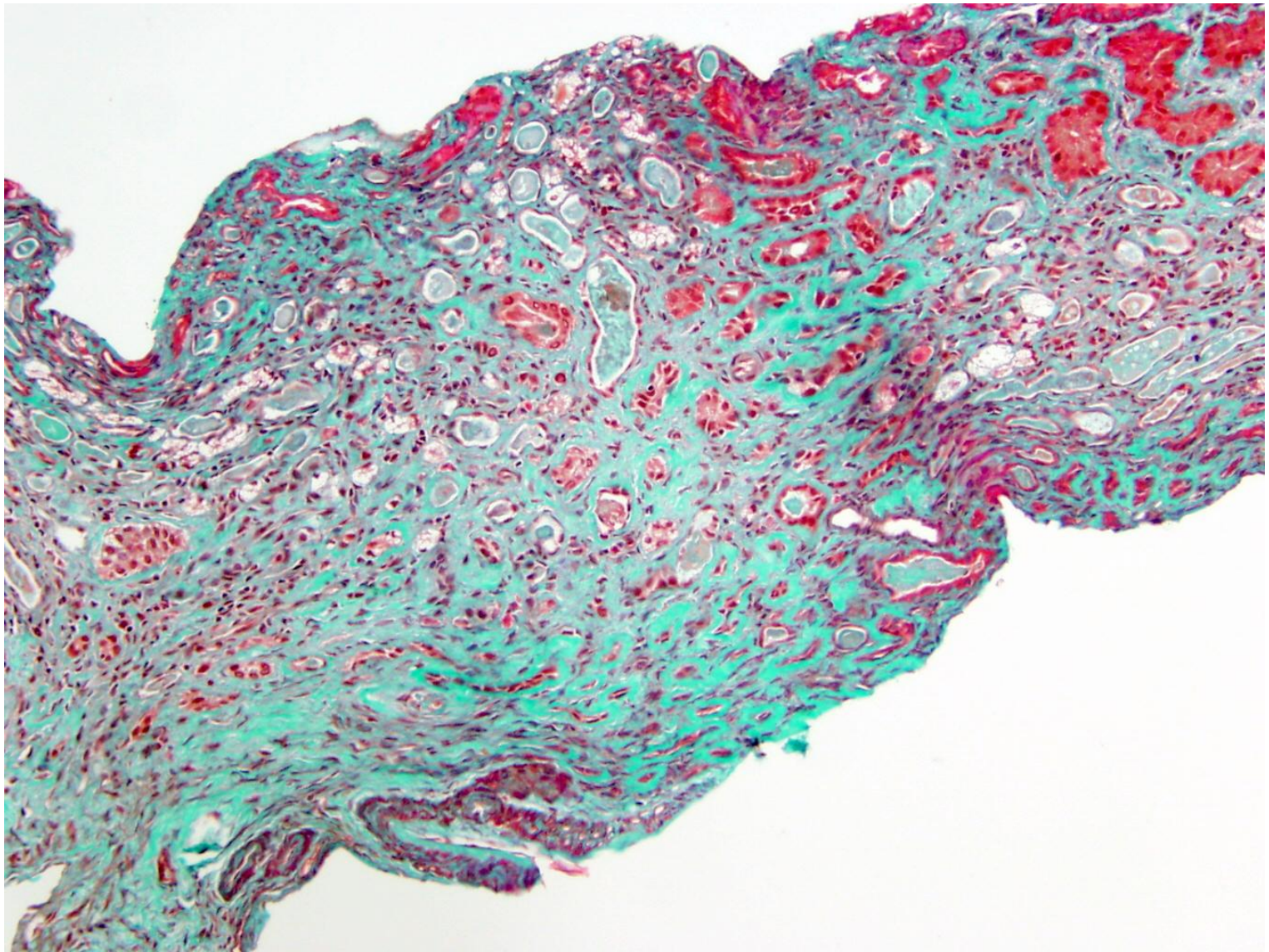




CONCLUSIÓN:

EXISTEN EVIDENCIAS DE QUE LA PRESENCIA DE CAPILARITIS PERITUBULAR AISLADA O ASOCIADA A GLOMERULITIS TIENE INFLUENCIA EN EL PRONÓSTICO A LARGO PLAZO DEL INJERTO RENAL

LA FIBROSIS INTERSTICIAL/ATROFIA TUBULAR (IF/TA)



LA FIBROSIS INTERSTICIAL/ATROFIA TUBULAR (IF/TA)

The NEW ENGLAND JOURNAL of MEDICINE

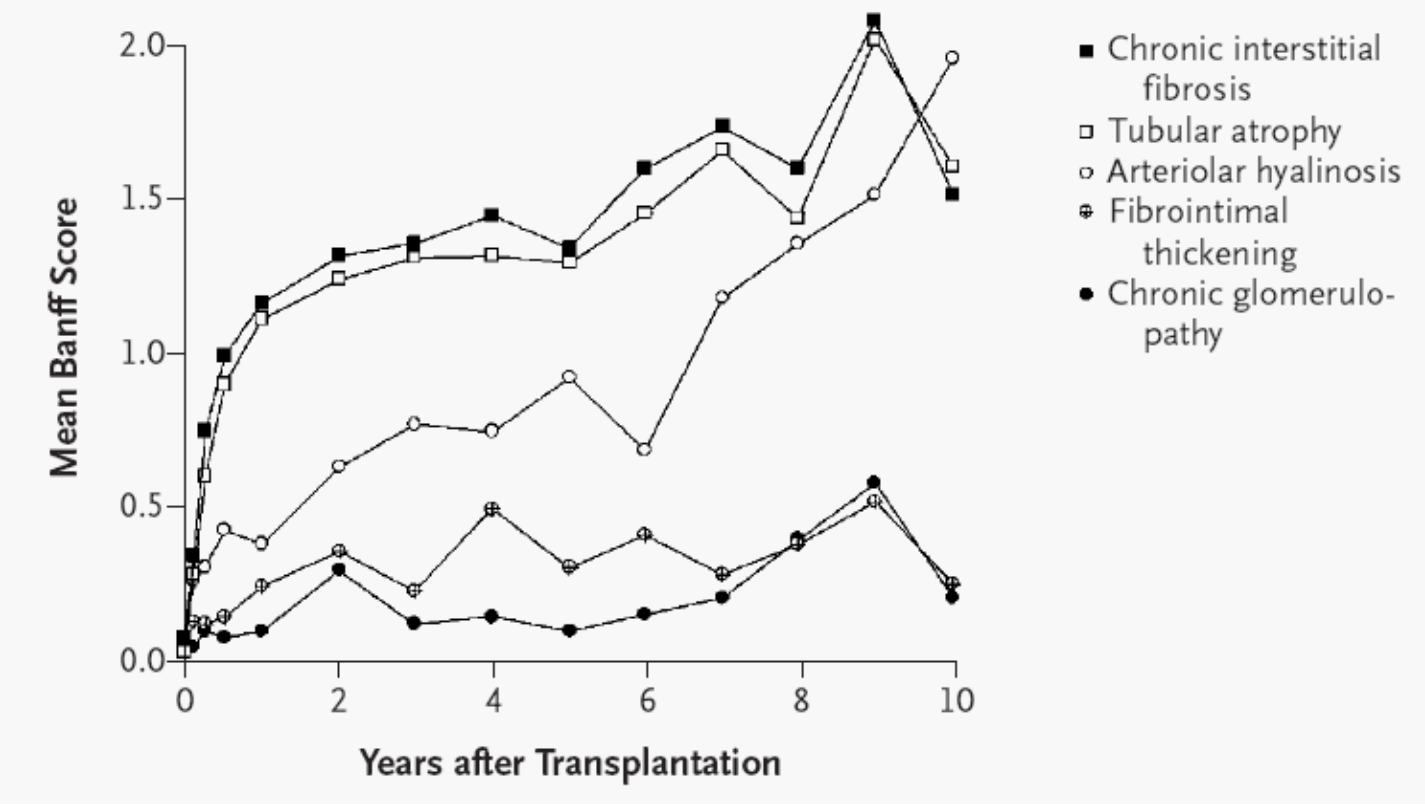
ORIGINAL ARTICLE

The Natural History of Chronic Allograft Nephropathy

Brian J. Nankivell, M.D., Ph.D., Richard J. Borrows, M.B., B.Chir.,
Caroline L.-S. Fung, M.B., B.S., F.R.C.P.A., Philip J. O'Connell, M.B., B.S., Ph.D.,
Richard D.M. Allen, F.R.A.C.S., and Jeremy R. Chapman, M.D., Ch.B.

N Engl J Med. 2003 Dec 11;349(24):2326-33

LA FIBROSIS INTERSTICIAL/ATROFIA TUBULAR (IF/TA)



Brian J. Nankivell, M.D., Ph.D., Richard J. Borrows, M.B., B.Chir., Caroline L.-S. Fung, M.B., B.S., F.R.C.P.A., Philip J. O'Connell, M.B., B.S., Ph.D., Richard D.M. Allen, F.R.A.C.S., and Jeremy R. Chapman, M.D., Ch.B.

N Engl J Med. 2003 Dec 11;349(24):2326-33

LA FIBROSIS INTERSTICIAL/ATROFIA TUBULAR (IF/TA)

Fibrosis with Inflammation at One Year Predicts Transplant Functional Decline

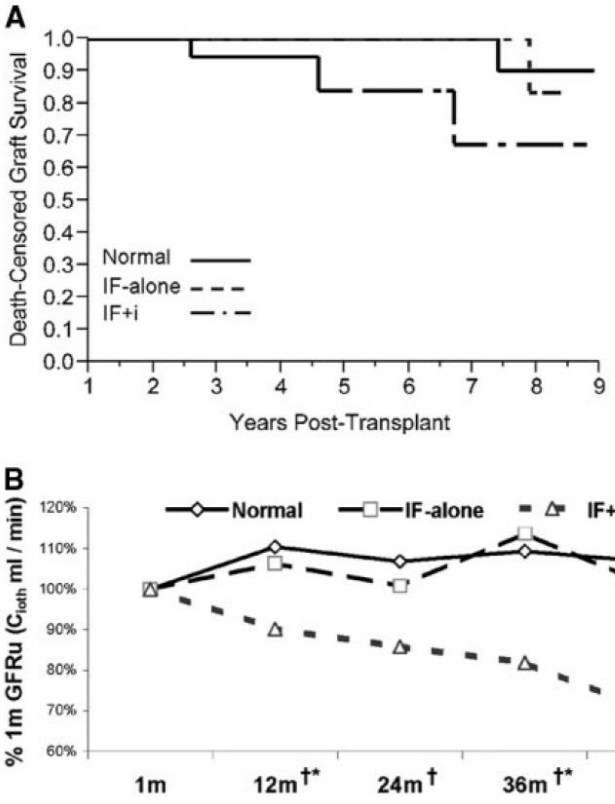
Walter D. Park,* Matthew D. Griffin,† Lynn D. Cornell,‡ Fernando G. Cosio,§ and Mark D. Stegall*

*Department of Surgery, Division of Transplantation Surgery, Mayo Clinic, Rochester, Minnesota; †Regenerative Medicine Institute, National Centre for Biomedical Engineering Science, National University of Ireland, Galway, Ireland; and ‡Department of Laboratory Medicine and Pathology, Division of Anatomic Pathology, and §Department of Medicine, Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota

ABSTRACT

Lack of knowledge regarding specific causes for late loss of kidney transplants hampers improvements in long-term allograft survival. Kidney transplants with both interstitial fibrosis and subclinical inflammation but not fibrosis alone after 1 year have reduced survival. This study tested whether fibrosis with inflammation at 1 year associates with decline of renal function in a low-risk cohort and characterized the nature of the inflammation. We studied 151 living-donor, tacrolimus/mycophenolate-treated recipients without overt risk factors for reduced graft survival. Transplants with normal histology ($n = 86$) or fibrosis alone ($n = 45$) on 1-year protocol biopsy had stable renal function between 1 and 5 years, whereas those with both fibrosis and inflammation ($n = 20$) exhibited a decline in GFR and reduced graft survival. Immunohistochemistry confirmed increased interstitial T cells and macrophages/dendritic cells in the group with both fibrosis and inflammation, and there was increased expression of transcripts related to innate and cognate immunity. Pathway- and pathologic process–specific analyses of microarray profiles revealed that potentially damaging immunologic activities were enriched among the overexpressed transcripts (*e.g.*, Toll-like receptor signaling, antigen presentation/dendritic cell maturation, IFN-γ–inducible response, cytotoxic T lymphocyte–associated and acute rejection–associated genes). Therefore, the combination of fibrosis and inflammation in 1-year protocol biopsies associates with reduced graft function and survival as well as a rejection-like gene expression signature, even among recipients with no clinical risk factors for poor outcomes. Early interventions aimed at altering rejection-like inflammation may improve long-term survival of kidney allografts.

J Am Soc Nephrol 21: 1987–1997, 2010. doi: 10.1681/ASN.2010010049



LA FIBROSIS INTERSTICIAL/ATROFIA TUBULAR (IF/TA)

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Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2010.03312.x

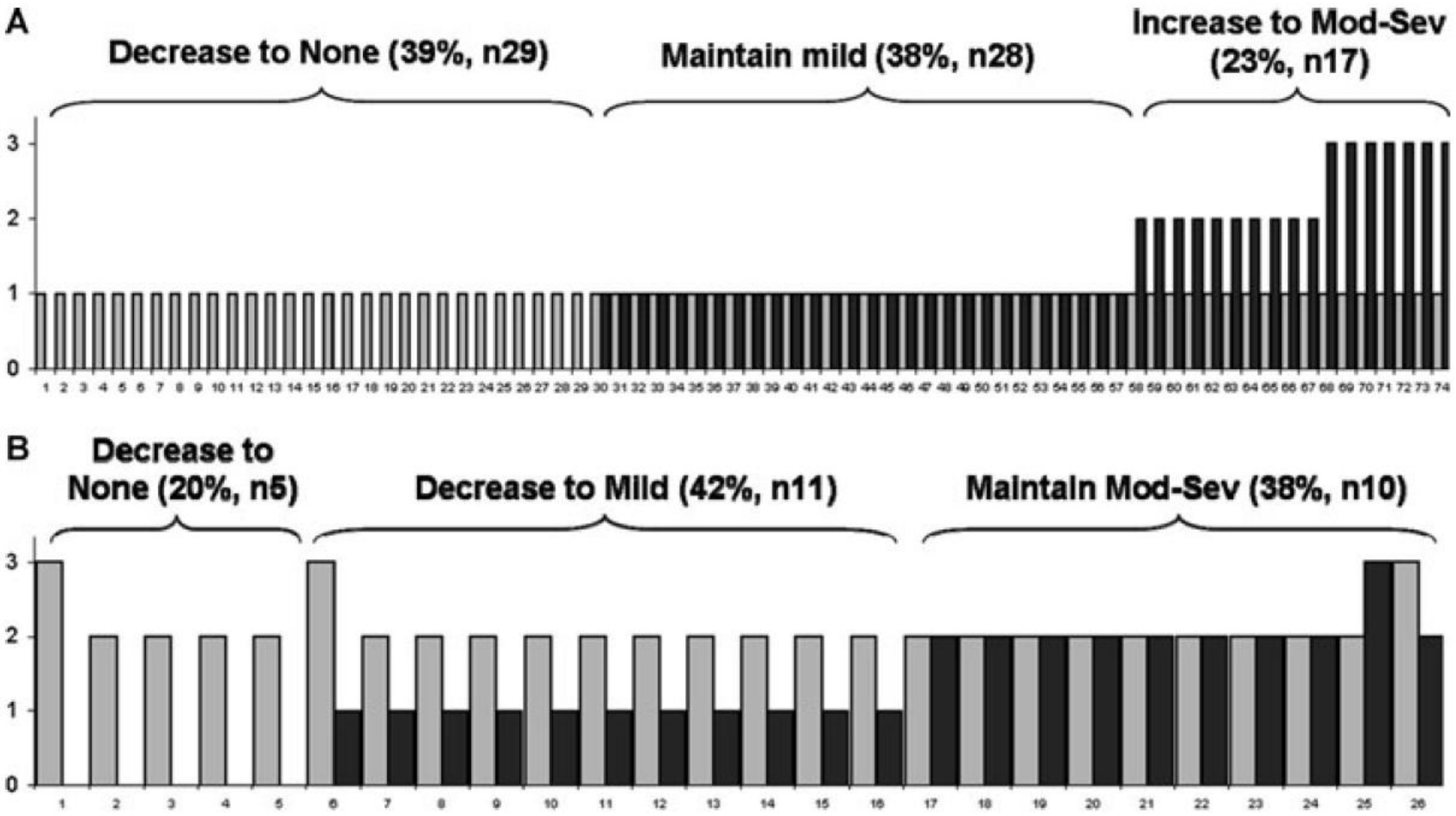
The Histology of Solitary Renal Allografts at 1 and 5 Years After Transplantation

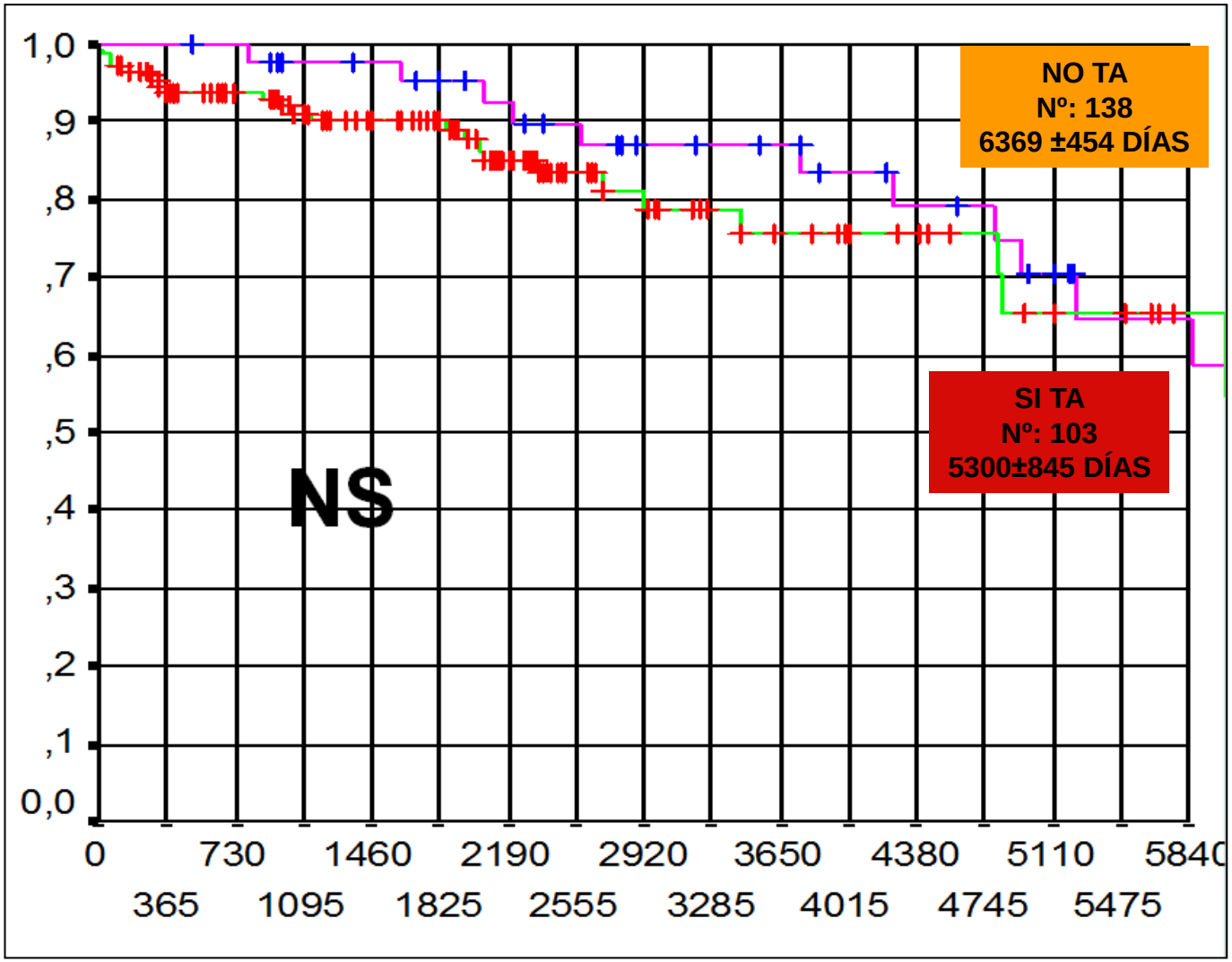
M. D. Stegall, W. D. Park, T. S. Larson, J. M. Gloor, L. D. Cornell, S. Sethi, P. G. Dean, M. Prieto, H. Amer, S. Textor, T. Schwab and F. G. Cosio

von Liebig Transplant Center, Division of Transplantation Surgery, Division of Nephrology and Hypertension, Department of Anatomic Pathology, Mayo Clinic, Rochester, MN
**Corresponding author: Mark D. Stegall, stegall.mark@mayo.edu*

fect the majority of renal allografts (1–4). A pivotal study by Nankivell et al. (1) outlined the natural history of "chronic allograft nephropathy" in 120 patients, 119 of which were recipients of bladder-drained simultaneous pancreas kidney transplants between 1987 and 2000. In these patients, maintained primarily on cyclosporine-based immunosuppression, 66% of protocol allograft biopsies obtained at 5 years demonstrated moderate-to-severe interstitial fibrosis (Banff scores of ci2 or 3 scores) and 90.3% showed arteriolar hyalinosis. On the basis of these findings, the authors described two phases of chronic allograft nephropathy in-

LA FIBROSIS INTERSTICIAL/ATROFIA TUBULAR (IF/TA)

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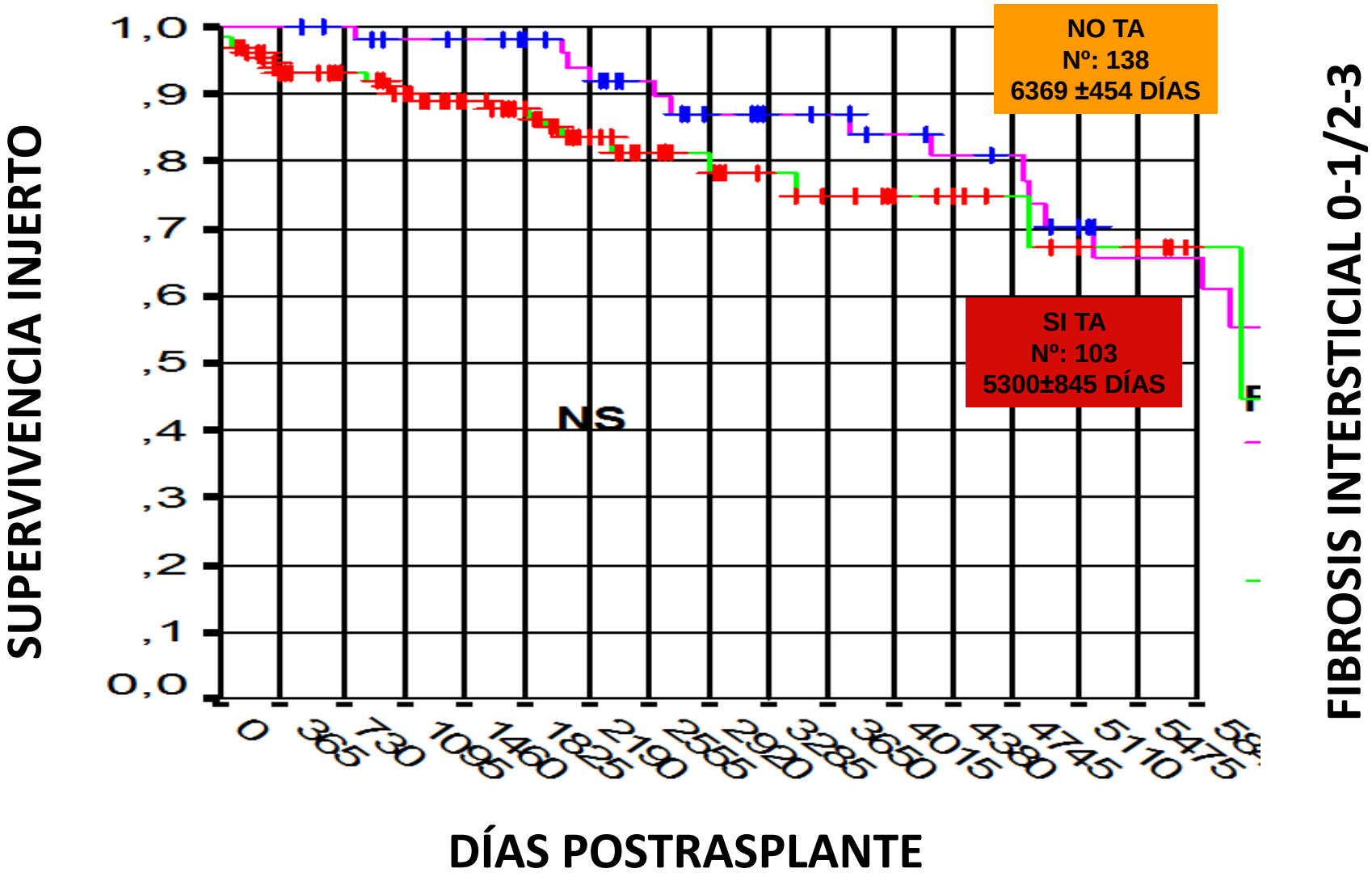
DÍAS POSTRASPLANTE
ARROFIA TUBULAR 0-1/2-3


SUPERVIVENCIA INJERTO
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NO TA
Nº: 138
6369 ±454 DÍAS
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Nº: 103
5300±845 DÍAS
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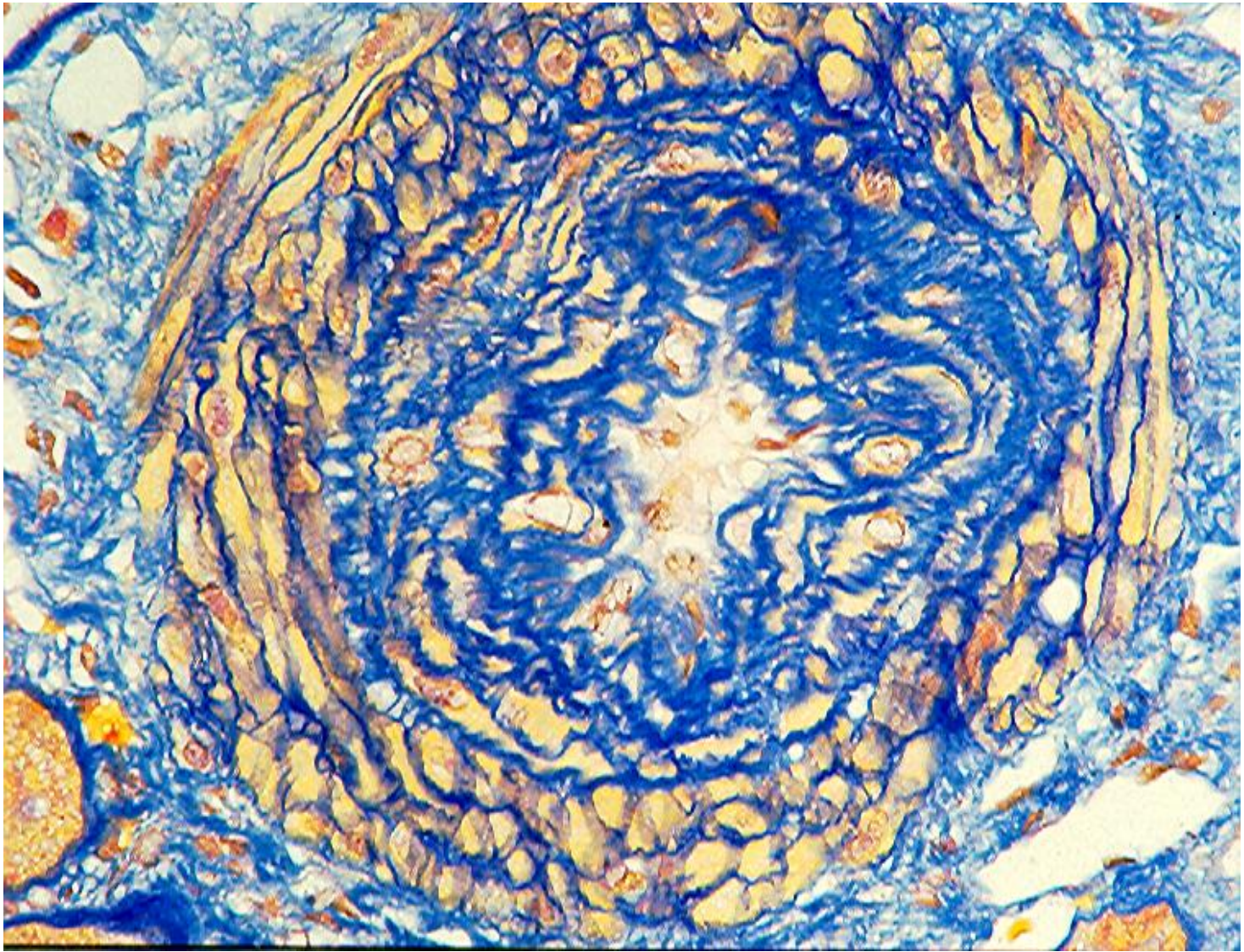
5475
DÍAS POSTRASPLANTE
FIBROSIS INTERSTICIAL 0-1/2-3

CONCLUSIÓN:

NO EXISTEN EVIDENCIAS SUFICIENTES PARA AFIRMAR QUE LA INTENSIDAD DE LA FIBROSIS INTERSTICIAL/ATROFIA TUBULAR TENGA INFLUENCIA EN EL PRONÓSTICO A LARGO PLAZO DEL INJERTO RENAL

LA FIBROSIS MIOINTIMAL VASCULAR



LA FIBROSIS MIOINTIMAL VASCULAR

Donor-Specific Antibodies Accelerate Arteriosclerosis after Kidney Transplantation

Gary S. Hill,* Dominique Nochy,*† Patrick Bruneval,*† J. P. Duong van Huyen,*† Denis Glotz,‡ Caroline Suberbielle,§ Julien Zuber,†‖ Dany Anglicheau,†‖ Jean-Philippe Empana,¶ Christophe Legendre,†‖ and Alexandre Loupy†‖¶

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ABSTRACT

In biopsies of renal allografts, arteriosclerosis is often more severe than expected based on the age of the donor, even without a history of rejection vasculitis. To determine whether preformed donor-specific antibodies (DSAs) may contribute to the severity of arteriosclerosis, we examined protocol biopsies from patients with (n = 40) or without (n = 59) DSA after excluding those with any evidence of vasculitis. Among DSA-positive patients, arteriosclerosis significantly progressed between month 3 and month 12 after transplant (mean Banff *cv* score 0.65 ± 0.11 to 1.12 ± 0.10, P = 0.014); in contrast, among DSA-negative patients, we did not detect a statistically significant progression during the same time-frame (mean Banff *cv* score 0.65 ± 0.11 to 0.81 ± 0.10, P = not significant). Available biopsies at later time points supported a rate of progression of arteriosclerosis in DSA-negative patients that was approximately one third that in DSA-positive patients. Accelerated arteriosclerosis was significantly associated with peritubular capillary leukocytic infiltration, glomerulitis, subclinical antibody-mediated rejection, and interstitial inflammation. In conclusion, these data support the hypothesis that donor-specific antibodies dramatically accelerate post-transplant progression of arteriosclerosis.

J Am Soc Nephrol 22: 975–983, 2011. doi: 10.1681/ASN.2010070777

LA FIBROSIS MIOINTIMAL VASCULAR

ENDOTHELIALITIS

INTIMAL HYPERPLASIA

MYOINTIMA HIPERPLASIA

} ***KIDNEY ALLOGRAFT OUTCOME***

APENAS EXISTEN REFERENCIAS EN LA LITERATURA

LA FIBROSIS MIOINTIMAL VASCULAR

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doi: 10.1111/ajt.12590

Meeting Report

Banff 2013 Meeting Report: Inclusion of C4d-Negative Antibody-Mediated Rejection and Antibody-Associated Arterial Lesions

M. Haas[1,*], B. Sis[2], L. C. Racusen[3], K. Solez[2], D. Glotz[4], R. B. Colvin[5], M. C. R. Castro[6], D. S. R. David[7], E. David-Neto[6], S. M. Bagnasco[3], L. C. Cendales[8], L. D. Cornell[9], A. J. Demetris[10], C. B. Drachenberg[11], C. F. Farver[12], A. B. Farris III[13], I. W. Gibson[14], E. Kraus[15], H. Liapis[16], A. Loupy[17], V. Nickeleit[18], P. Randhawa[10], E. R. Rodriguez[12], D. Rush[19], R. N. Smith[5], C. D. Tan[12], W. D. Wallace[20] and M. Mengel[2] as the Banff meeting report writing committee

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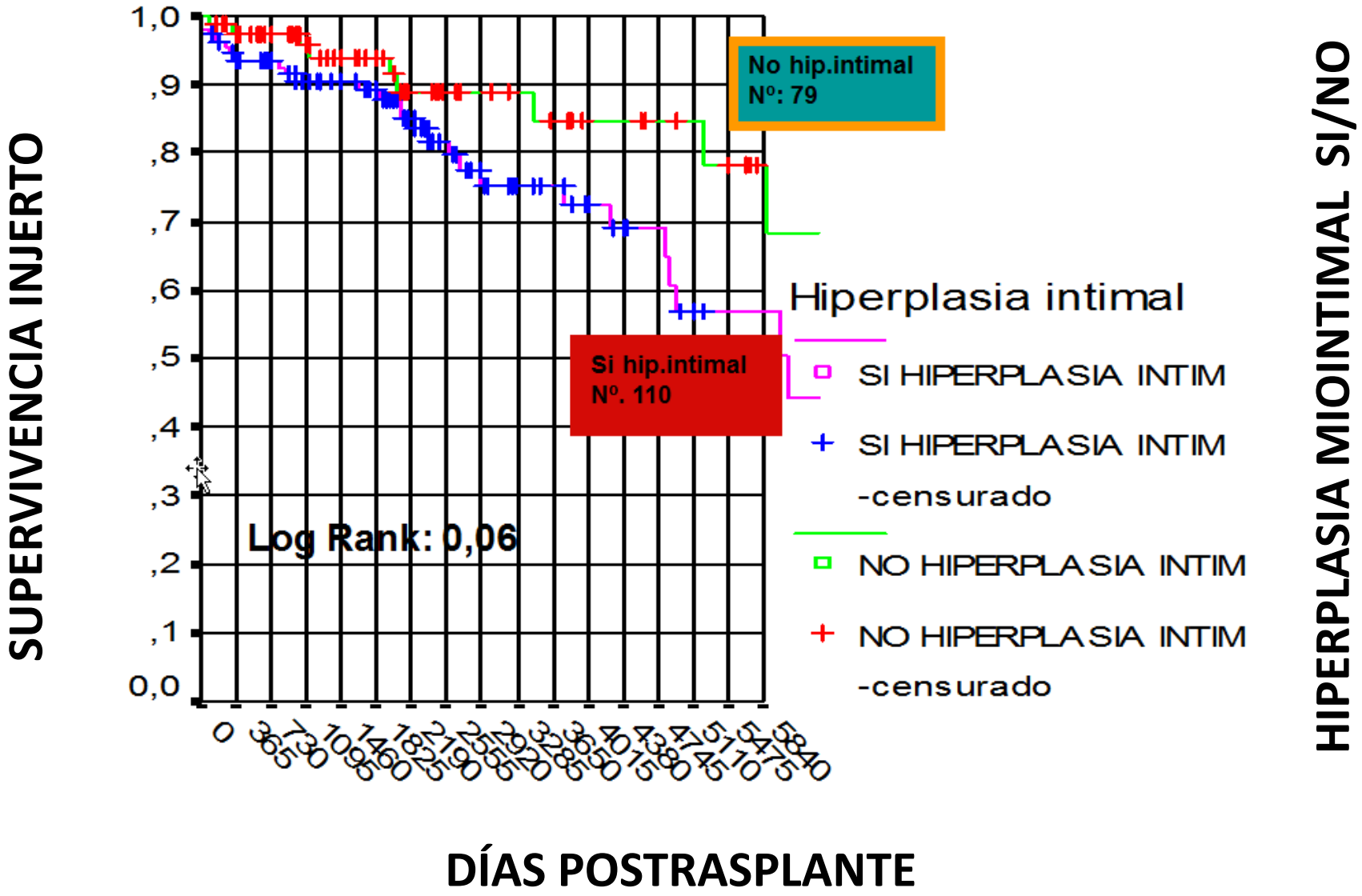
The 12th Banff Conference on Allograft Pathology was held in Comandatuba, Brazil, from August 19–23, 2013, and was preceded by a 2-day Latin American


SUPERVIVENCIA INJERTO
1,0
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,6
,5
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,3
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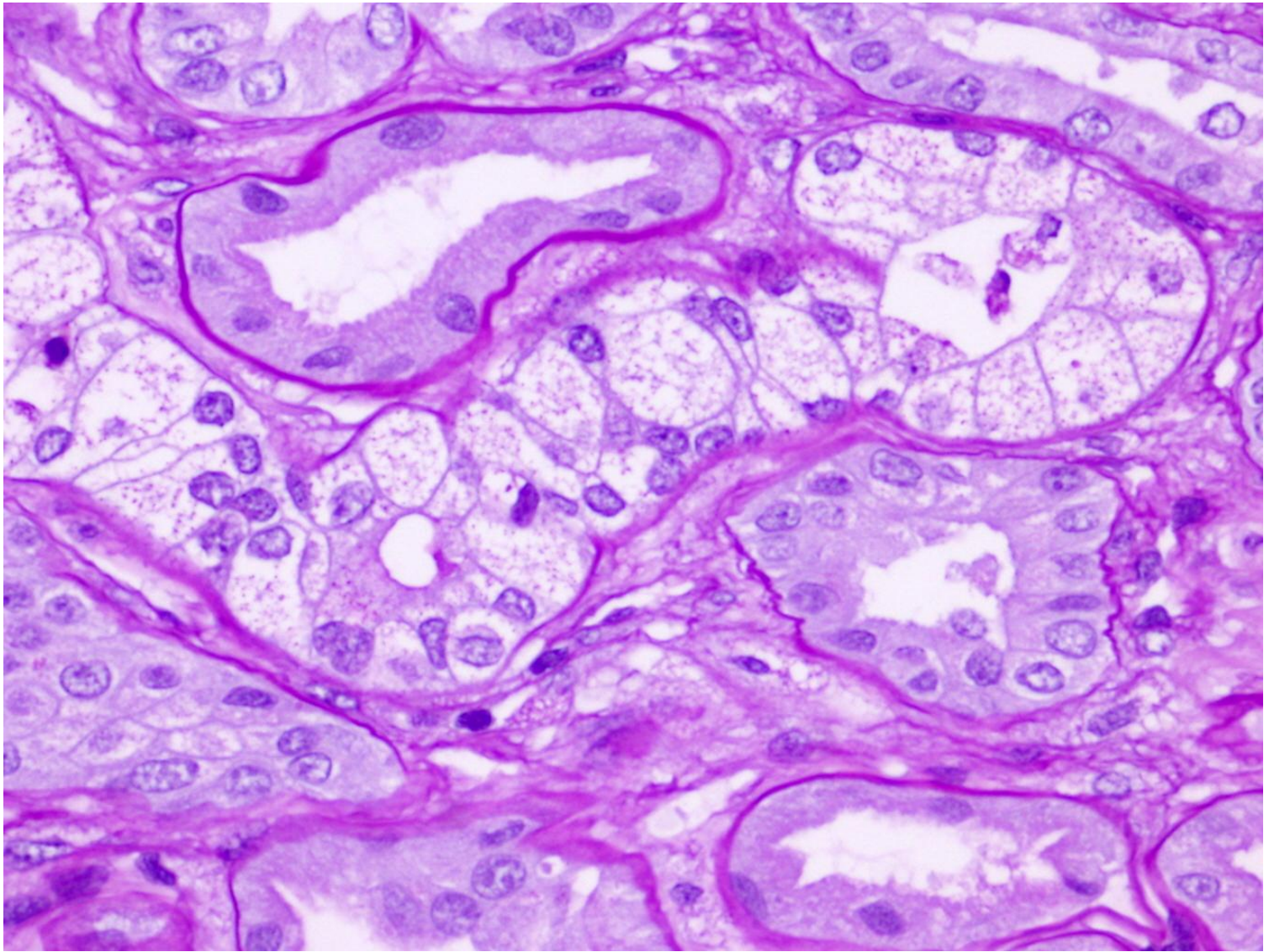
,1
0,0
No hip.intimal
Nº: 79
Si hip.intimal
Nº. 110
Log Rank: 0,06
Hiperplasia intimal
SI HIPERPLASIA INTIM
SI HIPERPLASIA INTIM -censurado
NO HIPERPLASIA INTIM
NO HIPERPLASIA INTIM -censurado
0
365
730
1095
1460
1825
2190
2555
2920
3285
3650
4015
4380
4745
5110
5475
5840
DÍAS POSTRASPLANTE
HIPERPLASIA MIOINTIMAL SI/NO

CONCLUSIÓN:

AUNQUE NO EXISTEN SUFICIENTES EVIDENCIAS EN LA LITERATURA PARA AFIRMAR QUE LA INTENSIDAD DE LA HIPERPLASIA MIOINTIMAL ARTERIAL TIENE INFLUENCIA EN EL PRONÓSTICO A LARGO PLAZO DEL INJERTO RENAL ES MUY POSIBLE QUE ASÍ SEA

LA NEFROTOXICIDAD POR ANTICALCINEURÍNICOS



LA NEFROTOXICIDAD POR ANTICALCINEURÍNICOS

1. Tradicionalmente ha sido considerada como uno de los principales factores no inmunitarios causantes de la disfunción crónica del injerto
2. Hoy día los factores inmunes se consideran el principal factor de influencia en el fracaso tardío del injerto

Our evolving understanding of late kidney allograft failure

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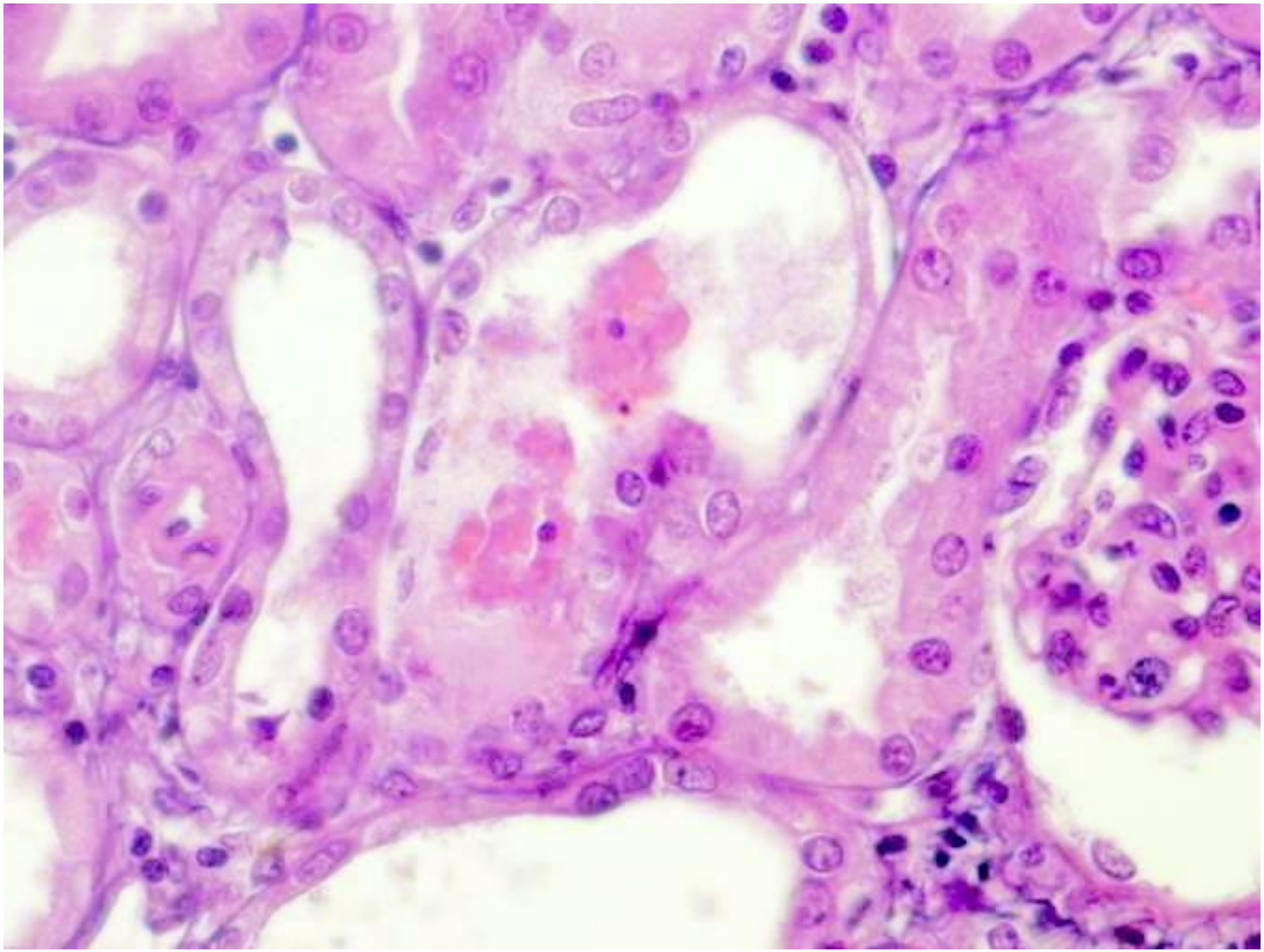
Current Opinion in Organ Transplantation 2011, 16:594–599

Purpose of review
Dramatic improvement in short-term results after kidney transplantation has fostered a change in focus for clinical research: further improvement in patient outcomes requires better understanding of late allograft failure.
Recent findings
As recently as a decade ago, with clinicians and investigators besot by the mistaken assumption that 'rejection' was under control, most late allograft failure was attributed to calcineurin inhibitor nephrotoxicity. Application of newer laboratory-based techniques (C4d staining, solid-phase antibody assays, and molecular profiling) has

LA NECROSIS TUBULAR AGUDA



Article

Preimplant Histologic Acute Tubular Necrosis and Allograft Outcomes

Isaac E. Hall,[*†] *Peter P. Reese,*[‡] *Francis L. Weng,*[§] *Bernd Schröppel,*[‖] *Mona D. Doshi,*[¶] *Rick D. Hasz,*[**] *William Reitsma,*[††] *Michael J. Goldstein,*[‡‡] *Kwangik Hong,*[*] *and Chirag R. Parikh*[*†§§]

Abstract

Background and objectives The influence of deceased-donor AKI on post-transplant outcomes is poorly understood. The few published studies about deceased-donor preimplant biopsy have reported conflicting results regarding associations between AKI and recipient outcomes.

Design, setting, participants, & measurements This multicenter study aimed to evaluate associations between deceased-donor biopsy reports of acute tubular necrosis (ATN) and delayed graft function (DGF), and secondarily for death-censored graft failure, first adjusting for the kidney donor risk index and then stratifying by donation after cardiac death (DCD) status.

Results Between March 2010 and April 2012, 651 kidneys (369 donors, 4 organ procurement organizations) were biopsied and subsequently transplanted, with ATN reported in 110 (17%). There were 262 recipients (40%) who experienced DGF and 38 (6%) who experienced graft failure. DGF occurred in 45% of kidneys with reported ATN compared with 39% without ATN (P=0.31) resulting in a relative risk (RR) of 1.13 (95% confidence interval [95% CI], 0.9 to 1.43) and a kidney donor risk index–adjusted RR of 1.11 (95% CI, 0.88 to 1.41). There was no significant difference in graft failure for kidneys with versus without ATN (8% versus 5%). In stratified analyses, the adjusted RR for DGF with ATN was 0.97 (95% CI, 0.7 to 1.34) for non-DCD kidneys and 1.59 (95% CI, 1.23 to 2.06) for DCD kidneys (P=0.02 for the interaction between ATN and DCD on the development of DGF).

Conclusions Despite a modest association with DGF for DCD kidneys, this study reveals no significant associations overall between preimplant biopsy-reported ATN and the outcomes of DGF or graft failure. The potential benefit of more rigorous ATN reporting is unclear, but these findings provide little evidence to suggest that current ATN reports are useful for predicting graft outcomes or deciding to accept or reject allograft offers.

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Clin J Am Soc Nephrol 9: 573–582, March, 2014

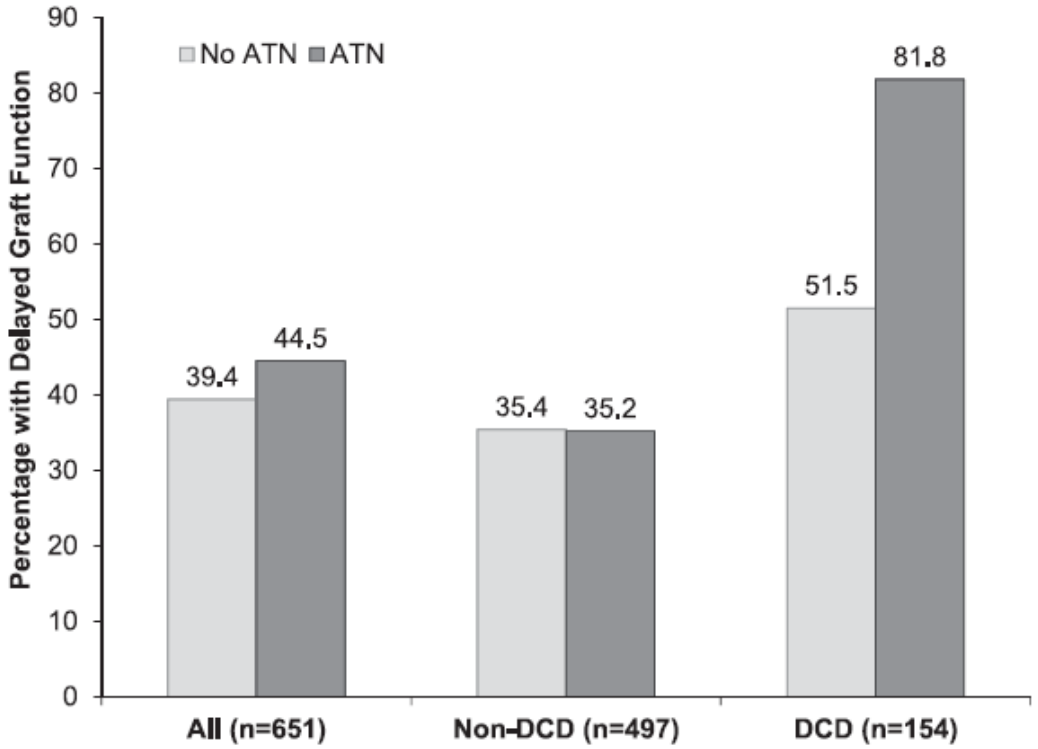
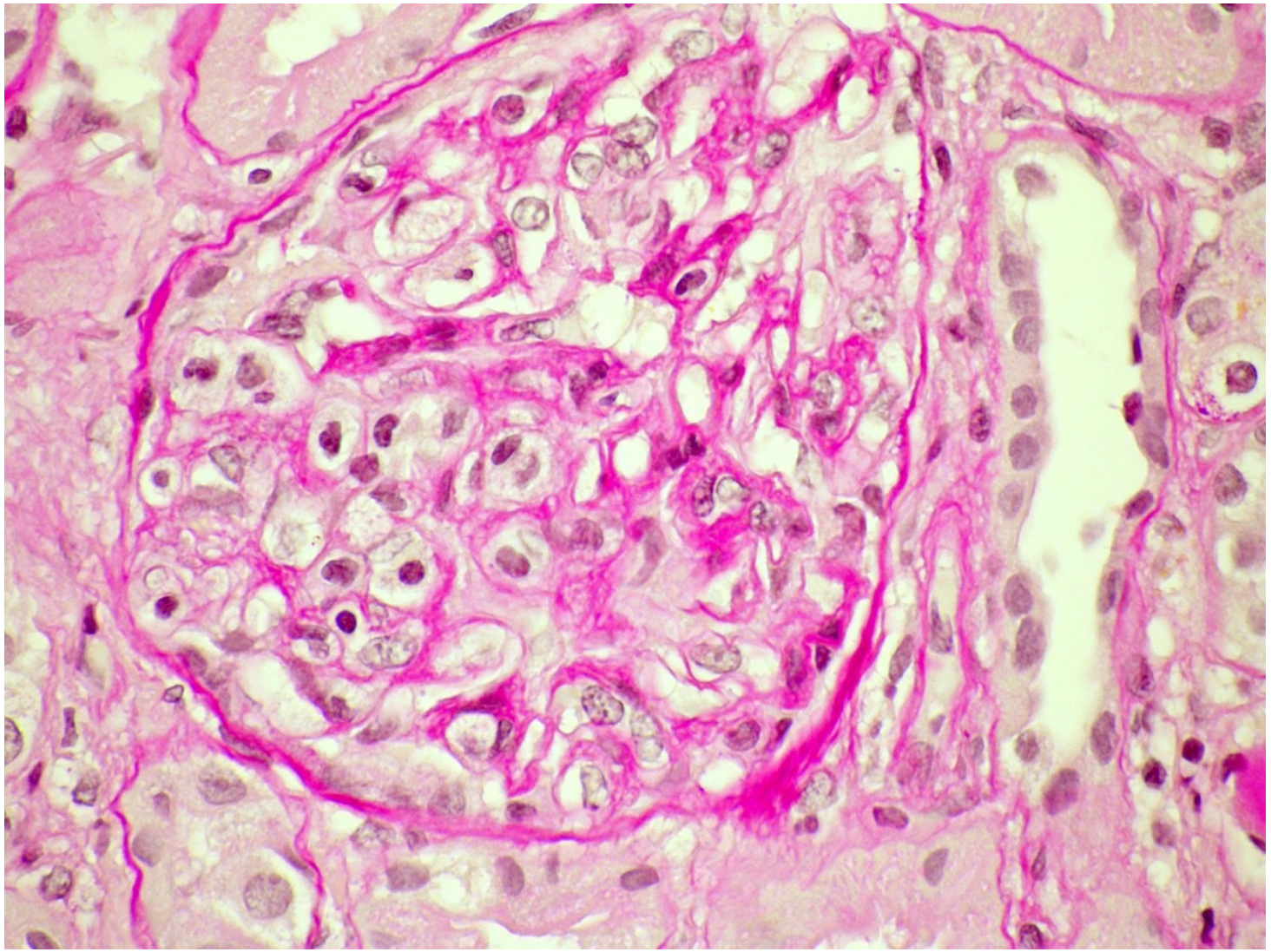


Figure 2. | Percentage of all recipients with DGF by preimplant biopsy-reported ATN and stratified by donation after DCD status. The *P* value for the interaction term (ATN*DCD) on the development of DGF was significant at 0.02. *P* values for the chi-squared tests comparing the proportion with DGF in kidneys with versus without ATN for the entire cohort, non-DCD kidneys and DCD kidneys were 0.31, 0.97, and 0.01, respectively. ATN, acute tubular necrosis; DCD, donation after cardiac death; DGF, delayed graft function.

CONCLUSIÓN:

NO EXISTEN EVIDENCIAS PARA AFIRMAR QUE LA PRESENCIA DE NECROSIS TUBULAR AGUDA TENGA INFLUENCIA EN EL PRONÓSTICO A LARGO PLAZO DEL INJERTO RENAL SALVO QUE SE ENCUENTRE EN EL CONTEXTO DE UN RECHAZO AGUDO MEDIADO POR ANTICUERPOS

GLOMERULOPATÍA DEL TRASPLANTE



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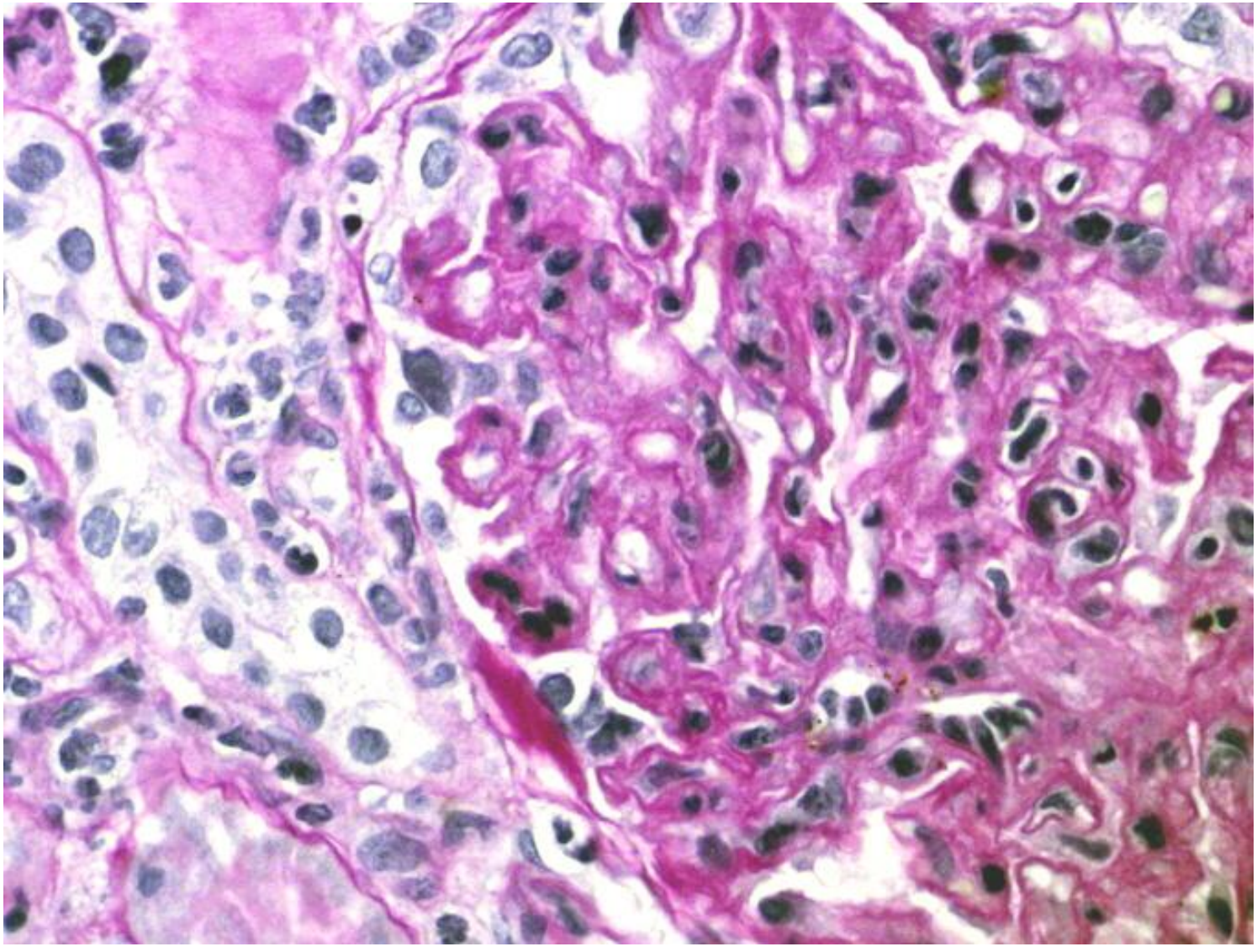

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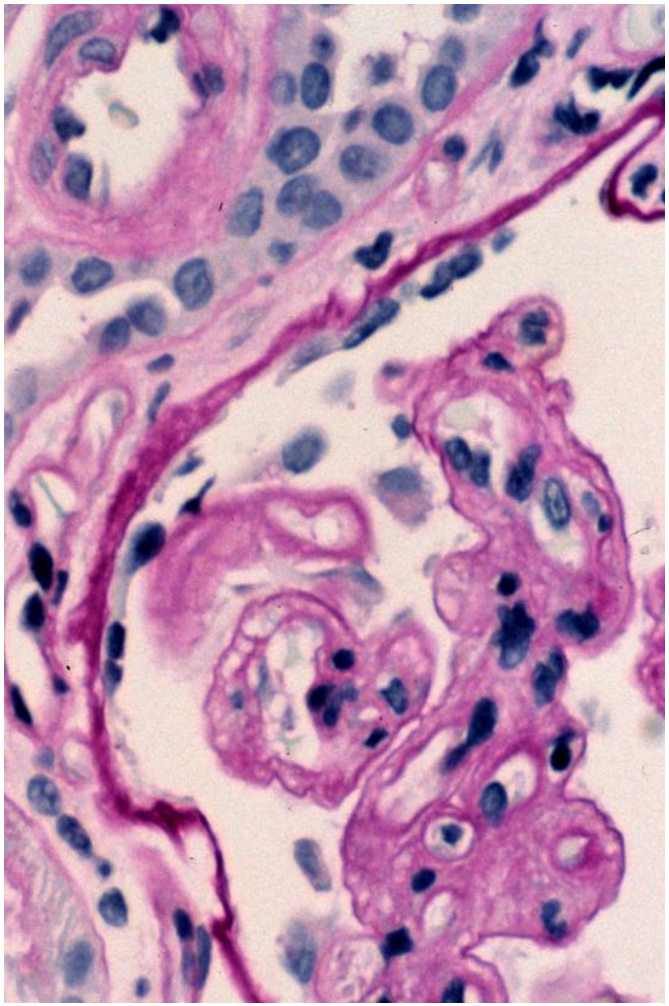
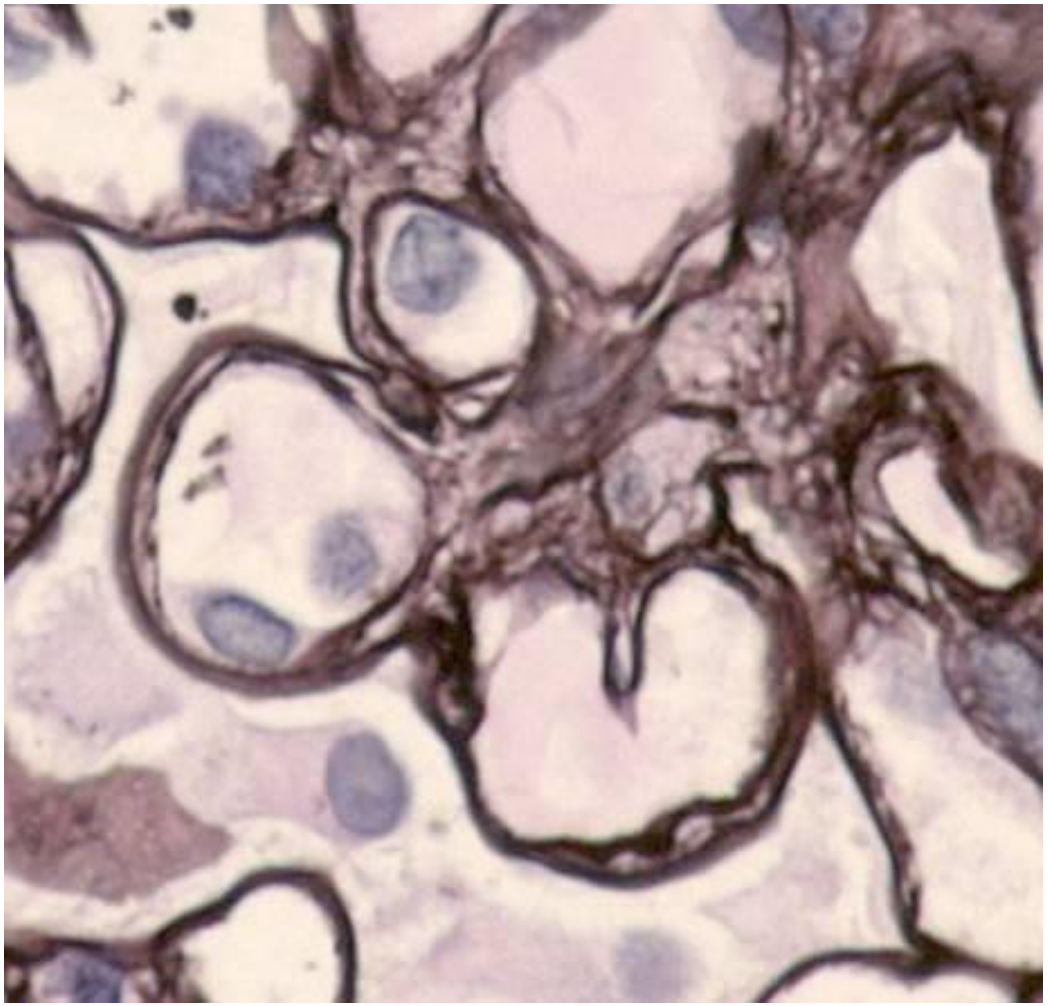
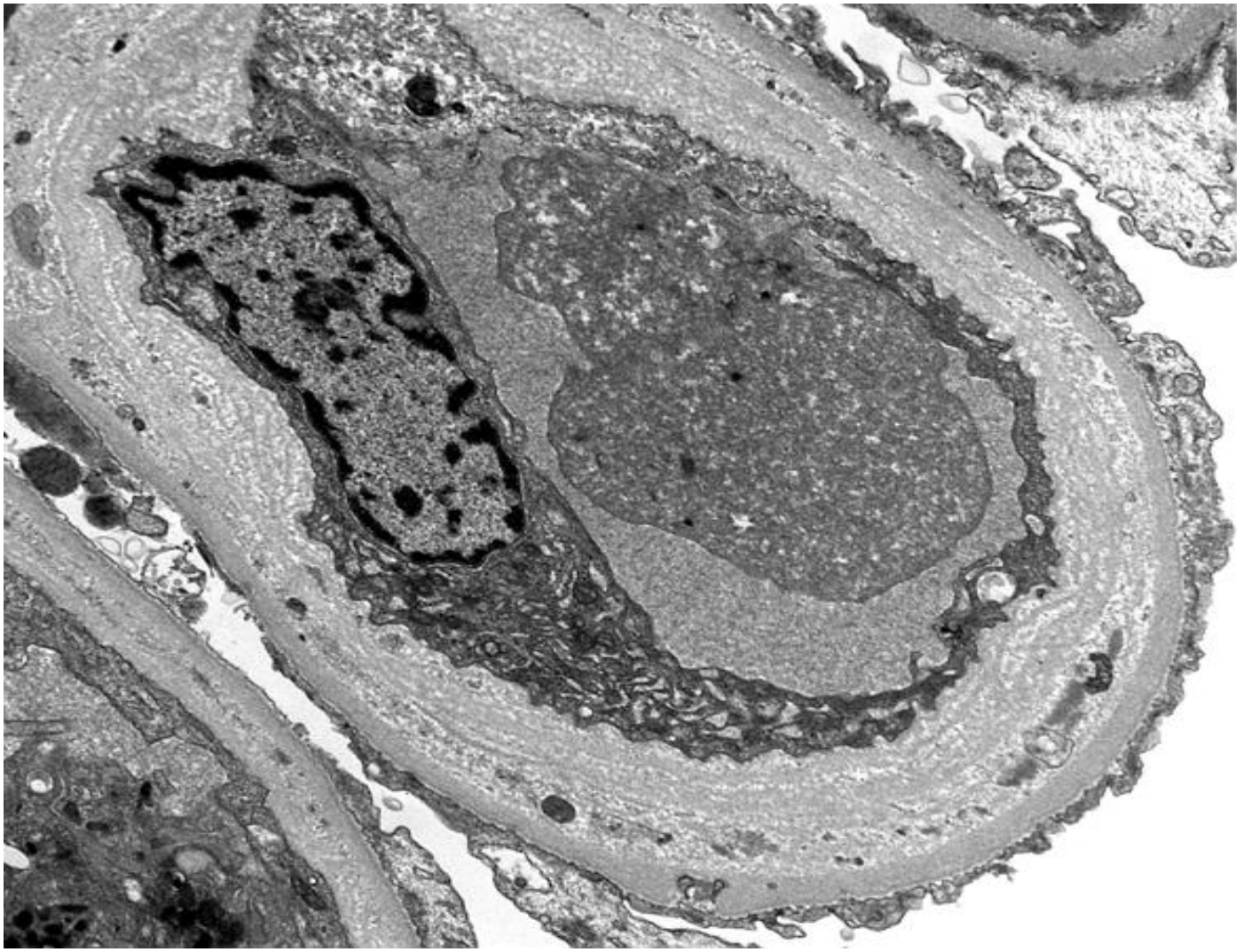


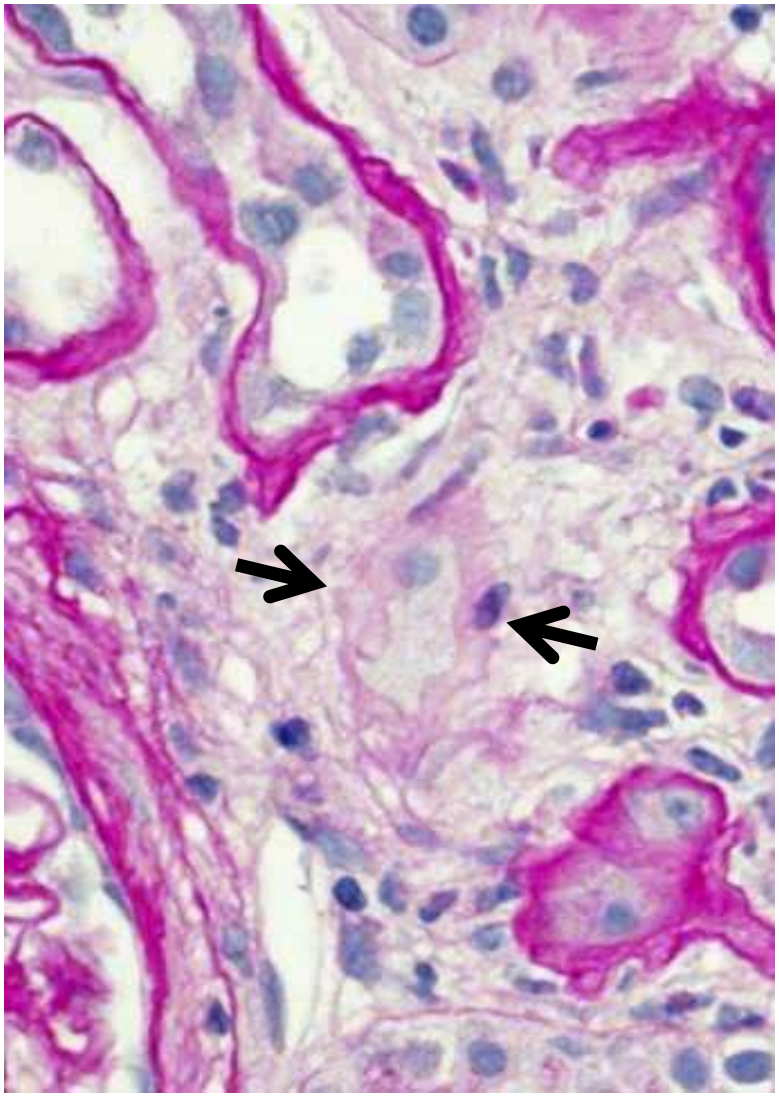


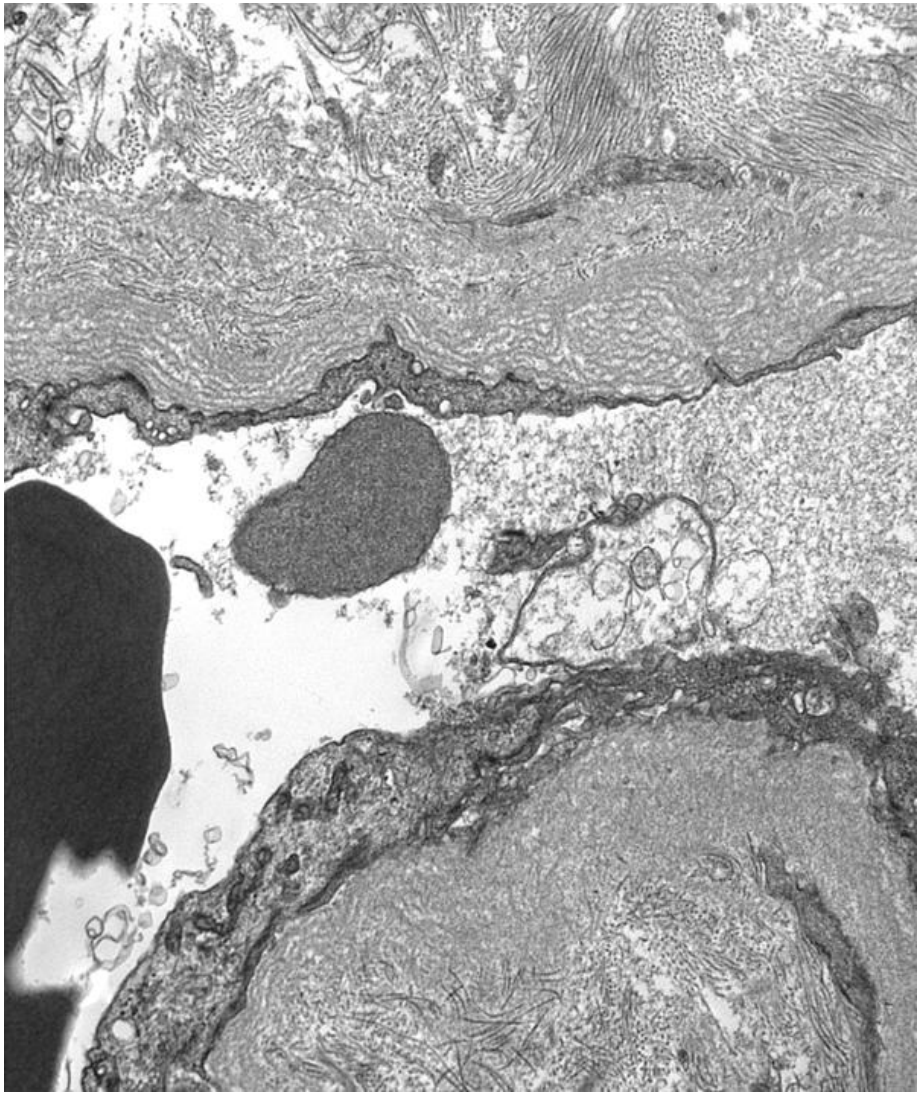
Imágenes tomadas de Enver Akalin MD, Banff'05: Morphologic Features of Transplant Glomerulopathy

GLOMERULOPATÍA DEL TRASPLANTE

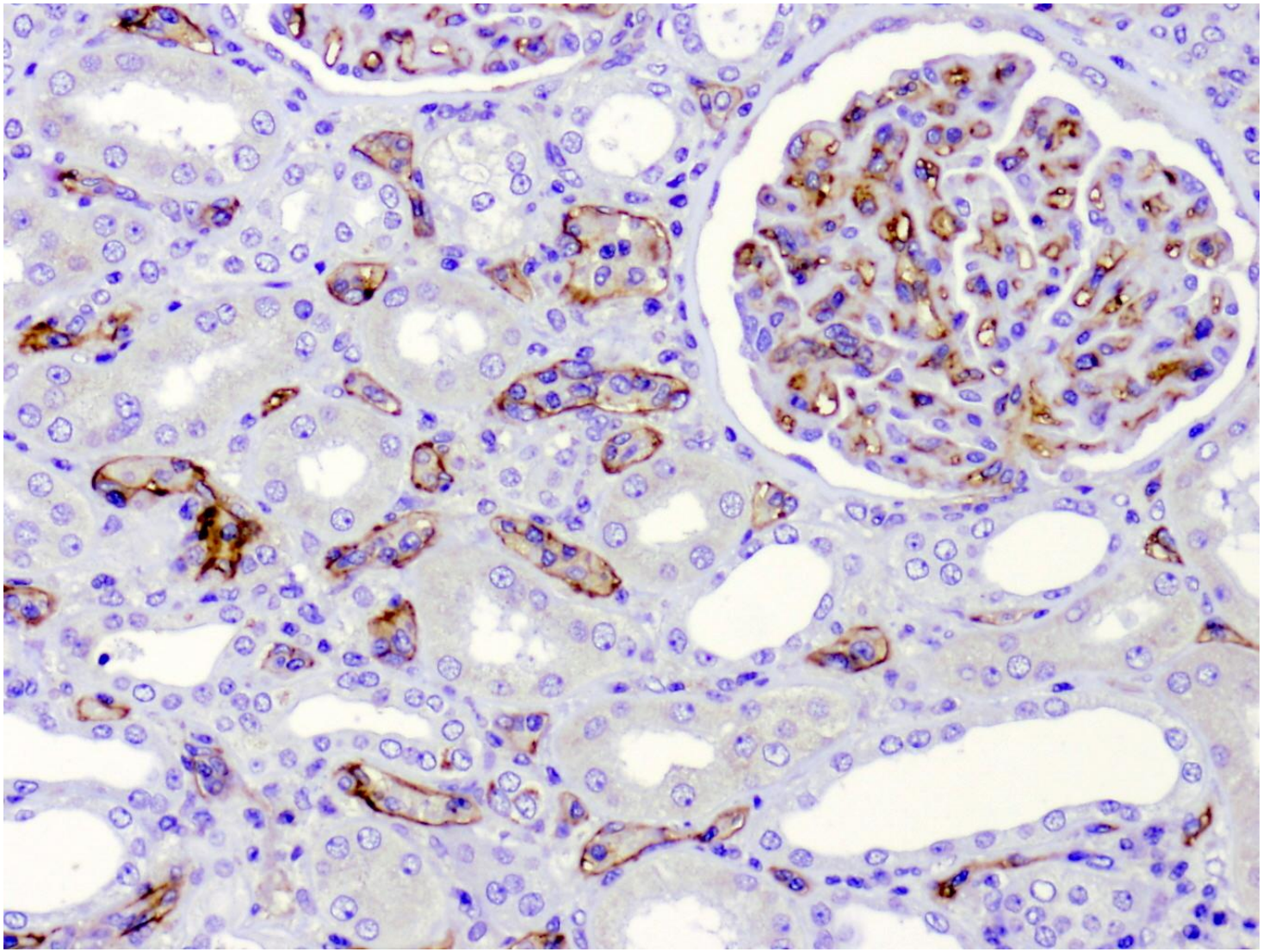


CAPILOROPATÍA DEL TRASPLANTE





GLOMERULOPATÍA DEL TRASPLANTE: DEPÓSITO DE C4d



CLINICAL AND TRANSLATIONAL RESEARCH

The Histology of Kidney Transplant Failure: A Long-Term Follow-Up Study

Maarten Naesens,[1,2,6] Dirk R.J. Kuypers,[1,2] Katrien De Vusser,[1,2] Pieter Evenepoel,[1,2] Kathleen Claes,[1,2] Bert Bammens,[1,2] Björn Meijers,[1,2] Ben Sprangers,[1,2] Jacques Pirenne,[2,3] Diethard Monbaliu,[2,3] Ina Jochmans,[2,3] and Evelyne Lerut[4,5]

Background. The relative impact on renal allograft outcome of specific histological diagnoses versus nonspecific chronic histological damage remains unclear.

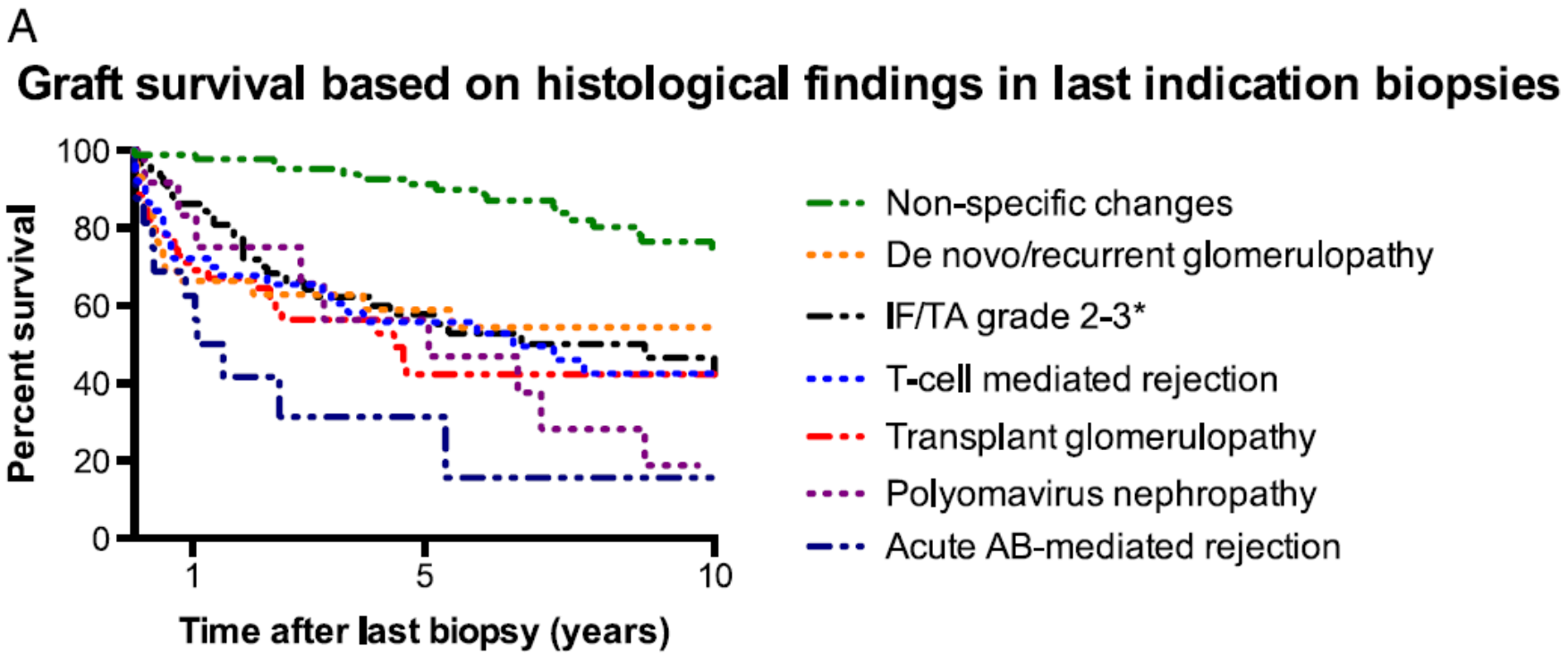
Methods. All 1,197 renal allograft recipients who were transplanted at a single center between 1991 and 2001 were included. All posttransplant renal allograft indication biopsies performed in this cohort during follow-up (mean, 14.5±2.80 years after transplantation) were rescored according to the current histological criteria and associated with death-censored graft outcome.

Results. In this cohort, 1,365 allograft indication biopsies were performed. Specific diagnoses were present in 69.4% of graft biopsies before graft loss, but 30.6% of grafts did not have specific diagnoses in the last biopsy before graft loss. Only 14.6% of the patients did never have any specific disease diagnosed before graft loss. Extensive interstitial fibrosis and tubular atrophy without a clear cause was identified as the single cause of graft loss in only 6.9% of the cases. Acute T-cell–mediated rejection and changes suggestive of acute antibody-mediated rejection, diagnosed after the first year posttransplant, associated independently with graft survival. Transplant glomerulopathy increased over time after transplantation and represented a major risk for graft loss, as well as de novo or recurrent glomerular pathologies and polyomavirus nephropathy. Chronic histological injury associated with graft outcome, independent of specific diagnoses.

Conclusion. Renal allograft loss is multifactorial. Chronic histological damage and specific diseases had additive and independent impact on graft outcome. Chronic damage should be taken into account in prognostication of renal allograft outcome and could be implemented in treatment algorithms for specific diseases of kidney allografts.

Keywords: Kidney transplantation, Histology, Graft outcome, Survival analysis.

(*Transplantation* 2014;98: 427–435)

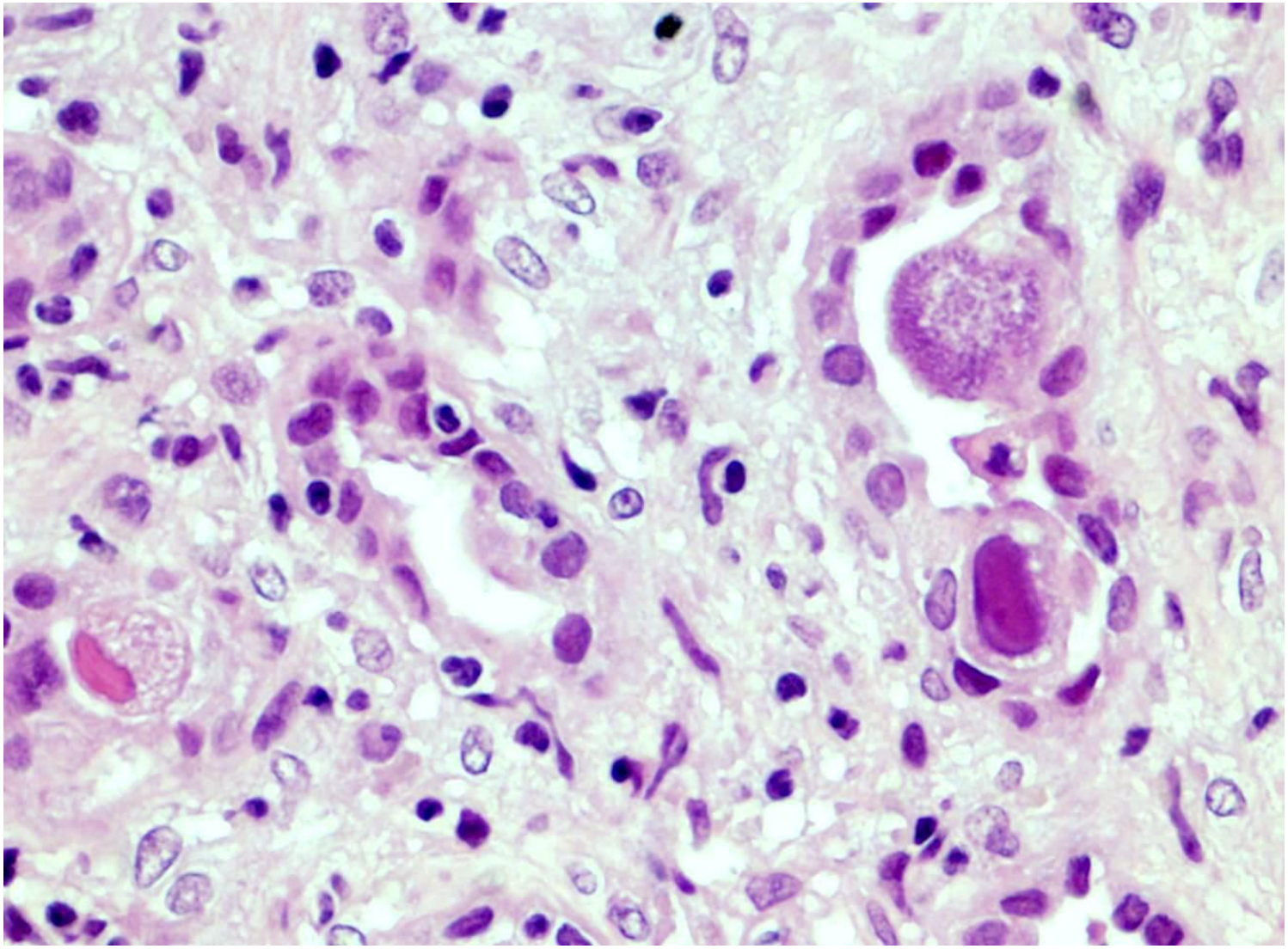


Naesens M, Kuypers DR, De Vusser K, et al. The histology of kidney transplant failure: a long-term follow-up study. Transplantation. 2014 Aug 27;98(4):427-35.

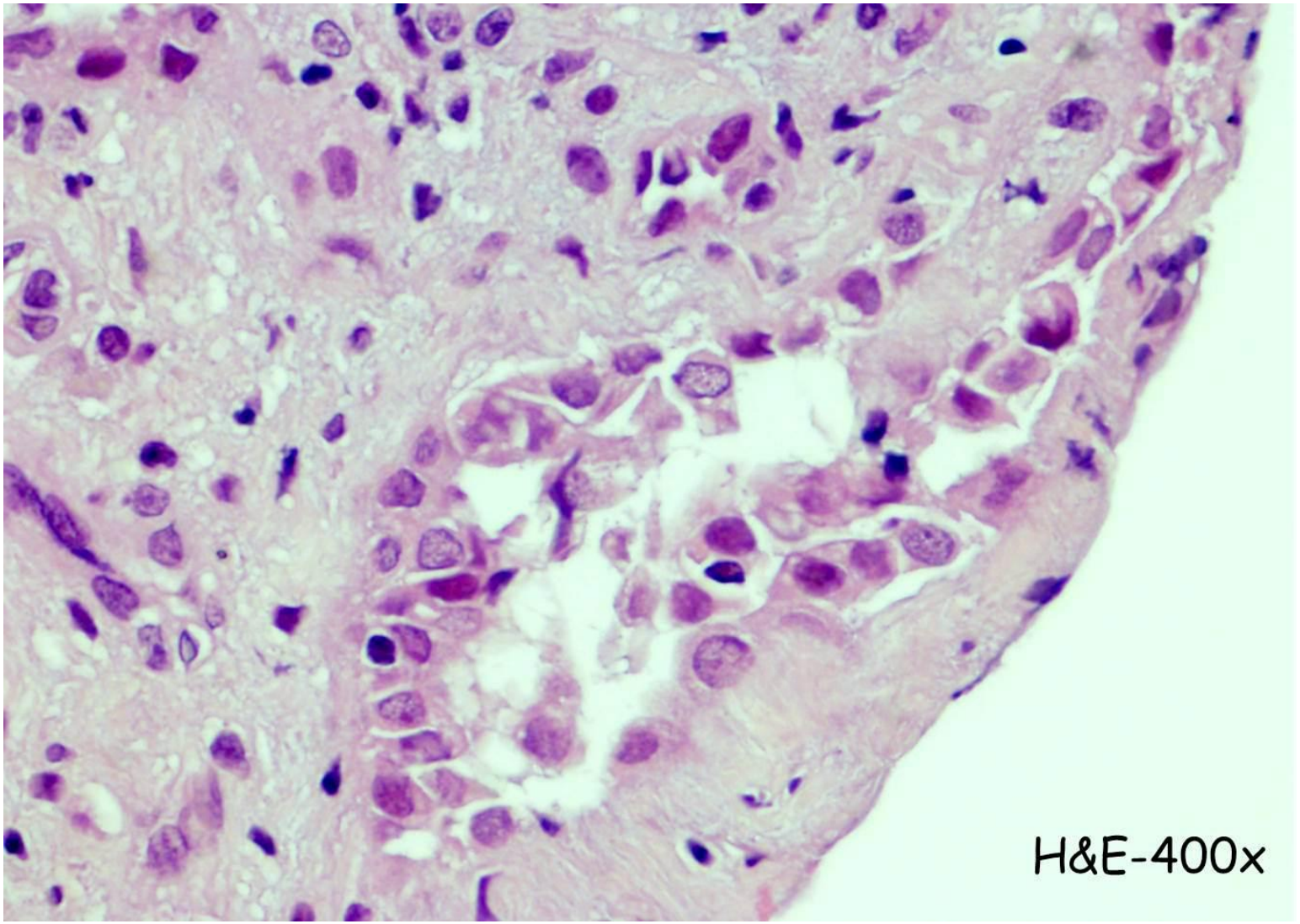
CONCLUSIONES:

1. ***EXISTE FUERTE EVIDENCIA DE QUE LA PRESENCIA DE GLOMERULITIS, ESENCIALMENTE POR CÉLULAS CON FENOTIPO CD68+, TIENE NOTABLE INFLUENCIA EN EL PRONÓSTICO A LARGO PLAZO DEL INJERTO RENAL***
2. ***SOBRE LA CAPILARITIS CRÓNICA NO EXISTEN EVIDENCIAS SUFICIENTES EN LA LITERATURA.***

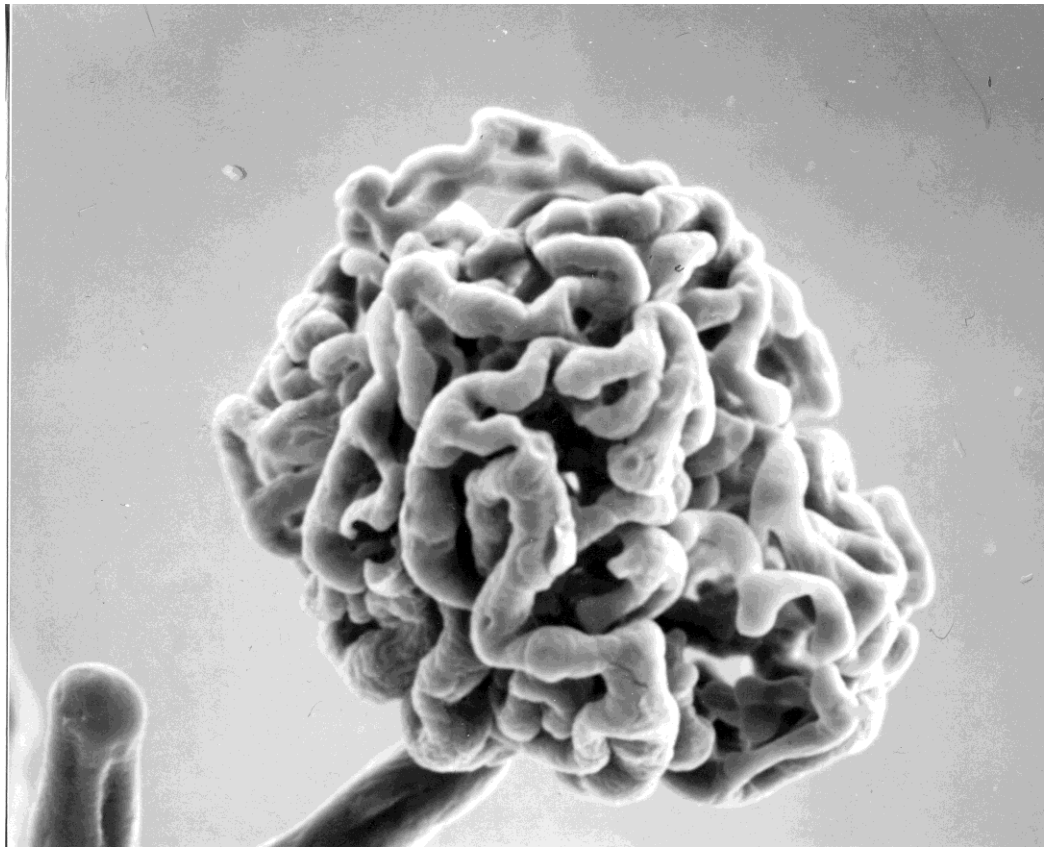
INFECCIÓN DEL INJERTO RENAL POR CMV



INFECCIÓN DEL INJERTO RENAL POR VIRUS BK DEL POLIOMA



LA CLAVE PRONÓSTICA DE LA BIOPSIA RENAL POSTINJERTO ESTÁ EN LAS LESIONES VASCULARES AGUDAS Y CRÓNICAS, CON ESPECIAL ÉNFASIS EN LA GLOMERULITIS/GLOMERULOPATÍA DEL TRASPLANTE



http://www.udel.edu/biology/Wags/histopage/vascularmodelingpage/sem/sempage.html