Protocol (Surveillance) Biopsies in Renal Transplantation

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The indications for transplant biopsy

1-Protocol biopsies that are performed at defined time points

2-those that are performed for acute or chronic graft dysfunction

Pretransplant biopsy

To judge the quality of a deceased donor organ at excision

To rule out the possibility of disease in live donors

30% of deceased donor kidneys are discarded by US Tx centers*

* Massie AB, Desai NM, Montgomery RA, Singer AL, Segev DL. Improving distribution efficiency of hard-to-place deceased donor kidneys: predicting probability of discard or delay. Am. J. Transplant. 2010; 10:1613–1620. [PubMed: 20642686]

Maryland Aggregate pathology Index

MAPI which is based on comprehensive pathologic scoring of both frozen and permanent tissue sections, followed by

sophisticated bioinformatics analysis of the most informative morphological para meters

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Munivenkatappa RB, et al. The Maryland aggregate pathology index: a deceased donor kidney biopsy scoring system for predicting graft failure. Am. J. Transplant. 2008; 8:2316–2324

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.

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Glomerulosclerosis

periglomerular fibrosis

TA and/or IF

Arteriolar hyalinosis

Arterial wall thickening

5-year survival was strikingly correlated with MAPI scores

Glomerulosclerosis-GS

GS (20%) is associated to the presence of DGF immediately after transplant, and also to a reduced kidney function or long-term graft loss.

The presence of TA damage inherited from the donor, is correlated to subsequent development of GS in the recipient

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Howie AJ, Ferreira MA, Lipkin GW, Adu D. Measurement of chronic damage in the donor kidney and graft survival. Transplantation .2004; 77 (7): 1058-65

Protocol renal allograft biopsy

A controversial issue

At fixed time points from Tx

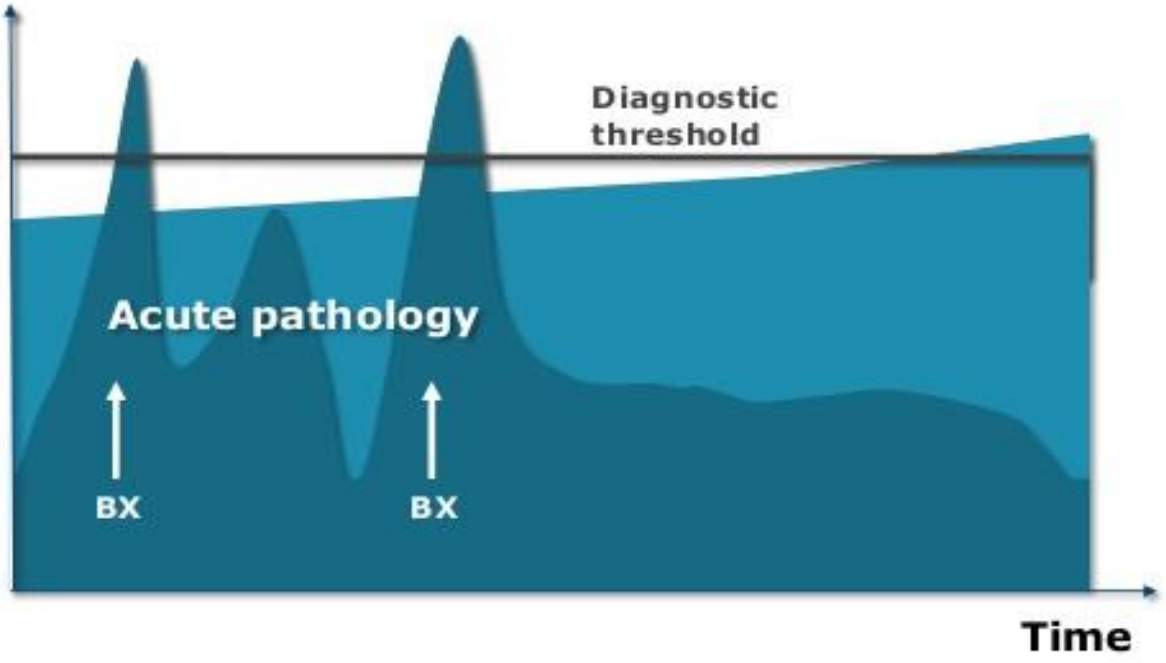
Their role is evolving from research to a clinical management tool

Subclinical pathology (especially SCR)

Individualization of therapy

Clinical vs. subclinical pathology

BX for cause



Subclinical Rejection (SCR)

The presence of histologic features of acute rejection on renal biopsy (tubulointerstitial mononuclear infiltration) in the absence of a decline in renal function:

1-SC-TCMR

2-SC-AMR (very rare)

B. J. Nankivell∗ and J. R. Chapman.The Significance of Subclinical Rejection and the Value of Protocol Biopsies . American Journal of Transplantation 2006; 6: 2006–2012


2016
AMERICAN
Transplant
CONGRESS
JUNE 11-15, 2016
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BOSTON

Histopathological Findings

The Banff grading on biopsy for the diagnosis of SC-TCMR can vary from borderline changes to Banff IA/ IB. Banff IIA or higher grades of rejection are relatively rare in SC-TCMR

Subclinical Rejection in Renal Transplantation: Reappraised Transplantation 2016;100: 1610–1618

Incidence

An SCR incidence of 30% in the late 1990s (Rush)

Incidence of SCR with a regimen containing tacrolimus and mycophenolate, with or without steroids, varies from 2.6% to 25% within the first year.

1-Rush D, Nickerson P, Gough J et al. Beneficial effects of treatment of early subclinical rejection: A randomized study. J Am Soc Nephrol 1998; 9: 2129–2134.
2-Subclinical Rejection in Renal Transplantation: Reappraised Transplantation 2016;100: 1610–1618

Pre-requisites to justify routine protocol biopsy surveillance for SCR

Very low risk of graft loss and a low risk of morbidity

Biopsy results must be diagnostically reliable and

Accurate.

SCR is detrimental to the allograft.

If SCR is found, a safe and effective suppressive treatment is available.

The risk-to-benefit ratio is justified by group

Must be individualized (In steroid avoidance and CNI withdrawal programs).

Safety and Value of Protocol Biopsy

Major complications from protocol

Biopsy is 1%

Minor complication rates (which resolve without intervention) include gross hematuria and …. is 3.5%

Skilled operator using ultrasound guidance and

an automated gun (rather than a manual needle biopsy).

A 16-gauge needle

single pass

Furness PN, Philpott CM, Chorbadjian MT et al. Protocol biopsy of the stable renal transplant: Amulticenter study of methods and complication rates. Transplantation 2003; 76: 969–973.

Reliability of protocol histology results

Variability between the pathologist's interpretation occurs using the Banff schema

Under or over-graded

Disappointingly resistant to feedback education

Furness PN, Taub N. International variation in the interpretation of renal transplant biopsies: Report of the CERTPAP Project. Kidney Int 2001; 60: 1998–2012.

Clinical Utility of Diagnostic Protocol Biopsies

The occurrence of SCR is time-dependent and maximal within the first months after Tx , falling to low levels after 1 year.

Interstitial lymphocytic infiltrate usually falls to low levels (Banff i1: 10–25% of cortex affected) or resolves completely beyond the first year in most compliant patients using CNI who are free of polyoma virus nephropathy.

Persistent SCR beyond 6 months thus represents a failure of baseline immunosuppression to control residual cellular immune activity.

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Recurrent and de novo GN

IFTA from unclear etiology

Recurrent disease

BK virus-associated nephropathy

CNI nephrotoxicity

Timing of Protocol Biopsies

IL-2R blocker

Depleting antibody agents

High-risk recipients such as those experiencing

DGF or those with elevated PRA, should undergo biopsy around 1 month.

A follow-up protocol biopsy should be done at 6 or 12 months post Tx.

Subclinical Rejection in Renal Transplantation: Reappraised Transplantation 2016;100: 1610–1618

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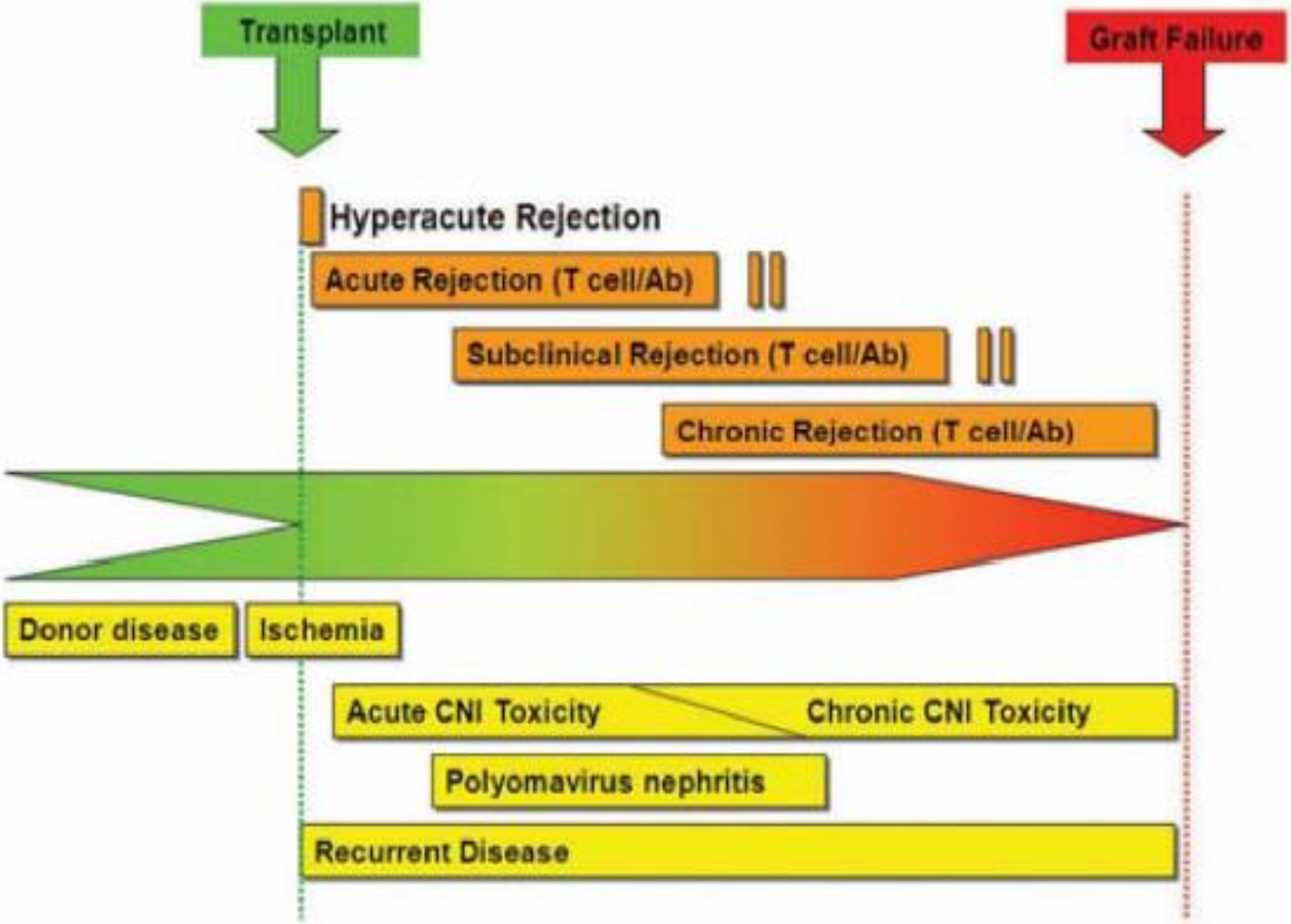
Optimum timing of surveillance biopsies depends on the pathology sought.

Biopsies up to 3months from transplant show a higher frequency of SCR with a greater incidence of IF/TA beyond 6 months and presentation of recurrent

and de novo GN, TG and CNI toxicity occurring at various time points from transplantation.

Early surveillance biopsy yields the greatest reversible pathology while biopsies beyond 1 year serve as prognostic indicators of graft survival and help tailor immunosuppression according to the individual.


Transplant
Graft Failure
Hyperacute Rejection
Acute Rejection (T cell/Ab)
Subclinical Rejection (T cell/Ab)
Chronic Rejection (T cell/Ab)
Donor disease
Ischemia
Acute CNI Toxicity
Chronic CNI Toxicity
Polyomavirus nephritis
Recurrent Disease

-Continued

The true incidence of kidney graft failure from acute rejection remains unclear. A study from Mayo Clinic identified specific causes of allograft failure in their **1317** recipients.

The overall incidence of graft loss due to acute rejection was **1.3%** (18/1317).

With a mean follow-up of 5 years annual allograft loss due to acute rejection

is 2.4%

El-Zoghby ZM, Stegall MD, Lager DJ, et al. Identifying specific causes of kidney allograft loss. Am J Transplant. 2009;9:527–535

-Continued

- Decreased prevalence of SCR with potent immunosuppression reduces this benefit in standard risk recipients, but utility is retained when transplanting high-risk patients and for monitoring steroid or CNI withdrawal

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Heilman RL, Devarapalli Y, Chakkera HA, et al. Impact of subclinical inflammation on the development of interstitial fibrosis and tubular atrophy in kidney transplant recipients. Am J Transplant 2010; 10: 563–570.

-Continued

Chronic rejection, either T cell– and/or antibody-mediated, causes late allograft failure in approximately 10% to 20% of renal allograft recipients

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El-Zoghby ZM, Stegall MD, Lager DJ, et al. Identifying specific causes of kidney allograft loss. Am J Transplant. 2009;9:527–535

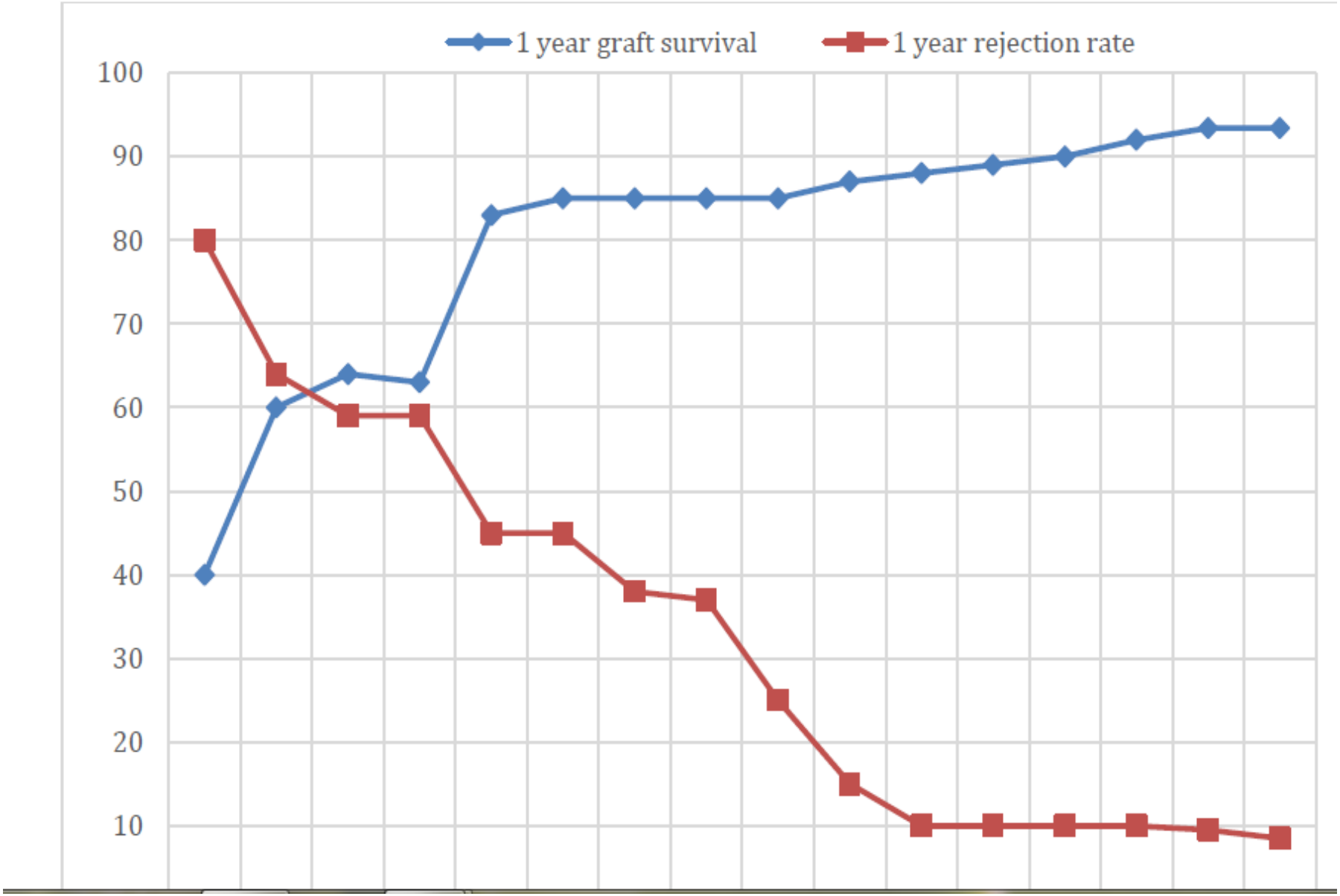
Short-term outcomes

Long-term outcomes :

- Death with a functioning graft (DWFG)
- TCMR or AMR
- Chronic TCMR or AMR
- CNI toxicity
- BKV nephritis
- Recurrent and de novo disease
- IFTA from unclear etiologies

Subclinical Rejection in Renal Transplantation: ReappraisedTransplantation 2016;100: 1610–1618

Figure 1. 1-year graft survival and rejection rates, 1960-2013[3]



Hart A, Smith JM, Skeans MA et al. OPTN/SRTR Annual Data Report 2014: Kidney. Am J Transplant. 2016; 16 (Suppl 2): 11-46

-Continued

The extent to which SCR influences long-term allograft dysfunction and survival remains controversial.

It is difficult to compare the true incidence of SCR

amongst centers because of differing immunosuppressive regimens.

Varying recipient immune risk factors

Not all transplant centers perform protocol biopsies, the timing of which also varies from center to center.

Few studies on SCR have been published over the past 2 decades.

TABLE 1.

Studies showing prevalence of SCR and treatment

Author/Publication, Year	No. patients (n)	Incidence	Treatment	Immunosuppression	Outcomes
Rush et al/JASN, 1998[22]	72	30% at 3 mo	Steroids	CsA, AZA, Pred. No induction	Improvement in chronicity scores at 6 mo and GFR at 2 y
Shapiro et al/AJT, 2001[23]	100	25% SCR at 1 wk, 21% borderline SCR	Steroids	Tac, steroids, MMF. Induction with Daclizumab or OKT3 in 18%	Not studied
Gloor et al/Transplantation, 2002[24]	114	2.6% SCR at 3 mo, 11% borderline SCR	Steroids	Tac, MMF, and steroids. Induction with Thymo or IL-2R blocker	Not studied
Shishido et al/JASN, 2003[25]	46	50% in patients with CAN at 1 y	Steroids	CsA/Aza/steroids	Worse graft survival in CAN associated with SCR
Nankivell et al/Transplantation, 2004[26]	120	60.8% and 45.7% at 1 and 3 mo	None	Four different IS protocols containing steroids which included combinations of cyclosporine, Tac, AZA, MMF	Tubulointerstitial damage decreased over time.
Kee, et al/Transplantation, 2006[27]	88	25% at 1 mo, 10.2% at 3 mo, 8.3% at 12 mo	Steroids	CNI inhibitor, MMF and steroids	Persistent SCR present in 46%. Lower Banff scores on follow up biopsy after treatment.
Scholten et al/JASN, 2006[28]	126	7.4% at 6 mo	Not treated	CsA or Tac along with MMF and steroids	No difference in GFR at 2 y
Moreso et al/AJT, 2006[29]	435	32% during first 6 mo	Not treated	Variable including CNI/MMF/ sirolimus/prednisone	Graft survival worse in patients with CAN and SCR
Anilkumar et al/AJT, 2008[30]	206	23% and 11% at 1 mo in AA and non-AA, respectively	Pulse steroids	CNI, MMF and steroid withdrawal at day 2	Higher incidence of SCAR in AA patients but no difference in graft survival at 5 y
Kurtkoti et al/AJT, 2008[31]	102	17.3% at 1 mo, 12% at 3 mo; all living donor transplants	Pulse Steroids	CsA/Tac, MMF/AZA, and prednisone	Lower serum creatinine in biopsy group at 6 mo and 1 y
Heilman et al/AJT, 2010[32]	256	7.4% at 1 or 4 mo	Steroids	Tac and MMF	IF/TA scores greater at 1 y in patients with SCI or SCR as compared with those with no inflammation on protocol biopsy
Loupy et al/JASN, 2015[33]	1001	13% SCR (T cell-mediated) at 1 y	Steroids	CNI, MMF, and prednisone	Good outcomes at 8 y for T cell–mediated SCR. Poor outcomes in patients who had antibody mediated SCR.
Gigliotti et al/J Nephrol, 2015[34]	169	10.7% at 30 d	Low-dose steroids	CNI/MMF/steroids	Treated SCR not associated with long-term graft failure

The impact and sequelae of SCR

1-Is associated with CAN using sequential biopsy analysis

2-Later tubulointerstitial damage

3-Reduced creatinine clearance

4-Shorter graft survival

Unlike clinical acute rejection, SCR does not immediately alter serum creatinine.

Nankivell BJ, Borrows RJ, Fung CL, O'Connell PJ, Allen RD, Chapman JR. Natural history, risk factors, and impact of subclinical rejection in kidney transplantation. Transplantation 2004; 78: 242–249.

Transplantation. 2004 Jan 27;77(2):214-20.

Natural history, risk factors, and impact of subclinical rejection in kidney transplantation.

Nankivell BJ[1], Borrows RJ, Fung CL, O'Connell PJ, Allen RD, Chapman JR.

Author information

Abstract

BACKGROUND: Subclinical rejection (SCR) is defined as histologically proven acute rejection in the absence of immediate functional deterioration.

METHODS: We evaluated the impact of SCR in 961 prospective protocol kidney biopsies from diabetic recipients of a kidney-pancreas transplant (n=119) and one kidney transplant alone taken regularly up to 10 years after transplantation.

RESULTS: SCR was present in 60.8%, 45.7%, 25.8%, and 17.7% of biopsies at 1, 3, 12, and greater than 12 months after transplantation. Banff scores for acute interstitial inflammation and tubulitis declined exponentially with time. SCR was predicted by prior acute cellular rejection and type of immunosuppressive therapy (P<0.05-0.001). Tacrolimus reduced interstitial infiltration (P<0.001), whereas mycophenolate reduced tubulitis (P<0.05), and the combination effectively eliminated SCR (P<0.001). Persistent SCR of less than 2 years duration on sequential biopsies occurred in 29.2% of patients and was associated with prior acute interstitial rejection (P<0.001) and requirement for antilymphocyte therapy (P<0.05). It resolved by 0.49 +/- 0.33 years and resulted in higher grades of chronic allograft nephropathy (CAN, P<0.05). True chronic rejection, defined as persistent SCR of 2 years or more duration and implying continuous immunologic activation was found in only 5.8% of patients. The presence of SCR increased chronic interstitial fibrosis, tubular atrophy, and CAN scores on subsequent biopsies (P<0.05-0.001). SCR preceded and was correlated with CAN (P<0.001) on sequential analysis.

CONCLUSIONS: Histologic evidence of acute rejection in the absence of clinical suspicion resulted in significant tubulointerstitial damage to transplanted kidneys and contributed to CAN.

American Journal of Transplantation 2006; 6: 2006–2012
Blackwell Munksgaard

doi: 10.1111/j.1600-6143.2006.01436.x

Minireview

The Significance of Subclinical Rejection and the Value of Protocol Biopsies

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Subclinical rejection (SCR) is diagnosed by protocol histology with a maximal prevalence occurring early after transplantation, falling to low levels by 1 year. Needle-core biopsy is safe, and the histology obtained fairly reflects subclinical immune activity. Several studies have consistently shown that SCR is associated with chronic tubulointerstitial damage, subsequent renal dysfunction and reduced graft survival. SCR is ef-

25% of baseline values) (2,3). SCR is therefore, by definition, diagnosed only on biopsies taken as *per protocol* at a fixed time after transplantation, rather than driven by clinical indication. It is distinct from clinical acute rejection, which is characterized by acute functional renal impairment. Some instances of SCR may represent the beginning or conclusion of an alloimmune infiltrate diagnosed fortuitously by protocol sampling (4,5), and some episodes of clinical rejection may actually represent SCR with an alterative cause of functional decline, such as concurrent calcineurin inhibitor (CNI) nephrotoxicity. SCR is subclassified into "acute" SCR (A-SCR, as Banff i2 and t2 or worse) or milder "borderline" SCR (e.g. i1 and t1), synonymously designated as "suspicious for acute rejec-

American Journal of Transplantation 2005; 5: 1354–1360
Blackwell Munksgaard

doi: 10.1111/j.1600-6143.2005.00830.x

Clinical Significance of an Early Protocol Biopsy in Living-Donor Renal Transplantation: Ten-Year Experience at a Single Center

Bum Soon Choi[a,*], Mi Jung Shin[a], Suk Joon Shin[a], Young Soo Kim[a], Yeong Jin Choi[b], Yong-Soo Kim[a], In Sung Moon[c], Suk Young Kim[a], Yong Bok Koh[c], Byung Kee Bang[a] and Chul Woo Yang[a,*]

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We report here our 10 year experience of a biopsy per

Introduction

The use of a protocol biopsy has documented the high prevalence of subclinical rejection in the early post-transplant period (1–5). It has provided timely treatment of allograft rejection that cannot be diagnosed on clinical grounds, and identifies patients who are insufficiently immunosuppressed. Moreover, subclinical rejection is associated with chronic allograft nephropathy, which is the most common cause of late renal allograft failure (6). Therefore, early detection and treatment of subclinical rejection reduces the incidence of chronic allograft nephropathy and the increase of graft survival.

Between July 1993 and July 2003

10-year experience

At day 14 after Tx

304 patients

Stable graft function

incidence of subclinical rejection was 13.2%

HLA-DR antigen mismatch (odds ratio, 2.39)
Unrelated donor (odds ratio, 2.10)

115 patients (37.8%) showed borderline changes and 40 patients (13.2%) showed acute rejection according to the Banff classification.

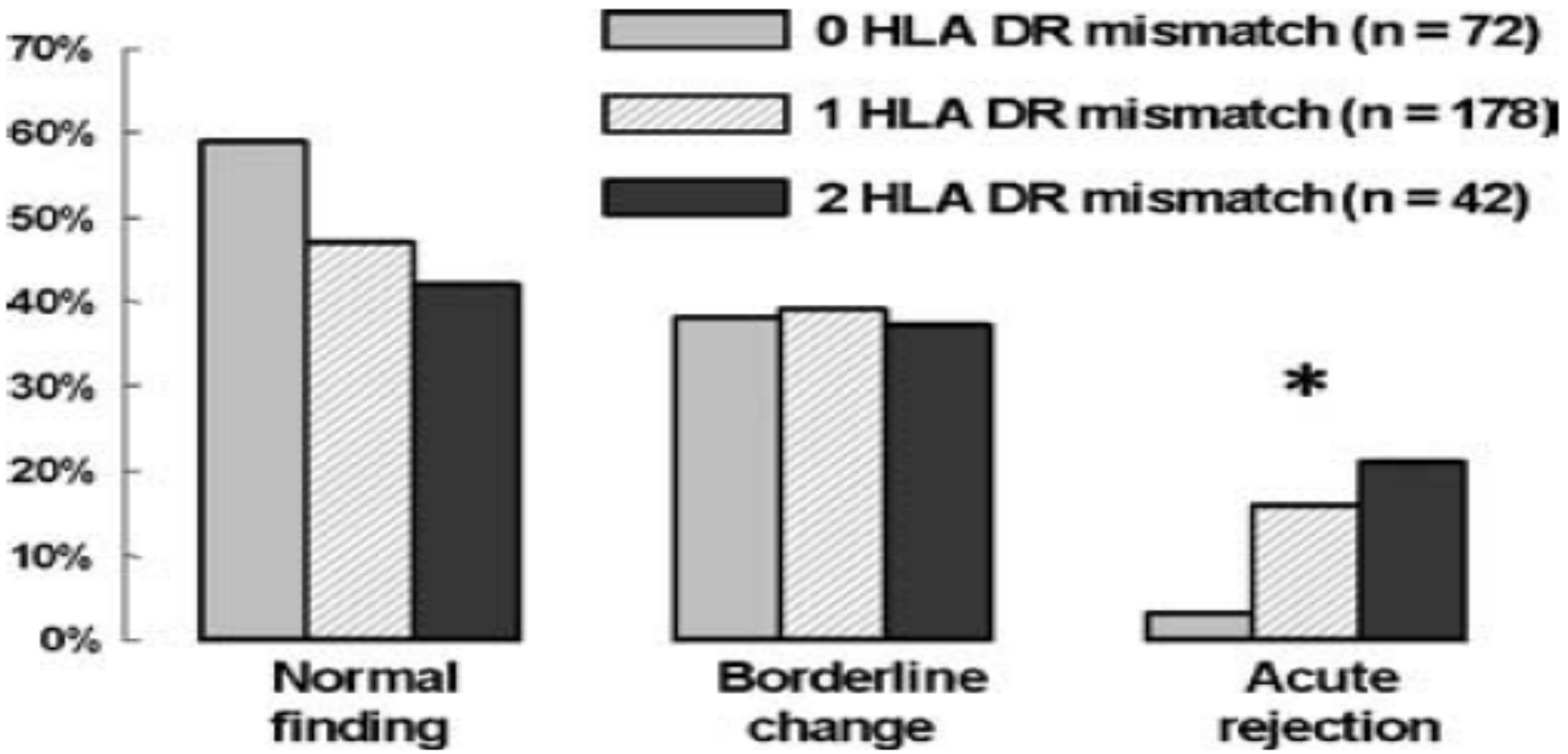

Figure 3: Histological findings of renal graft biopsies according to the number of HLA-DR mismatches. Note the significant increase of subclinical rejection in the patients with two HLA-DR mismatches compared with other groups. *$p < 0.05$ versus one or two HLA-DR mismatches.

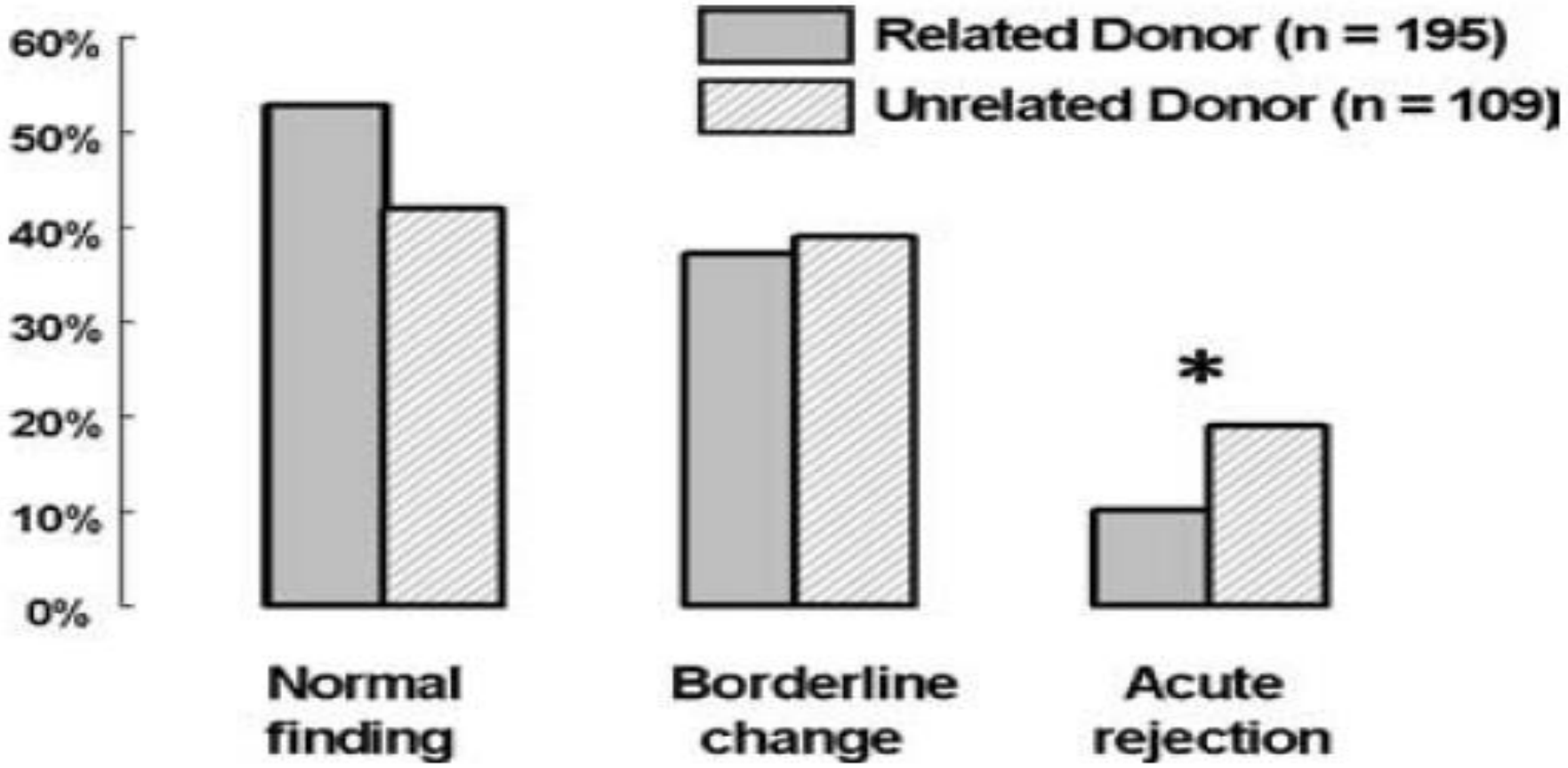

Figure 4: Histological findings of renal graft biopsies according to related versus unrelated donors. Note the significant decrease of subclinical rejection in patients with related donor compared with patients with unrelated donor. *$p < 0.05$ versus patients with unrelated donor.

Graft survival

62.3% : subclinical rejection group

93.7% : borderline change groups

96.2% : the normal finding group (88.4%

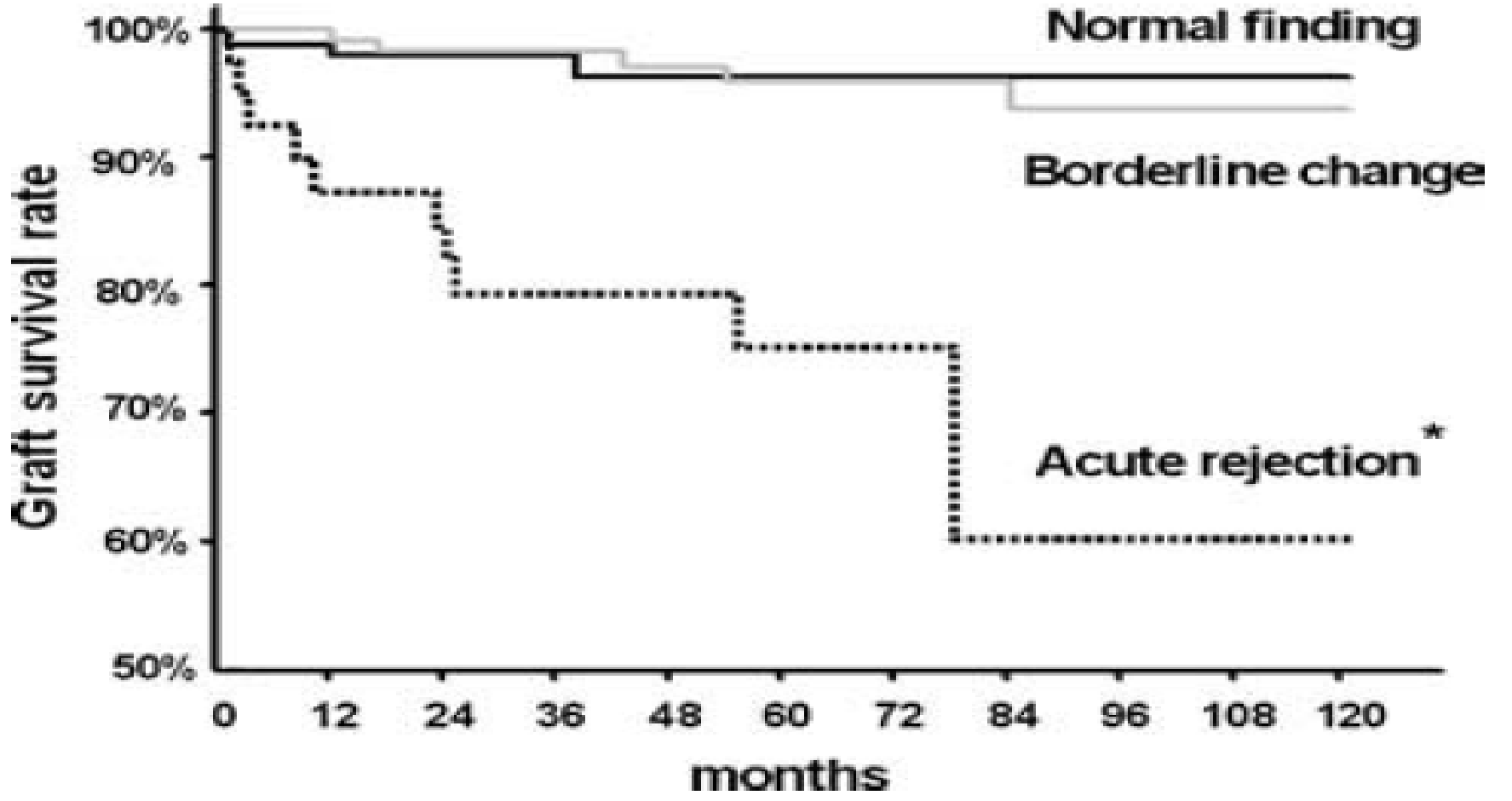

Figure 6: Graft survival rate in patients with normal, borderline changes and subclinical rejection. Note the significant decrease in graft survival rate in patients with subclinical rejection compared with the other groups. *$p < 0.05$ versus normal or borderline change groups.

Importance of SCR

- Early detection and treatment of SCR, before renal dysfunction, improves outcomes

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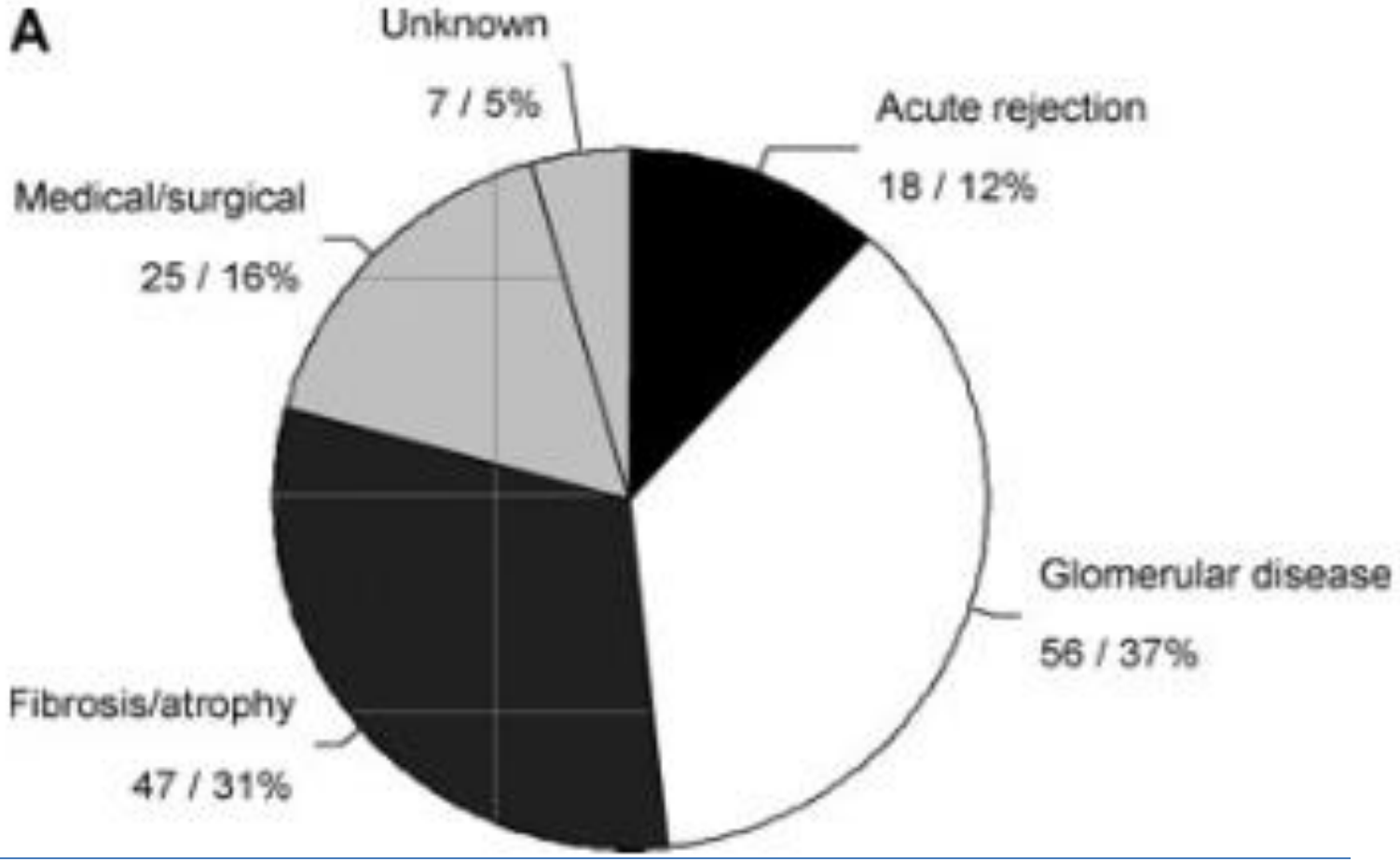
Kurtkoti J, Sakhuja V, Sud K, et al. The utility of 1- and 3-month protocol biopsies on renal allograft function: A randomized controlled study. Am J Transplant 2008; 8: 317–323.



El-Zoghby ZM, Stegall MD, Lager DJ, et al. Identifying specific causes of kidney allograft loss. Am J Transplant. 2009;9:527–535

Significance of IF/TA

The detection of IF/TA in protocol biopsies

procured as early as three to six months posttransplant in well functioning transplants has been correlated with later allograft dysfunction and loss.

Patients with concomitant interstitial inflammation and fibrosis may have a greater risk of graft dysfunction and loss than those patients with fibrosis alone.

1-Nankivell BJ. Delta analysis of posttransplantation tubulointerstitialdamage.Transplantation 2004;78(3):434-41.

2-Moreso F. Subclinical rejection associated with chronic allograft nephropathy in protocol biopsies as a risk factor for late graft loss. Am J Transplant 2006;6(4): 747-52.1-

-Continued

Burdick found lymphocytic infiltrates in protocol biopsies at 1 and 4 weeks after transplantation from patients with normal graft function.

Termed SCR by Rush using the Banff schema, it occurred in 30% of well-functioning grafts by 3months after transplantation using cyclosporine based immunosuppression .

Nankivell noted **SCR** in 45.7% at 3 months was associated with greater IF/TA by 12 months.

Legendre confirmed the association of clinically silent persistent inflammation with chronic tubulointerstitial damage and others have reported impact on survival of fibrosis and inflammation compared with fibrosis alone.

SCR and IF/TA

Silent progression of IF/TA

Simultaneous presence of SCR and IF/TA could be associated with a poorer graft survival when compared with grafts with SCR without IF/TA or with grafts with IF/TA but without SCR

Table 1. Risk Factors for the Development of CAN/IFTA[10,12]

Donor Derived	Recipient Derived
Deceased donor kidney	Obesity
Non-heart beating donor kidney	Polyomavirus nephropathy
Donor age > 60	CNI toxicity
Female Donor	Recurrent renal disease or de novo glomerulopathy
Donor with prior cardiac history or vascular disease	Hypertension
Cold ischemic time	Hyperlipidemia
DGF	Proteinuria
	Diabetes
	Medication non-compliance
	HLA mismatch
	Recipient pre-sensitization/panel reactive antibody (PRA)
	Presence of donor specific antibody (DSA)
	Acute rejection
	Subclinical rejection

American Journal of Transplantation 2006; 6: 747–752
Blackwell Munksgaard

doi: 10.1111/j.1600-6143.2005.01230.x

Subclinical Rejection Associated with Chronic Allograft Nephropathy in Protocol Biopsies as a Risk Factor for Late Graft Loss

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sions in renal allografts with otherwise stable renal function (1–5). There is agreement that subclinical rejection (SCR), that is, the presence of histological lesions of rejection in well functioning grafts, peaks during the initial months of post-transplantation and declines thereafter (6,7). The incidence of SCR is rather variable between centers and is influenced by the timing of protocol biopsy, the presence of an episode of acute rejection before the protocol biopsy and immunosuppressive treatment (6,8–10). The potential influence of other variables on the incidence of SCR such as donor source (deceased vs. living) or recipient type (pediatric vs adult) has not been properly evaluated (11,12).

Treatment of SCR

Steroids (intravenous or oral).

Depleting agents (ATG would be restricted

to those rare and severe cases of SC-TCMR involving arteritis or t3 tubulitis).

Combination of IVIG/ PLEX, Rituximab, and Bortezomib in SC-AMR.

Subclinical Rejection in Renal Transplantation: ReappraisedTransplantation 2016;100: 1610–1618

The American Journal of Pathology, Vol. 176, No. 4, April 2010

DOI: 10.2353/ajpath.2010.090411

Cardiovascular, Pulmonary and Renal Pathology

Intragraft Expression of the IL-10 Gene Is Up-Regulated in Renal Protocol Biopsies with Early Interstitial Fibrosis, Tubular Atrophy, and Subclinical Rejection

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From the Departament de Nefrologia, Hospital Universitari de*

associated with silent progression of interstitial fibrosis and tubular atrophy (IF/TA).[1–2] Furthermore, there is evidence that the simultaneous presence of subclinical rejection, interstitial fibrosis and tubular atrophy (SCR+IF/TA) could be associated with a poorer graft survival when compared with grafts with subclinical rejection without IF/TA (SCR), or with

protocol biopsies with SCR associated with IF/TA presented a **more severe infiltrate of B lymphocytes**, a similar degree of T-cell activation, and **higher IL-10 mRNA levels** than protocol biopsies with SCR but without chronic lesions

Data in Brief

A pathogenesis-based transcript signature in donor-specific antibody-positive kidney transplant patients with normal biopsies

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ARTICLE INFO

Article history:
Received 30 September 2014
Received in revised form 2 October 2014
Accepted 2 October 2014
Available online 12 October 2014

Keywords:
Kidney
Transplant
Antibody-mediated rejection
Donor-specific antibodies
Gene expression

ABSTRACT

Affymetrix Human Gene 1.0-ST arrays were used to assess the gene expression profiles of kidney transplant patients who presented with donor-specific antibodies (DSAs) but showed normal biopsy histopathology and did not develop antibody-mediated rejection (AMR). Biopsy and whole-blood profiles for these DSA-positive, AMR-negative (DSA+/AMR−) patients were compared to both DSA-positive, AMR-positive (DSA+/AMR+) patients as well as DSA-negative (DSA−) controls. While individual gene expression changes across sample groups were relatively subtle, gene-set enrichment analysis using previously identified pathogenesis-based transcripts (PBTs) identified a clear molecular signature involving increased rejection-associated transcripts in AMR− patients. Results from this study have been published in Kidney International (Hayde et al., 2014 [1]) and the associated data have been deposited in the GEO archive and are accessible via the following link: http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE50084

- Increased levels of rejection-associated transcripts, including those related to interferon,T-cell, B-cell, natural killer cell, and macrophage function. Despite this increased level of rejection-associated transcripts, during a three-year follow-up, only four patients (17%) developed AMR

Whether gene expression profiles in donor biopsy samples might help to assess the quality of the organ ?

gene expression profiles in donor biopsy samples

At present, no gene expression profile that should prompt a donor kidney to be declined has been identified.

kidneys from African-American donors who carry two copies of a genetic variant in **APOL1** associated with FSGS had a significantly shorter graft survival.

Monitoring Patients With SCR

We do not have a cellular, immunological, chemical, or genomic markers that are reliable, inexpensive, and reproducible and that can correlate with SCR so that a need for a biopsy could be eliminated.

Rebiopsy

Diagnostic Strategies

No protocol biopsies : vast majority of transplant units (they assume that either SCR is unimportant or that is relevant but can be controlled by high-dose anti-rejection therapy

Biopsies only in high-risk individuals : While individual selection is easy at the extremes of immunological risk, the difficulty arises with the large number of intermediate risk individuals—

Universal screening protocol biopsy program :

Current endpoints

FDA : composite of BPAR, graft loss, death, and loss to follow up.

European authorities : renal function at 1 year

It is time to convince the FDA to use SCR as a short-term surrogate marker.

Summary and Future Research

SCR results in chronic tubulointerstitial damage, impaired renal dysfunction and reduced graft survival. It is relatively common and easily and safely diagnosed by protocol biopsies.

Corticosteroid treatment in a single randomized clinical trial and other cohort studies demonstrated improved structural, functional and graft survival outcomes.

Kidney Transplant