LONG-TERM DETERIORATION OF KIDNEY ALLOGRAFT FUNCTION (DeKAF): HISTOPATHOLOGIC CORRELATES

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Long-term deterioration of kidney allograft function (DeKAF) is an ongoing multicenter study to define, in grafts with late post transplant dysfunction ("creeping creatinine"), clinicopathologic entities that predict rate of progression of chronic graft dysfunction and graft loss. Collectively, the participating centers perform over 1,000 renal transplants per year and currently follow over 10,000 transplant patients. The study population consists of all recipients of a kidney transplant prior to initiation of this study and with serum creatinine level < 2.0 mg/dL who develop new onset deterioration of function (as defined by a greater than 25% increase in serum creatinine level or new onset of proteinuria). The study also includes an inception cohort – those transplanted after study initiation who reached creatinine baseline (defined as the average of 3 serum creatinine levels after 3 months post-transplant) and then have a >25% increase in serum creatinine level that persists after potential confounding factors have been eliminated.

Objective: The objective of this interim analysis is to define histopathologic findings in renal biopsies obtained from the first 179 patients entered into this study.

Methods: Representative histologic sections from clinically indicated biopsies (obtained from patients who had a >25% increase in serum creatinine) were read in a blinded fashion, in the absence of clinical information or local pathology reports (which may have included immunofluorescence and/or electron microscopic data). Semiquantitative analysis was performed according to the Banff '97 Classification Scheme. An attempt was made to classify each biopsy according to the predominant morphologic alteration.

Results: Prevalence of Banff '97 acute and chronic scores are as follows:

	0	**1**	**2**	**3**
Inflammation (i)	100	34	26	19
Glomerulitis (g)	126	42	6	5
Tubulitis (t)	97	32	35	15
Vasculitis (v)	170	8	1	0
Interstitial fibrosis (ci)	58	94	17	10
Tubular atrophy (ct)	12	135	22	10
Transplant glomerulopathy (cg)	159	11	7	2
Vascular sclerosis (cv)	82	76	20	1
Hyalinosis (ah)	98	64	12	5

Predominant histopathologic findings are as follows:

	N	%		N	%
Minimal alterations	11	6%	Mild fibrosis (ci1, ct1)	27	15%
Isolated tubulitis (i0, t1-2)	2	2%	Moderate fibrosis (ci2, ct1-2)	6	3%
Suspicious (i1, t1-2)	18	10%	Severe fibrosis (ci3, ct3)	6	3%
Type IA Rejection	15	8%	Transplant glomerulopathy	9	5%
Type IB Rejection	13	10%	Arteriolar hyalinosis	19	11%
Type IIA Rejection	4	2%	Acute Tubular Necrosis	26	15%
Type IIB Rejection	1	0%	Viral cytopathic effects (BK)	8	4%
			Miscellaneous*	14	8%

*thrombotic arteriopathy (3), focal segmental glomerulosclerosis (7), ischemic nephropathy (1), cortical necrosis (1), acute pyelonephritis (2).

Conclusions: We report the predominant histopathologic findings in a group of 179 patients with graft dysfunction, as evidenced by a 25% increase in baseline serum creatinine levels 3 months or more after receiving a renal transplant. Studies to correlate histopathologic findings with markers of inflammation, fibrosis, humoral immunity, and clinical parameters are ongoing.