Does Histopathology of Implanted Kidney According to Banff 07 Help Predict Long-term Transplantation Outcome?

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ABSTRACT

Analyses of peritransplant biopsies of deceased-donor kidneys show high incidence of chronic abnormalities. The question arises whether chronic abnormalities present at implantation determine engrafted kidney fate regardless of other concomitant variables. The aim of this study was to identify risk factors of graft loss considering histopathological changes present at implantation scored according to Banff 07 criteria.

Patients and methods. Inclusion criteria (n = 300) was engraftment between years 2000 and 2008 and availability of implantation biopsy. Analyzed abnormalities present in donor biopsy were arteriolar hyalinization, interstitial fibrosis, intimal sclerotization, tubular atrophy, total inflammation, and percentage of sclerotic glomeruli (Banff classification). Allograft function was estimated by abbreviated Modification of Diet in Renal Disease formula and proteinuria semi-quantitatively by standard dip-stick test. Kaplan-Meier estimate was used to assess graft survival. Searching for independent risk factors of graft survival was performed by means of Cox proportional hazards models (SAS System, SAS Institute Inc, Cary, NC, United States).

Results. In one-factor analyses, predictors of kidney allograft loss were donor age, donor history of diabetes, kidney allograft dysfunction within first posttransplant year, and recipient chronic hepatitis C. In terms of chronic abnormalities, arteriolar hyalinization of any intensity nearly doubled the risk of allograft loss.
Independent risk factors of kidney allograft loss in multivariate analysis were donor age, posttransplant diabetes mellitus, proteinuria after engraftment, and recipient hepatitis C.

Conclusion. The effect of arteriolar hyalinization on renal transplant survival is probably interwoven with other predictors of graft loss. Recognizing the negative impact of recipient chronic hepatitis C on graft survival, hepatitis C virus treatment should be provided to patients with advanced chronic kidney disease, patients on wait lists, or patients already transplanted.

DURING the last few decades, due to the introduction of potent immunosuppressive agents, the incidence of acute rejection decreased and substantial improvement in 1-year graft survival was observed. However, short-term excellent results do not necessarily translate into prolonged survival and there is an ongoing search for more precise predictors of long-term kidney graft function.

There is a substantial number of well-recognized clinical characteristics known to influence deceased-donor kidney transplant survival [1] and the risk of graft failure depends on immunological and nonimmunological factors [2]. Donor age has been identified as one of the key determinants of prolonged transplanted kidney survival, not only as an important risk factor of chronic allograft dysfunction, but

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also as undermining acute rejection episodes [3]. At the same time, due to organ shortage, transplanting suboptimal kidneys has become routine [4], making an implantation biopsy a potentially useful tool to predict both short- and long-term graft function.

Former analyses of peritransplant biopsies of deceased-donor kidneys show high incidence of chronic abnormalities, especially glomerular sclerosis and vascular changes, and increasing evidence indicates their impact on graft function [5]. The question arises whether chronic abnormalities present at implantation determine engrafted kidney fate regardless of other concomitant variables.

STUDY AIM, DESIGN, AND PARTICIPANTS

The aim of the study was to identify risk factors of graft loss considering histopathological changes present at implantation and scored according to Banff 07 criteria.

We conducted an observational prospective cohort study of kidney recipients with the following inclusion criteria: successful kidney transplantation between years 2000 and 2008 (immediate or delayed graft function), availability of preimplantation graft biopsy, and posttransplant observation at the local outpatient clinic. Patients were accepted for the engraftment in concordance with national criteria for enlistment for kidney transplantation. As preimplantation biopsy results were not available before engraftment, they were not considered during the allocation process.

In all cases the procedure was performed at the Institute of Transplantation of the Medical University of Warsaw. Data were retrieved from the standard clinical charts. Peritransplant biopsies were evaluated by a local renal pathologist who was blinded to all clinical data. Biopsy specimens were processed and stained routinely (hematoxylin-eosin, periodic acid–Schiff, acid fuchsin orange G-stain) and evaluated by light microscopy. Histopathological evaluation was performed according to the Banff 07 classification for renal allograft pathology. The following chronic changes were analyzed: arteriolar hyalinization, interstitial fibrosis, intimal sclerotization, tubular atrophy, total inflammation score, and percentage of sclerotic glomeruli. The following donor clinical variables were included: type (living/deceased), basic demographic data, cause of death, body mass index, history of hypertension and other cardiovascular disease, diabetes mellitus, and serum creatinine concentration before harvesting. Procedure characteristics included cold ischemia time, number of HLA mismatches, and panel reactive antibodies. The following recipient characteristics were included: demographic data, weight and body mass index, primary kidney disease, renal replacement treatment before transplantation, retransplants, chronic hepatitis, diabetes as primary disease or occurring after implantation, rejection episodes within first year, and cytomegalovirus infection/disease within the first year of follow-up.

Allograft function within the first posttransplant year was estimated by abbreviated modification of diet in renal disease formula and proteinuria semi-quantitatively by standard dip-stick test.

STATISTICAL METHODS

Kaplan-Meier estimate was used to assess graft survival. Searching for independent risk factors of graft survival was performed by means of Cox proportional hazard models (SAS System).

RESULTS

After fulfilling inclusion criteria, 300 recipients were included in the study with mean observation time of 7.5 years. Among study patients, 42 (14%) lost the graft and required other modes of renal replacement therapy (hemodialysis or peritoneal dialysis), and 45 (15%) were lost to follow-up. Detailed description of the study group, their donors, and characteristics of kidney transplantation procedure are provided in Table 1.

In one-factor analyses we identified the following predictors of kidney allograft loss: donor age, donor history of diabetes, kidney allograft dysfunction within first posttransplant year (given as proteinuria occurrence or estimated glomerular filtration rate in Modification of Diet in Renal Disease <50 mL/min), and recipient chronic hepatitis C (details given in Table 2). In terms of chronic abnormalities present at implantation, arteriolar hyalinization of any intensity nearly doubled the risk of allograft loss.

We identified independent risk factors of kidney allograft loss in multivariate analysis: donor age with additional 4% of entering dialysis per 1 year, posttransplant diabetes mellitus, proteinuria at third month after engraftment, which nearly doubled the risk of dialysis, and recipient chronic hepatitis C (Table 3).

DISCUSSION

Our study aimed to elucidate whether histological evaluation of the kidney to be transplanted would enhance prediction of graft survival. In one-factor analyses we found that arteriolar hyalinization of any intensity doubled the risk of kidney loss (Table 2). Arteriolar hyalinization is a nonspecific abnormality that may be found in kidney tissue specimens originating from healthy individuals; it is also suggested that it accompanies healthy aging [6]. The very same but more pronounced pathology is found in kidney specimens harvested from individuals with hypertension, other cardiovascular diseases, lipid abnormalities, or diabetes [7].

According to our one-factor analysis arteriolar hyalinization diminishes long-term kidney survival, while this effect vanishes after adjustment for such prominent predictors of successful transplantation as donor age, diabetes, proteinuria, and chronic hepatitis. It may be the case that the same factors presenting in history as hypertension or aging are shown as proteinuria or hyperglycemia in laboratory results, and are detected as arteriolar hyalinization on a histological level.