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A retrospective analysis of the utility and safety of kidney transplant biopsies by nephrology trainees and consultants

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ABSTRACT

Background and aims: Dysfunction of a kidney transplant often requires histological sampling by percutaneous ultrasound-guided core needle biopsy. Transplant biopsy is more specialized than native kidney biopsy, the indications and complications are less well defined and in England are performed mainly by nephrologists. The aims of the study were to evaluate the adequacy and complication rate in living and deceased donor recipients according to training status of the nephrologist, assess the accuracy of physicians in predicting rejection, the threshold creatinine rise for biopsy, and the change in drug management post-biopsy.

Materials and methods: We performed a retrospective analysis of all adult patients undergoing a kidney transplant biopsy in 2015 at a major teaching hospital in the UK as part of a service evaluation program. The primary outcome measure was the rate of major complications and secondary measures included sample adequacy, seniority of operator, clinician-predicted diagnosis, biopsy diagnosis and change in drug management.

Results: One hundred and seven (n = 107) transplant biopsies were performed across 27 living donor (LD) recipients and 57 deceased donor (DD) recipients. LDs were statistically less likely to have diabetes, more likely to take azathioprine. Biopsies were performed by trainees rather than consultants at a ratio of 3:1. The complication rate was low with no major bleeding complications. Visible haematuria occurred in 4.7% and 2.8% of patients developed transplant pyelonephritis. 3.7% of biopsies contained no glomeruli. There was no effect attributed to training status. The pre-biopsy rise in creatinine was significantly less for LD compared to DD recipients (45% vs 70%). A clinician-suspected diagnosis of rejection was confirmed on biopsy in 42.9% of cases and overall about 47.9% of biopsies led to a change in drug management.

Conclusions: Kidney transplant biopsies were safe, performed adequately by trainee nephrologists and were often associated with a change in drug management.

1. Introduction

Kidney transplantation is the optimal treatment for many patients with end-stage renal failure [1]. Episodes of renal dysfunction are common during the lifetime of a transplanted kidney and often mandate histological sampling of the organ [2]. A percutaneous ultrasound-guided kidney transplant biopsy is the 'gold standard' method for determining the cause of allograft dysfunction after obstructive and major vascular causes have been excluded [3].

The indications for transplant biopsy are divided between protocol biopsies that are performed at defined time points and those that are performed for acute or chronic graft dysfunction [3]. The threshold reduction in kidney function leading to a non-protocol biopsy is largely unknown and may vary across different transplant units and for donor types. Information on the reasons for initiating a biopsy could be helpful for developing more standardized guidelines for transplant biopsy. Percutaneous kidney transplant biopsies in England are performed predominantly by nephrologists and not radiologists or surgeons. The extent to which biopsies are performed by trainees versus certified consultants in nephrology is unknown and could impact on biopsy quality and safety. In England, competency with renal transplant biopsy is an optional part of the nephrology training program (https://www.jrcptb.org.uk/specialties/renal-medicine).

Percutaneous kidney transplant biopsy is an invasive procedure that confers a risk of major and minor complications. Major complications of transplant biopsies are variously described in the literature but predominantly comprise haemorrhage requiring transfusion, radiological intra-arterial embolization or surgical intervention. Recent studies of native kidney biopsies have described the risk of such bleeding complications as 2.2 to 7.4% [4–6]. Fewer data exist for transplant biopsies. One study described a composite major complication rate of 1.9%, comprising predominantly a need for transfusion due to bleeding [7].

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Another study described a composite severe or life-threatening complication rate of 0.4% and that the risk of bleeding was 311% higher for biopsies within the first week after transplantation [8]. In addition to complications, biopsy adequacy is a major factor in the overall utility of performing a biopsy [9]. Although precise criteria for an adequate biopsy are difficult to define the Banff criteria recommend several parameters such as a minimum of 10 glomeruli [10].

We conducted a service evaluation to analyse the utility and safety of kidney transplant biopsies performed over 12 months at a major kidney transplant centre in England. We examined the complication and adequacy rate stratified by donor status and biopsy operator grade. We also examined the value of biopsies with regards confirming the clinicians' suspected diagnosis of rejection and effect on drug treatment.

2. Methods

We evaluated all percutaneous inpatient and outpatient renal transplant biopsies for patients aged > 16 years old performed from 1st January 2015 to the 31st of December 2015 at the Oxford Kidney and Transplant Unit. Data were collected in January 2017 allowing at least 1 year of follow-up for each patient. Data were obtained from the local online renal patient database (Proton), from the electronic patient record (EPR) and where available from the paper medical notes. A list of patients having undergone a biopsy was ascertained by examining the local paper biopsy diary, and electronic annotation of biopsies on Proton and EPR. Transplant biopsies were performed under ultrasound guidance with 18 gauge needles and a spring loaded re-usable biopsy gun. Biopsies were performed in the supine position and all patients had laboratory blood tests within 2 weeks prior and following the biopsy. All anti-coagulants were stopped prior to biopsy with a suitable washout period but continuation of aspirin was permitted. Our protocol recommended patients receive Desmopressin 0.4 mcg/kg (max dose 28 mcg) intravenously prior to the biopsy if the creatinine was more than 250 μmol/L unless there was active coronary artery disease or recent stroke. Biopsies were performed on the renal day-case unit with 6 h post-biopsy observation or on the renal/transplant wards. The data were entered into an Excel Spreadsheet and analysed using the R software environment. The rise in creatinine from baseline to the time of biopsy was based on a comparison of the nadir creatinine within the last 6 months and last creatinine preceding or on the biopsy date. Statistical tests were conducted within R using default software parameters. A Fisher's exact test was used to compare count data between groups with a P value threshold for significance of 0.05. Alternatively, a Student's *t*-test, with a threshold for significance of 0.05, was used to compare means for the following data variables: age (at first biopsy), time from transplant to first biopsy, baseline creatinine, proportion globally sclerosed glomeruli, change in haemoglobin post-biopsy, absolute rise in creatinine prior to biopsy, fold change in creatinine rise prior to biopsy, and differences in sampled glomeruli numbers. The project and manuscript were evaluated by the Oxford University Hospitals NHS Trust Research and Development department and the work deemed a 'service evaluation' and that further external ethical permissions were not required. Where applicable the study format adheres to the STROCSS guideline (https://www.strocssguideline.com).

3. Results

3.1. Baseline characteristics of patients undergoing renal transplant biopsy

We analysed 107 (100%) kidney transplant biopsies that were performed in 84 patients during the 1 year study period. The majority of patients had a deceased donor kidney that was biopsied (57, 67.9%) and two of these patients had a simultaneous kidney-pancreas transplant. Biopsies were predominantly performed on an outpatient basis with 66 (61.7%) biopsies occurring on the renal day-case unit. Several patients underwent more than one biopsy of the same kidney transplant within this year – 66 (62%) patients underwent 1 biopsy, 14 (13.1%) patients underwent 2 biopsies, 3 (2.8%) patients under went 3 biopsies and 1 (0.9%) patient underwent 4 biopsies. The baseline demographic and clinical details are shown on a per patient basis comparing deceased donors and living kidney donors (Table 1). DD recipients undergoing a biopsy were more likely than LD recipients to have diabetes and to have diabetes as their primary renal diagnosis whereas LD recipients were more likely to be taking azathioprine.

Table 1
Baseline demographic and clinical parameters of patients with living or deceased donor kidneys who underwent a kidney transplant biopsy during the evaluation period (HLA = human leucocyte antigen, NA indicates missing data).

Variable	Living Donor (%)	Deceased Donor (%)	P value
Number of patients	27	57	
Number of biopsies	38 (35.5)	69 (64.5)	
Gender male	19 (70)	30 (52.6)	0.16
Age (mean)	48.78	54.37	0.06
HLA mismatches			0.87
0	1 (3.7)	3 (5.3)	
1	1 (3.7)	2 (3.5)	
2	4 (14.8)	7 (12.3)	
3	8 (29.6)	20 (35.1)	
4	8 (29.6)	9 (15.8)	
5	2 (7.4)	2 (3.5)	
6	0 (0)	1 (1.8)	
NA	3 (11.1)	13 (22.8)	
Comorbidity			
Cardiovascular	4 (14.8)	12 (21.1)	0.57
Respiratory	2 (7.4)	5 (8.8)	1.00
Diabetes	2 (7.4)	19 (33.3)	0.014
Other	4 (14.8)	11 (19.3)	0.76
Ethnicity			
White	23 (85)	39 (68.4)	0.12
Asian	2 (7.4)	8 (14)	0.49
Black	0 (0)	2 (3.5)	1.00
Other	2 (7.4)	8 (14)	0.12
Primary renal disease			
Diabetes	1 (3.7)	13 (22.8)	0.03
Hypertension	3 (11.1)	4 (7)	0.66
Polycystic Kidney Disease	2 (7.4)	6 (10.5)	1.00
Glomerulonephritis	7 (25.9)	18 (31.6)	0.80
Reflux Nephropathy	4 (14.8)	2 (3.5)	0.08
Other	10 (37)	14 (24.6)	0.20
Time from transplant to first biopsy (days)			
Min	4	4	
Median	160	536	
Mean	969	1368	
Max	6218	10067	0.39
Baseline creatinine (μmol/L, mean)	194	238	0.19
Mortality (at last follow-up)	0 (0)	7 (12.3)	0.09
Immunosuppression			
Tacrolimus	23 (85.2)	50 (87.7)	0.74
Ciclosporin	2 (7.4)	7 (12.3)	0.71
Sirolimus	1 (3.7)	0 (0)	0.32
Mycophenolate	15 (55.6)	40 (70.2)	0.22
Azathioprine	12 (44.4)	11 (19.3)	0.02
Prednisolone	11 (40.7)	15 (26.3)	0.21

3.2. Baseline haematological parameters in living and deceased donor recipients at the time of biopsy

To begin to assess the safety of kidney transplant biopsy we ascertained the baseline haematological profile of patients using blood tests performed within 2 weeks preceding the biopsy (Table 2 - data are shown on a per biopsy basis). We also assessed the number of patients who continued on aspirin and the use of desmopressin. Patients were generally permitted to continue aspirin at the clinician's discretion, but other anticoagulants or anti-thrombotic agents were discontinued. Our policy was to give desmopressin pre-biopsy if the creatinine was more