Evaluation of Renal Allograft Fibrosis by Transient Elastography (Fibro Scan)

T. Nakao[a,*], H. Ushigome[a], T. Nakamura[a], S. Harada[a], K. Koshino[a], T. Suzuki[b], T. Ito[a], S. Nobori[a], and N. Yoshimura[a,b]

[a]Department of Organ Transplantation and General Surgery, Kyoto Prefectural University of Medicine, Kajii-cho 465, Kamigyo-ku, Kyoto, Japan; and [b]Department of Organ Interaction Research Medicine, Kyoto Prefectural University of Medicine, Kajii-cho 465, Kamigyo-ku, Kyoto, Japan

ABSTRACT

Background. Chronic allograft injury (CAI) is one of the most important factors for graft failure after renal transplantation. Protocol biopsy is the most valuable tool for revealing subclinical renal allograft failure. Transient elastography (TE) is a noninvasive technique that has shown utility for the assessment of hepatic and renal fibrosis. This study sought to evaluate whether TE was a viable and effective method for the assessment of renal allograft failure.

Patients and Methods. Thirty-five patients underwent TE by Fibro Scan (Echosense, Paris, France). Biopsies were performed in 27 patients, allowing classification according to Banff chronic changes in the interstitium grade 0, grade 1 or grade 2.

Results. Measurement of parenchymal stiffness was successful in 31of 35 patients (91%). Stiffness was significantly correlated with interstitial fibrosis ($P < .05$) and inversely related with estimated glomerular filtration rate (eGFR; $P < .05$). Stiffness values of patients with eGFR > 50 mL/min were lower than those of patients with eGFR < 50 mL/min ($P < .05$). Patients classed as CAI Banff grade 0 had significantly less parenchymal stiffness than patients with Banff grade 1 or grade 2 CAI ($P < .05$). Parenchymal stiffness measured by TE reflected interstitial fibrosis in renal allograft.

Conclusion. Assessment of parenchymal renal allograft stiffness by TE was effective for identifying patients with CAI who may subsequently benefit from biopsy and modification of the immunosuppressive regimen. Assessment of parenchymal renal allograft stiffness can be effective for identifying patients with CAI. TE has the potential to reduce the number of renal allograft biopsies required for accurate assessment of CAI.

CHRONIC ALLOGRAFT INJURY (CAI) is one of the most important factors for graft failure after renal transplantation [1]. An early diagnosis of CAI is important to prevent further deterioration of renal function, which may lead to chronic and permanent elevation of creatinine levels in patients. Currently, only protocol biopsy can accurately reveal subclinical renal allograft failure and, for this reason, our hospital, as well as other transplantation centers nationwide, has well-established protocol biopsy programs. Protocol biopsy is widely regarded as a valuable tool for detecting subclinical disease in renal transplantation patients who may then benefit from a modification of therapy [2,3]. However, protocol biopsy has the potential to cause complications, such as vasovagal reactions, hematuria, perirenal hematomas, arteriovenous fistula, and injury to other organs, especially the gut. Indeed, major complications requiring invasive procedures, such as blood transfusions or urinary catheter, were reported in 1% of all

*Address correspondence to Toshimasa Nakao, MD, Department of Organ Transplantation and General Surgery, Kyoto Prefectural University of Medicine, 02-8566, Kajii-cho 465, Kamigyo-ku, Kyoto-prefecture, Japan. E-mail: toshi876@koto.kpu-m.ac.jp

0041-1345/15
http://dx.doi.org/10.1016/j.transproceed.2014.12.034

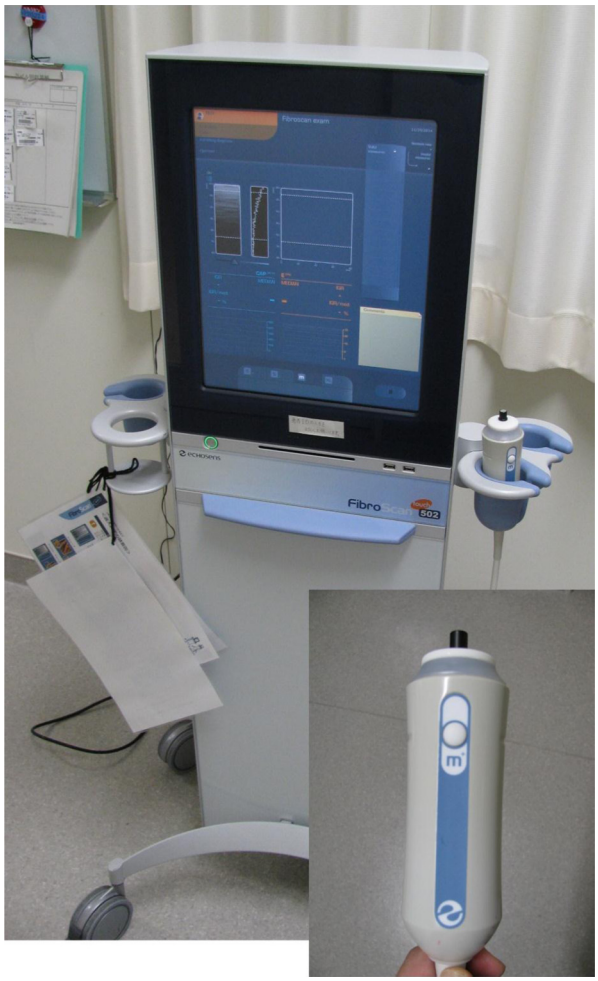

Fig 1. The transient elastography machine (Fibro Scan), which measures organ stiffness. The cylinder is 10 mm wide and 25 to 30 mm long.

protocol biopsy specimens [2,3]. Transient elastography (TE) is a noninvasive technique that originally showed effectiveness in the assessment of liver fibrosis [4–6]. As a result, there has been increasing interest in the use of TE as a noninvasive tool in place of renal allograft biopsy for evaluating CAI and renal allograft failure [7–9]. This study sought to evaluate whether TE was viable as an alternative method to renal allograft biopsy for assessing CAI and renal allograft failure.

PATIENTS AND METHODS

Thirty-five patients underwent TE from October 2013 to August 2014. Blood tests were performed in all patients and serum creatinine, estimated glomerular filtration rate (eGFR), hemoglobin, hematocrit, calcium, total cholesterol, and phosphorus levels were measured. Biopsies were performed in 27 patients and their renal allograft tissue was classified according to the Banff changes in interstitium (ci) classification scheme (grade 0, grade 1, or grade 2). TE stiffness was compared between patients in the three different Banff grades. Furthermore, patients were divided into two groups according to their eGFR: >50 mL/min (first group) or <50 mL/min (second group). Tissue stiffness was compared between these two groups. Finally, patients were divided into two groups according to time since transplantation, with the first group being >24 months post-transplantation and the second group being <24 months post-transplantation.

TE was performed using the Fibro Scan (Echosense Paris, France) (Fig 1). All measurements were made by the same operator, and measurements were taken with patients lying in a supine position. Before starting TE, a conventional ultrasound examination of the renal allograft was performed to define the optimal position for the probe. A transducer transmitted vibration and low frequency through the underlying tissue. TE measured parenchymal stiffness in a volume that approximated a cylinder of 10 mm in width and 25–30 mm in length (Fig 1).

Statistical Analysis

Two different groups were compared using the Student *t*-test. Tukey's tests were used to analyze for multiple comparisons. *P* values less than .05 were considered to indicate statistical significance. All statistical analyses were performed by JMP 11 version (SAS Institute Inc., Cary, NC).

RESULTS

The total number of patients included in this study was 35. The demographic and baseline characteristics of recipients and donors are shown in Table 1. In this cohort, 7 patients had diabetes mellitus; 4 patients had immunoglobulin A nephropathy; two patients had focal segmental glomerulosclerosis, and one patient had polycystic kidney disease. The mean serum creatinine level was 1.79 ± 1.21 mg/dL; the mean eGFR level was 41.9 + 20.6 mL/min; the mean hemoglobin level was 10.57 ± 1.59 g/dL; the mean hematocrit level was 32.0 + 4.93%; the mean phosphorus level was 41.9 + 20.6 mg/dL; the mean calcium level was 2.99 + 1.21 mg/dL; and the mean total cholesterol level was

Table 1. Study Population and Graft Characterization

Total number of subjects	35
Female	12
Male	23
Diabetes mellitus	7
IgA nephropathy	4
FSGS	2
PKD	1
Mean age of patient (y)	51.3 ± 12.8
Mean age of donor (y)	56.9 + 10.9
Mean time since transplantation (mo)	23.12 ± 9.86
Mean parenchymal stiffness (kPa)	32.97 ± 19.08
Serum creatinine (mg/dL)	1.79 ± 1.21
eGFR (mL/min)	41.9 + 20.6
Hemoglobin (g/dL)	10.57 ± 1.59
Hematocrit (%)	32.0 + 4.93
K (mg/dL)	3.18 + 1.58
Ca (mg/dL)	9.19 + 0.88
Mean total cholesterol (mg/dL)	187.37 + 48.0

Abbreviations: IgA, immunoglobulin A; FSGS, focal segmental glomerulosclerosis; PKD, polycystic kidney disease; K, potassium; Ca, calcium.