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CLINICAL INVESTIGATION

Transjugular Renal Biopsy: Our Experience and Technical Considerations

Teik Choon See · Barbara C. Thompson · Alexander J. Howie · M. Karamshi · Anthie M. Papadopoulou · Neil Davies · Jonathan Tibballs

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Abstract The purpose of this study was to describe the indications for and technique of transjugular renal biopsy (TJRB) and evaluate the efficacy and complications of this method. We performed a retrospective review of 59 patients who underwent TJRB using the Quick-core needle biopsy system (Cook, Letchworth, UK) over a 4-year period. The indications for obtaining renal biopsy included acute renal failure, chronic renal failure, nephrotic syndrome, and proteinuria with or without other associated disease. Indications for the transjugular approach included coagulopathy, biopsy of a solitary kidney or essentially single functioning kidney, simultaneous renal and hepatic biopsy, morbid obesity, and failed percutaneous biopsy. All but four cases were performed via the right internal jugular vein. The right, left, or both renal veins were cannulated in 41, 14, and 4 cases, respectively. Combined liver and renal biopsies were obtained in seven cases. Diagnostic biopsy specimens were obtained in 56 of 59 patients (95%). The number and size of tissue cores ranged from 1 to 9 mm and from 1 to 20 mm, respectively. The mean numbers of glomeruli per procedure on light microscopy and electron microscopy were 10.3 and 2.6, respectively. Specimens for immunohistology were acquired in 49 cases, of which 40 were adequate. Of the 56 successful TJRB procedures, 34 (61%) were associated with isolated capsular perforation (19), contained subcapsular leak (10), isolated collecting system puncture (1), and concurrent collecting system and capsular perforation (4). There was a significant increase in capsular perforation with six or more needle passes, although no significant correlation was seen between number of needle passes and complication. Six patients had minor complications defined as hematuria or loin pain. Seven patients developed major complications, of whom five received blood transfusion alone. Two required intervention: in one an arteriocalyceal fistula was embolized and the patient was temporarily dialyzed; the remaining patient required ureteric stenting. In conclusion, TJRB provides an adequate yield for diagnosis. Complication rates are relatively high, but patients are also at high risk from the conventional percutaneous approach. Patient selection and optimization are critical to avoid major complications.

Keywords Transjugular · Renal biopsy · Tru-cut needle

T. C. See (✉)
Radiology Department, Addenbrookes Hospital, Hills Road, Box 219, Cambridge CB2 2QQ, UK
e-mail: teikchoon.see@addenbrookes.nhs.uk

T. C. See
Departments of Radiology, Cambridge University Hospitals NHS Trust, Cambridge, UK

B. C. Thompson
Department of Nephrology, Royal Free Hospital, Pond Street, London NW3 2QG, UK

A. J. Howie
Department of Pathology, University College London, London WC1E 6JJ, UK

M. Karamshi · A. M. Papadopoulou · N. Davies · J. Tibballs
Department of Radiology, Royal Free Hospital, Pond Street, London NW3 2QG, UK

Introduction

Renal biopsy may form part of the clinical workup for diagnosis of renal parenchymal disease. Percutaneous technique remains the preferred method for obtaining renal tissue. The efficiency and safety of this technique have

been further improved by image guidance, with tissue yields of up to 98.8% [1–3] and reported major complication rate of 3.5%–6.4% [4]. However, percutaneous biopsy is considered too risky to be justified in patients with deranged clotting, thrombocytopenia, a single functioning kidney, or small kidneys and can be technically too challenging in patients with a particularly high body mass index (BMI) or patients who are unable to cooperate with the procedure or lie prone. Transjugular renal biopsy (TJRB) is a feasible alternative in these high-risk patient groups, in whom a pathological diagnosis would provide valuable information needed to guide their clinical management. The needle is directed away from larger vessels, and in theory any bleeding will bleed back into the vein unless arterial puncture or a significant capsular perforation or collecting system puncture occurs. It may be performed using an aspiration needle or the less commonly described core biopsy system, although there is limited expertise worldwide. A diagnostic yield of 73%–95% and major complication rate of 1%–18% [1, 5–7] have been reported using the aspiration needle, compared with yields of 89%–96.5% and major complications of 2.7%–27% with the core biopsy needle [8–11]. The aspiration biopsy technique is, however, difficult to learn and requires a particularly high level of expertise. The core biopsy technique is easy to use and the new blunt-tipped biopsy needle may be less traumatic, hence avoiding significant complications [12]. The Tru-cut biopsy needle (Cook, Letchworth, UK) with a 2-cm throw used in our series is not dissimilar in principle to the needle used in other core biopsy series [8–11], although we use a flexible Arrows sheath (Kimal, Uxbridge, UK) instead of the rigid 7-Fr sheath with a rigid 14-gauge inner stiffening cannula [9–11]. We describe the technique, indications, sampling effectiveness, and complications of our experience in 59 patients.

Materials and Methods

This is a retrospective review of 59 consecutive patients referred by our renal physicians for TJRB from August 2000 to December 2004. Informed consent was obtained for TJRB, but as this was not a clinical trial, formal ethics committee approval was not required.

Transjugular Renal Biopsy Technique

The procedures were performed in the interventional radiology suite with selective utilization of conscious sedation and intravenous analgesia. Patency of the internal jugular veins (IJVs) was assessed with the patient in the supine position using ultrasound. The right IJV was preferred due to its straight course to the inferior vena cava (IVC). However, a left-sided approach was necessary when there was stenosis of the right IJV or brachiochephalic vein, usually from multiple previous line insertions. Following infiltration with local anesthetic, IJV puncture was performed with an 18-gauge needle. Using the Seldinger technique a 7-Fr Arrows sheath (Kimal, Uxbridge, UK) was advanced into the IVC. A 5-Fr Cobra catheter (Cordis Europa N.V., Roden, Netherlands) was then introduced and engaged on a main renal vein. The right renal vein is preferred due to the more favorable angle and shorter course from the IVC. A guide wire was advanced as distally as possible in a subcortical vein, followed by the catheter and the Arrows sheath. The catheter and wire were then removed. A limited venogram was performed via the sheath to assess the venous anatomy and to ensure that the system was peripherally wedged (which manifests as cortical enhancement distal to the sheath) (Fig. 1). This increases the likelihood of true cortical sampling. A 60-cm-long, 19-gauge Quick-core biopsy needle with a beveled end and a 2-cm specimen notch (Cook, Letchworth, UK) was inserted into a 70-cm, 5-Fr straight catheter (Cook), which was shortened by approximately 15 cm in order to accommodate the length of the biopsy needle. Both were inserted into the selected renal vein until it reached the tip of the Arrows sheath. The sheath and catheter were withdrawn slightly to expose the needle tip and samples were taken with the aid of the spring-loaded gun. Biopsy specimens were immediately examined by an on-site pathology technician who made an initial assessment of the adequacy of the samples using a dissecting microscope, and in this manner guided how many tissue cores were obtained.

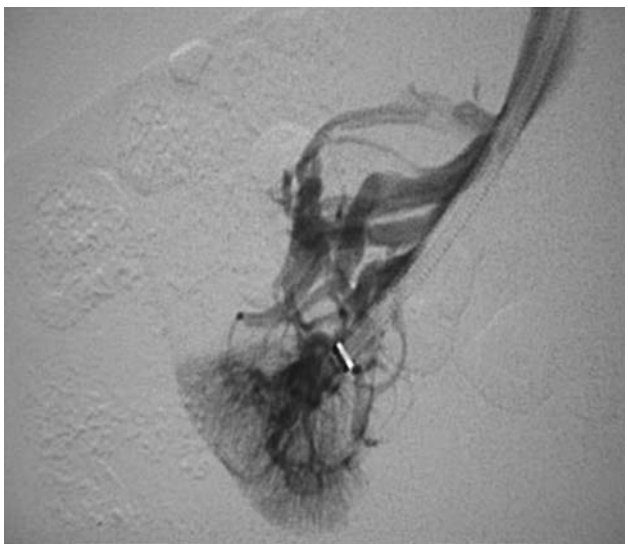

Fig. 1 Venogram confirms peripheral wedging of the sheath

Nearly all the tissue was fixed in formalin for light microscopy (LM). A small piece of tissue was fixed in glutaraldehyde for electron microscopy (EM). In the first half of the series, another small sample was frozen for immunoflourescence (IF), but later, immunoperoxidase (IP) was performed on the formalin-fixed material.

The catheter was left in situ and a small volume of contrast medium was injected to exclude a capsular perforation. Elective embolization of the biopsy track in asymptomatic patients was performed in five cases during our early experience with TJRB, but with increasing experience we found that this is unnecessary, and currently we reserve the practice for patients with significant extravasation accompanied by hemodynamic compromise while on the table, where venous access to the biopsy track is still maintained. No intervention was performed for patients with significant extravasation who remained clinically stable, nor did we perform repeat contrast injection to assess the progression of extravasation. All patients returned to the ward for routine 24-h bed rest and hemodynamic observation, which took place every 15 min for the first 2 h, then half-hourly for 4 h, then hourly.

Tissue Adequacy

The numbers of needle passes and cores obtained per procedure were ascertained. The tissue cores were considered adequate when a sufficient number of intact glomeruli was present to make a pathological diagnosis. At first we aimed to obtain about 10 glomeruli, although this was not achieveable in all cases, and with increasing experience we realized that a diagnosis could be made with fewer glomeruli. The number of glomeruli available for LM, IF/IP, and EM was assessed for each procedure.

Complications

Complications were considered major if they resulted in clinical sequelae, requiring blood transfusion, an intervention, or therapeutic embolization and minor if they were of minimal clinical consequence or no treatment was required. The lowest hemoglobin (Hb) level within the 72-h period following the procedure was documented, in order to estimate blood loss related to the biopsy.

Statistical Analysis

Student *t*-tests were performed to compare the length of cortical tissue and the number of glomeruli obtained between patients with capsular and/or subcapsular perforation and patients without. Fischer's exact test was performed to compare the incidence of complications in patients with five or fewer passes with patients who underwent six or more needle passes. Chi-square test was performed to assess the number of needle passes in relation to major complications.

Results

Of the 59 patients there were 33 males and 26 females, with a mean age of 50 years (range, 16–82 years). All patients were referred by nephrologists who requested renal biopsy specifically via the transjugular route, due to relative contraindications to percutaneous biopsy. During the same period, 544 percutaneous renal biopsies (including 106 in transplant kidneys) were performed at our institution, making the incidence of the transjugular approach 10.8%.

Indications

The medical reasons for renal biopsy are summarized in Table 1. These included patients with recent acute deterioration in renal failure, patients with multiple comorbidities investigated for chronic renal failure, and new presentations of nephrotic syndrome or significant proteinuria. Among our cohort were 12 patients for liver transplant assessment and 3 patients with bone marrow transplants. The indications for the transjugular approach are summarized in Table 2. Twenty-six patients (44%) had more than one indication for TJRB. The most common indication (33 patients) was a bleeding diathesis due to thrombocytopenia and/or coagulopathy (raised international normalized ratio [INR] or APTT). Seven patients were on anticoagulant medication (warfarin). Ten patients were deemed uncooperative or unable to lie prone. The causes included ventilatory problems, tracheostomy, encephalopathy, subarachnoid hemorrhage, and recent liver transplantation. However, there was a further indication for a TJRB in eight of these patients. Eight patients had a single functioning/anatomical kidney, of whom three had associated factors rendering them unsuitable for the percutaneous approach. Five patients had previous failed attempts at percutaneous biopsy due to high BMI, high kidney position, poor patient coordination, difficult patient positioning, and tiny fragmented samples. Seven patients required concomitant liver biopsy. Five patients had a high BMI, of whom three had a further indication for TJRB. Three patients had small kidneys. TJRB was thought to be a safer option in one patient with massive hepatosplenomegaly associated with myelodysplasia, a further patient

Table 1 Medical indications for renal biopsy

Patient No.	Age	Gender	Renal presentation	Clinical features / Comorbidity
1	73	F	ARF (CCl, 36.3 ml/min) UP (5.3 g/day)	Skin vasculitis, liver dysfunction, pancytopenia, previous TB
2	54	M	CRF (Cr, 194 μmol/L) UP (1 g/day)	OLTx workup, cryptogenic cirrhosis, myelopdysplasia
3	38	F	ACRF (Cr, 562 μmol/L)	Subarachnoid hemorrhage, alveolar hemorrhage, arthralgia
4	72	F	ARF (Cr, 168 μmol/L) NS, UP (7.9 g/day)	Relapsing nephritic syndrome
5	55	M	CRF (Cr, 230 μmol/L) UP (3.5 g/day)	Workup for second OLTx, hepatitis C, diabetes, hypertension, atrial fibrillation
6	47	F	ACRF (Cr, 344 μmol/L)	OLTx , autoimmune hepatitis
7	55	M	ACRF (Cr, 243 μmol/L) UP (9.6 g/day)	Diabetes, ischemic heart disease, gross edema
8	50	M	CRF (Cr, 417 μmol/L) UP (3 g/day)	Bone marrow transplant, graft vs host disease
9	46	F	ARF (Cr, 127 μmol/L)	Diabetes, myelopdysplasia, veno-occlusive disease, TIPSS
10	49	M	CRF (Cr, 150 μmol/L)	Hepatitis C cirrhosis, OLTx workup?, renal TB
11	66	F	ACRF (Cr, 190 μmol/L)	Arthralgia, diabetes, hypertension
12	33	M	ARF (Cr, 130 μmol/L)	Liver dysfunction, small bowel obstruction, splenomegaly, retinal infarcts
13	26	M	ARF (Cr, 152 μmol/L) UP (9.3 g/day)	Bone marrow transplant, graft vs host disease, cytomegalovirus
14	81	M	ACRF (Cr, 410 μmol/L)	Sepsis, trash feet, previous urine infection
15	50	M	ACRF (Cr, 176 μmol/L)	OLTx workup, cirrhosis, TIPSS, ↑IgA
16	36	F	ARF (Cr, 134 μmol/L) UP (5.8 g/day)	Bone marrow transplant, sepsis
17	67	M	CRF (Cr, 310 μmol/L) UP (5.6 g/day)	Previous renal artery stenosis, coronary disease, atrial fibrillation
18	70	F	ACRF (Cr, 314 μmol/l) NS (7.3 g/day)	Hypertension, on lithium
19	24	F	ARF (Cr ,417 μmol/L)	Sickle cell trait, pneumonia, eosinophilia, retinal vasculitis
20	53	M	UP (1.2 g/day)	Portal hypertension, TIPSS, OLTx workup
21	20	F	ARF (CCl, 98.6 ml/min) UP (3.6 g/day)	Discoid lupus erythematosus, pancytopenia
22	16	F	ARF (Cr, 192 μmol/L) UP (3.7 g/day)	OLTx workup, cryptogenic cirrhosis, portal hypertension, sickle cell disease
23	49	F	ARF (Cr, 168 μmol/L) NS, UP (7.9 g/day)	Relapsing nephritic syndrome
24	82	M	CRF (Cr ,260 μmol/L)	Hypertension, family history of glomerulonephritis
25	43	M	CRF (hemodialysis dependent)	Recurrence of hepatitis C following OLTx
26	48	M	CRF (CCl, 16.2 ml/min), UP (2.5 g/day)	Alcoholic cirrhosis, immunology negative
27	46	F	NS, UP (17 g/day)	Diabetes, hypertension, hepatitis cirrhosis, worsening NS post OLTx
28	41	M	CRF (Cr, 267 μmol/L)	Hepatitis C cirrhosis, previous IV drug abuser, OLTx workup
29	28	F	ARF (Cr, 294 μmol/L) UP (1.8 g/day)	Hemoptysis, vasculitic rash, Jehovah's witness
30	52	M	UP (4 g/day)	Obese, diabetes, heart failure
31	77	M	ARF (hemodialysis dependent)	Chronic bronchiectasis, IgG λ band

Table 1 continued

Patient No.	Age	Gender	Renal presentation	Clinical features / Comorbidity
32	59	M	ARF (hemodialysis dependent)	Reaction to chemotherapy drug, failure, disseminated coagulopathy liver
33	66	F	ARF (Cr, 233 μmol/L)	New Wegener's granulomatosis
34	56	M	CRF (Cr, 250 μmol/L) UP (2.6 g/day)	Alcoholic cirrhosis
35	32	M	ARF (Cr, 253 μmol/L) UP (6.2 g/day)	HIV, lymphoma on chemotherapy, fever, deranged liver function
36	69	M	CRF (Cr, 148 μmol/L), UP (1.5 g/day)	Diabetes, previous nephrectomy for renal cancer, IgA λ paraprotein
37	26	F	NS, UP	Systemic lupus, ascites
38	53	M	ARF (Cr, 153 μmol/L) UP (4.8 g/day)	Hepatitis C cirrhosis, IgG λ paraprotein
39	77	F	ARF (Cr, 247 μmol/L)	AFR following septicemia, loculated pleural effusion
40	38	F	ARF (hemodialysis dependent)	ARF post OLTx, anuria
41	35	F	UP (1.7 g/day)	Leukocytoclastic vasculitic rash, immunology negative
42	32	F	ARF (hemodialysis dependent)	Alcoholic cirrhosis, TIPSS
43	45	M	ACRF (Cr, 232 μmol/L) NS (9.6 g/day)	Hepatitis B cirrhosis, HIV, retroviral therapy, IgA nephropathy on earlier biopsy
44	46	M	NS (11 g/day)	Diabetes, hypertension, hepatitis B
45	41	M	ARF (Cr 321 μmol/L) UP (1.7 g/day)	Hemoptysis, disseminated coagulopathy, accelerated phase hypertension
46	79	M	ARF (hemodialysis dependent)	Renal artery stenosis
47	32	F	ACRF (Cr, 385 μmol/L), UP (2.5 g/day)	Sickle cell trait, systemic lupus
48	47	F	CRF (Cr, 119 μmol/L), NS, UP	Deep vein thrombosis, chronic pyelonephritis, nonfunctioning right kidney
49	73	M	CRF (Cr, 124 μmol/L)	Warfarin, hypertension, bladder cancer
50	54	M	ARF (hemodialysis dependent)	Primary biliary cirrhosis, OLTx workup
51	71	M	CRF (Cr, 230 μmol/L) UP (2.8 g/day)	Previous gastric cancer, anemia, chest infection
52	63	M	CRF (Cr, 130 μmol/L)	Hepatitis B & C cirrhosis, OLTx, steroid-induced diabetes, hypertension
53	59	F	CRF	Cyclosporin for connective tissue disease, steroid-induced diabetes
54	79	M	ARF (Cr, 530 μmol/L)	Myeloma
55	28	F	UP (1.2 g/day)	No renal scars on DMSA isotope scan
56	38	M	CRF (Cr, 238 μmol/L) UP (5.7 g/day)	OLTx, previous cyclosporin treatment
57	23	F	NS (Cr, 279 μmol/L) UP (8.7 g/day)	Relapsing steroid-resistant nephrotic syndrome since age 2 yr
58	27	M	ARF (Cr, 275 μmol/L) NS (11 g/day)	Aortic valve replacement, endocarditis, aminoglycosides, hepatitis C, iv drug user
59	56	F	ARF (Cr, 226 μmol/L)	Alcohol-associated fatty liver disease, recent stroke, chronic lung disease, microhematuria/proteinuria

Note. ARF, acute renal failure; CRF, chronic renal failure; ACRF, acute-on-chronic renal failure; NS, nephrotic syndrome; UP, urinary protein; Cr, creatinine; CCl, creatinine clearance; OLTx, liver transplant; TIPSS, transjugular intrahepatic portosystemic shunt

with advanced renal impairment and known renal microaneurysms, and a third patient, a Jehovah's Witness, who was profoundly anemic with a coagulopathy. All indications and diagnoses are presented in Table 3.

Access

Access is summarized in Table 4. Right IJV access was achieved in 55 of 59 patients (93%); the remainder, via the

Table 2 Indications for transjugular renal biopsy

Indication	No. of patients
coagulation profile	24
Thrombocytopenia	22
Uncooperative/unable to lie prone/ventilated/ tracheostomy	10
Warfarin treatment	7
Single kidney	8
Failed percutaneous biopsy	5
Simultaneous liver and renal biopsy	7
High BMI	5
Small kidneys	3
Massive hepatosplenomegaly and myelodysplasia	1
Renal microaneurysms	1
Anemic Jehovah's Witness	1

Note. BMI, body mass index

left IJV. Specimens were obtained (or biopsy attempted) from the right, left, or both kidneys in 41, 14, and 4 patients, respectively. The mean duration of the procedure was 58 min (range, 25–125 min) including the time for transferring the patient to and from the couch in the interventional radiology room.

Tissue Availability and Diagnoses

Renal tissue was successfully obtained by the transjugular route in 56 of 59 (95%) patients. TJRB was unsuccessful in three patients due to failed renal vein cannulation. One of these patients subsequently had a successful biopsy via a transfemoral approach. The number of needle passes per case ranged from 1 to 13, with a mean of 5.3. The number of core specimens obtained per procedure ranged from 1 to 9 (mean, 4.3). The specimen length varied from 1 to 20 mm. The mean number of glomeruli per procedure on LM and EM was 10.3 (range, 0–33) and 2.6 (range, 1–8), respectively. Tissue was available for IF/IP studies in 49 cases and these were adequate in 40 cases (71%). Specimens were sufficient to make a pathological diagnosis in 53 of 56 patients (94.6%) as reported in Table 3. In three patients, the TJRB was inadequate for diagnosis due to lack of tissue for EM and/or IF.

Blood Loss

The mean preprocedure Hb was 10.1 g/dl (range, 6.3–18.1 g/dl) and the mean lowest level of the Hb within 3 days of the procedure was 9.7 g/dl (range, 5.4–17.8 g/dl).

Complications

Six patients (10.2%) had minor complications with no clinical consequence. These included four cases of hematuria and two cases of loin pain localized to the renal region.

Seven patients (12.5%) developed major complications, of whom five required only blood transfusion, as described below. Patient 57 had a normal coagulation profile. Three passes were made and resulted in capsular perforation. She was transfused for a fall in Hb of 3.2 g/dl. Patient 54 was uremic and had thrombocytopenia and abnormal clotting. Peripheral wedging of the biopsy system was difficult due to angulation of the renal veins. Nine passes were performed (seven on the right and two on the left) with both capsular perforation and collecting system puncture on the right. The patient had macroscopic hematuria for 1 week. A blood transfusion was administered despite a small drop in the Hb level (0.6 g/dl). Patient 25 had thrombocytopenia. This was a technically difficult biopsy, with 13 attempts at needle passes which yielded only 3 glomeruli. No extravasation was recorded on check venography, but the patient subsequently required blood transfusion for a drop of Hb of 3 g/dl. Patient 1 had thrombocytopenia and abnormal clotting. He had a concomitant transjugular liver biopsy. It was difficult to access the renal veins due to their horizontal position. A single biopsy attempt was made on the right kidney, with no extravasation demonstrated. The sample turned out to be inadequate for diagnosis and this patient also required blood transfusion for a Hb fall of 3 g/dl. Patient 35 was an unwell, HIV-positive patient with a high C-reactive protein and lactate, who received chemotherapy for non-Hodgkin lymphoma. At TJRB five needle passes were made, with no extravasation noted. Over the subsequent 48 h, his Hb decreased by 2 g/dl, with a transient rise in creatinine. This may have been due to sepsis and not necessarily related to the procedure.

The other two patients with major complications required invasive intervention. Patient 8 had a single functioning right kidney and a bleeding diathesis due to uremia (urea, 43 mmol/L) and disseminated intravascular coagulation. Eight passes were made with capsular and collecting system punctures (Fig. 2a). Elective embolization of the biopsy track was attempted using 100-μm PVA particles (Cook, Letchworth, UK) via the catheter which was still left in situ at the site of biopsy following removal of the trucut needle. Shortly after the procedure the patient developed gross hematuria, clot retention, and a tachycardia. Subsequent arteriography showed a communication between a peripheral branch of the right lower pole artery and a lower pole calyx. Angiographic closure of the arteriocalyceal communication was achieved with coil embolization using a coaxial system (Figs. 2b–d). He required blood transfusion and temporary dialysis but made a full renal recovery. Patient 28 had a solitary right kidney, thrombocytopenia, and an

Table 3 Individual indications and diagnoses

Patient No.	Age	Gender	Indication(s)[a]	Diagnosis
1	73	F	Thrombocytopenia, coagulopathy, uncooperative, liver biopsy	None: no tissue for EM/IF
2	54	M	Thrombocytopenia, uncooperative	IgA nephropathy with vasculitic glomerulonephritis
3	38	F	Renal microaneurysms, (uremia)	Late renal damage. No active vasculitis
4	72	F	Failed percutaneous biopsy	Focal segmental glomerulosclerosis
5	55	M	Single kidney	Diabetic glomerulopathy
6	47	F	Failed percutaneous biopsy	Suggestive of cyclosporine toxicity
7	55	M	Warfarin for apical mural thrombus, (uremia, gross edema)	Diabetic glomerulopathy
8	50	M	Thrombocytopenia, coagulopathy, single functioning kidney, (uremia)	Disseminated intravascular coagulation
9	46	F	Myelodysplasia with massive hepatosplenomegaly	Non-immune-mediated glomerular disease
10	49	M	Thrombocytopenia, coagulopathy	Recovering ATN. Not TB
11	66	F	Single functioning kidney	None: no tissue for IF. Suggestive of IgA nephropathy
12	33	M	Coagulopathy, liver biopsy	Thrombotic microangiopathy
13	26	M	Thrombocytopenia, coagulopathy	Thrombotic microangiopathy
14	81	M	Solitary kidney	Embolic disease with patchy infarction
15	50	M	Coagulopathy	Membranoproliferative glomerulonephritis
16	36	F	Thrombocytopenia, coagulopathy	Thrombotic microangiopathy
17	67	M	Warfarin for atrial fibrillation	Hypertensive glomerulosclerosis, non-immune-mediated
18	70	F	Solitary kidney	Overload glomerular changes
19	24	F	Thrombocytopenia, coagulopathy, ventilated	Thrombotic microangiopathy
20	53	M	Coagulopathy, unable to lie prone	Non-immune-mediated disease
21	20	F	Thrombocytopenia	Failed TJRB
22	16	F	Thrombocytopenia, coagulopathy	ATN
23	49	F	Warfarin for central vein thrombosis	IgA nephropathy with diffuse interstitial fibrosis suggestive of ischemia
24	82	M	Warfarin for AF	Late nonglomerulonephritic renal damage
25	43	M	Thrombocytopenia, (uremia)	Late nonglomerulonephritic renal damage
26	48	M	Coagulopathy, liver biopsy	ATN with IgA nephropathy
27	46	F	Unable to lie prone	Membranoproliferative glomerulonephritis and diabetic changes
28	41	M	Thrombocytopenia, coagulopathy, solitary kidney	None: single glomerulus in samples
29	28	F	Jehovah's Witness, coagulopathy (Hb, 6.3 g/dl)	Pauci-immune crescentic necrotizing glomerulonephritis
30	52	M	High BMI	Diabetic glomerulopathy
31	77	M	Coagulopathy	AA amyloidosis
32	59	M	Thrombocytopenia, liver biopsy, (uremia)	ATN
33	66	F	Failed percutaneous biopsy	Pauci-immune crescentic necrotizing glomerulonephritis
34	56	M	Thrombocytopenia, coagulopathy, (uremia)	IgA nephropathy with ATN
35	32	M	Thrombocytopenia, coagulopathy, liver biopsy	Lymphomatous infiltration
36	69	M	Single kidney on hemodialysis	Late nonglomerulonephritic renal damage
37	26	F	Thrombocytopenia, (ascites)	Lupus nephritis
38	53	M	Thrombocytopenia, coagulopathy	AL amyloidosis
39	77	F	Failed percutaneous biopsy	ATN with IgA nephropathy
40	38	F	High BMI, tracheostomy, liver biopsy	Severe ATN
41	35	F	High BMI	IgA nephropathy with vasculitic glomerulonephritis
42	32	F	Thrombocytopenia, coagulopathy, liver biopsy	ATN, lupus nephritis
43	45	M	Coagulopathy	IgA nephropathy with vasculitic glomerulonephritis
44	46	M	Warfarin for recent PE	Membranous nephropathy
45	41	M	Thrombocytopenia	Severe ATN. Non-immune-mediated disease

Table 3 continued

Patient No.	Age	Gender	Indication(s)[a]	Diagnosis
46	79	M	Small kidneys	Advanced hypertensive nephropathy
47	32	F	Uncooperative	Lupus nephritis
48	47	F	Small single kidney	Advanced membranous nephropathy
49	73	M	Anticoagulation	Resolving minimal-change disease, hypertensive nephropathy
50	54	M	Thrombocytopenia, coagulopathy	Membranous nephropathy with ATN
51	71	M	Coagulopathy, (uremia)	Advanced IgA nephropathy
52	63	M	Thrombocytopenia	Advanced membranoproliferative

Note. ATN, acute tubular necrosis; BMI, body mass index; Hb, hemoglobin level; PE, pulmonary embolus; DVT, deep vein thrombosis; AVR, aortic valve replacement; EM, electron microscopy; IF, immunofluorescence

[a] Factors in parentheses are not indications per se

Table 4 Transjugular renal biopsy access

Access	No. of patients
Right IJV; right kidney	38
Right IJV; left kidney	13 (1 failed)
Left IJV; right kidney	3
Left IJV; left kidney	1
Right IJV; both kidneys	4 (2 failed)

Note. IJV, internal jugular vein

abnormal coagulation profile. Five passes were made, resulting in limited extravasation. The patient subsequently developed frank hematuria with deteriorating renal function. Imaging showed right hydronephrosis and cystoscopy revealed a clot in the distal right ureter, requiring stenting and bladder irrigation.

There was one further complication where the TJRB may have been implicated. Patient 21 had systemic lupus erythematosus and nephrotic syndrome, with positive lupus anticoagulant (negative anticardiolipin antibodies). She was not anticoagulated due to thrombocytopenia. An attempt at TJRB failed, as it was not possible to stabilize the Arrows sheath in either renal vein. She developed left loin pain 6 days later. Ultrasound and MRI studies revealed left renal vein thrombosis. It has not been possible to establish whether the patient's underlying prothrombotic tendency or the attempted biopsy was responsible.

Significance of Capsular Perforation

The association between capsular perforation in TJRB is well recognized [1, 2] and this has not been considered a complication per se [1]. Of the 56 successful TJRB procedures, 33 (59%) were associated with pericapsular extravasation: isolated capsular perforation (19 cases), contained subcapsular leaks (10 cases), and concurrent capsular perforation and collecting system puncture (4 cases). In addition, there was a case of isolated collecting system puncture. Of this group of 34 patients, 24 had no clinical sequelae, 6 had minor complications, and 4 developed major complications, as detailed above. However, three patients with no extravasation on check venography subsequently required blood transfusion (patients 1, 25, and 35).

Elective coil embolization of the biopsy track was performed in five of the early cases of isolated capsular perforation (two further patients without extravasation were empirically embolized). Pre-emptive particle embolization was attempted in the patient who subsequently developed the arteriocalyceal fistula.

Capsular or subcapsular perforation should theoretically indicate that the biopsy included cortex and was likely to allow a diagnosis to be made. The mean maximum length of the specimen containing the cortex (in entirety or mixed with medulla or fat) was 12.6 mm in the 33 patients with capsular and subcapsular puncture (with or without collecting system puncture), compared with 12.2 mm in the remaining 23 patients without radiological evidence of the above. No significant difference was found between the two groups (Student's *t*-test). The mean number of glomeruli was 9.9 and 11.6 in the two groups, respectively. Again, no significant difference was found in the two groups (Student's *t*-test).

Significance of Collecting System Puncture

Collecting system puncture at the time of TJRB occurred in five cases, with or without concurrent pericapsular extravasation. In a further four cases, subsequent macrohematuria implied that the collecting system was breached. This group of nine patients therefore comprised three of the seven cases of major complications and all six minor complications, by definition.

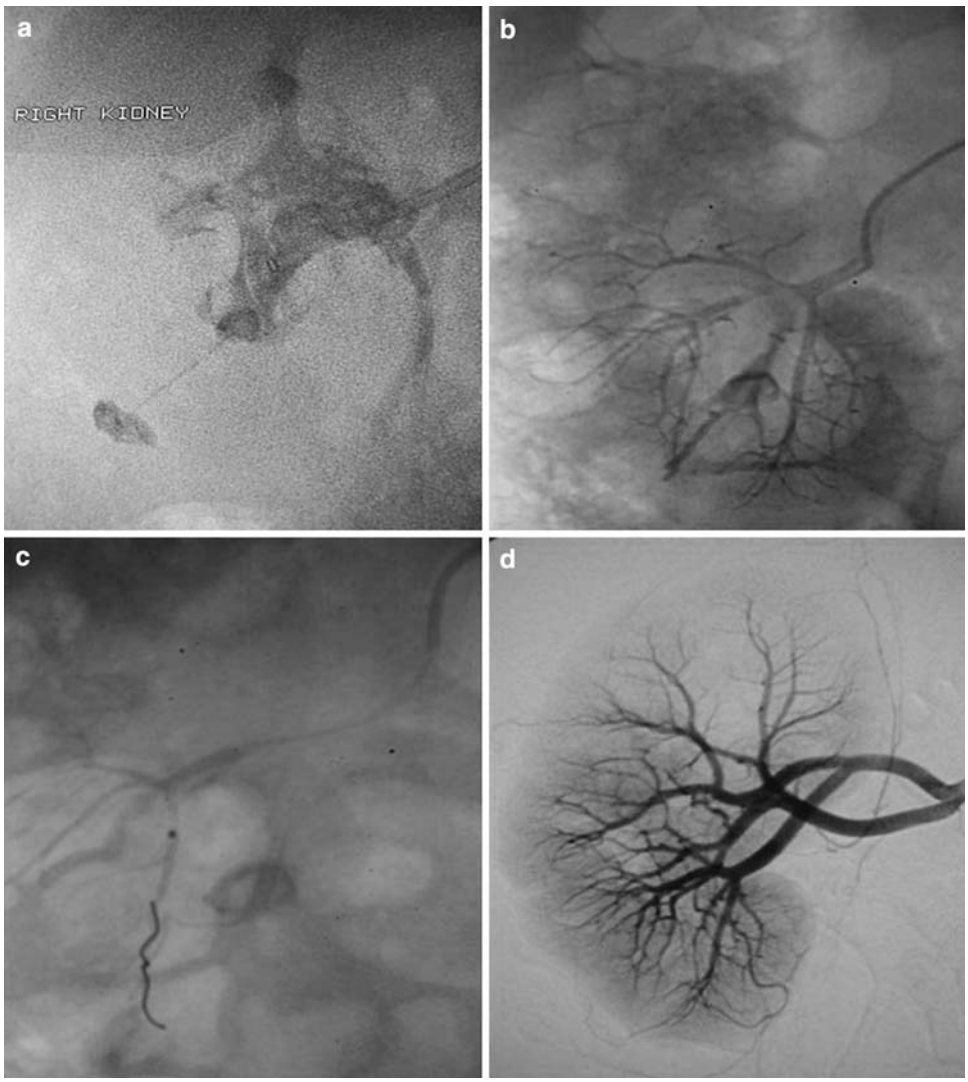

Fig. 2 (**a**) Subcapsular and collecting system filled with contrast medium following biopsy (66 × 73 mm; 150 × 150 DPI). (**b**) Selective renal arteriography confirms an arteriocalyceal fistula (66 × 73 mm; 150 × 150 DPI). (**c**) Coil embolization of the arteriocalyceal fistula track via a microcatheter (64 × 73 mm; 150 × 150 DPI). (**d**) Check renal arteriography shows closure of the arteriocalyceal fistula (62 × 73 mm; 150 × 150 DPI)

Significance of Number of Needle Passes

Fifty-seven percent (32/56) of patients had five or fewer needle passes. Capsular perforation occurred in nine of these patients (28%), while two developed major complications (patient 57 required blood transfusion and patient 28 underwent ureteric stenting). Two patients with five or fewer needle passes did not show extravasation on check venography but both required blood transfusion (patients 1 and 35). The remaining 24 patients (43%) required six or more needle passes. Capsular perforation occurred in 14 patients (58%), with 2 of them sustaining major complications (patient 54 required blood transfusion and patient 8 underwent coil embolization for an arteriocalyceal communication and temporary hemodialysis). Patient 25, who had 13 passes but no noticeable extravasation, was transfused following a drop in Hb. The rate of major complications did not differ between patients who had five or fewer needle passes (4/32 = 12.5%) and patients with more than five passes (3/24 = 12.5%; Fischer's exact test, p value = 1). However, the incidence of capsular perforation was significantly higher in patients with six or more needle passes (58%) compared to those who had five or fewer needle passes (28%; χ^2 test).

Cortical tissue (in entirety or mixed with medulla or fat) was obtained in 36 patients (64.3%) with the first pass of the needle. In nine patients (16.1%) a cortical specimen was obtained following a second needle pass, and in three (5%), following the third. This was based on the findings of the on-site pathology technician. Hence cortical tissue could be obtained within three needle passes in 86% of cases. The specific needle pass that resulted in a diagnostic yield could not be determined in four patients.

Discussion

Percutaneous renal biopsy is a commonly performed, safe procedure, with an excellent yield, ranging from 95.5% to

98.8% in the published literature [1–3], and is the routine method of acquiring renal tissue in patients. The main risk of the procedure is bleeding due to the high vascularity of the kidneys. Diseased kidneys are frequently small, with some degree of cortical thinning, and therefore, the tamponade effect may be minimal. In addition, early clinical detection of retroperitoneal hemorrhage is difficult. Pathological diagnosis is an integral part of the management of patients with renal parenchymal disease. In patients in whom a percutaneous biopsy is contraindicated, when the pathological diagnosis alters clinical management, TJRB provides an alternative approach. There are limited published data on the transjugular approach using both the aspiration [1, 5–7] and the core biopsy [8–12] techniques.

Patients were referred with varying degrees of renal impairment, proteinuria, and/or hematuria as illustrated in our patient population in Table 1. Many of them were unwell with significant comorbidity, necessitating a biopsy in order to decide on the optimal clinical management.

All patients in this series had risk factors which contraindicated percutaneous biopsy, of whom 26 (44%) had more than one indication for TJRB. A bleeding diathesis (thrombocytopenia and/or coagulopathy) was the most common indication. Other recognized indications for a TJRB include inability to cooperate with the percutaneous procedure, severe hypertension, a solitary or horseshoe kidney, end-stage renal disease or bilaterally small kidneys, and morbid obesity [13]. In the latter, a high diagnostic yield and low complication rates have been reported [10]. Obese patients have thickened perirenal fat, which may exceed 2 cm and contains the bleeding and, therefore, reduces complications [14]. In patients with acute renal failure requiring hemodialysis, TJRB can be usefully combined with central venous dialysis catheter placement [15]. Concomitant TJRB can be performed in conjunction with transjugular liver biopsy in patients undergoing assessment for potential liver transplantation, to differentiate between hepatorenal syndrome and other renal lesions that may progress [16–18].

Careful patient preparation is important prior to TJRB, given that any renal biopsy is not without risk and those patients deemed to be suitable only for biopsy via the transjugular route are therefore inherently more complex and at higher risk of complications. We now recommend optimization with correction of abnormal coagulation, where possible, and platelet replacement to minimize bleeding complications. All our patients were routinely observed for 24 h postprocedure so that any major complication could be detected and intervened early.

Cluzel et al. stated that a rigid biopsy system precludes a left IJV approach [1]. Although we agree that access via the right IJV is less demanding, using the flexible Arrows sheath and the Quick-core system, successful biopsy via the left IJV approach was performed in four patients, one of these in the left kidney. The three cases of failed TJRB were all due to failure to access or stabilize the biopsy system in the renal vein. A lower pole renal vein is preferred due to optimal angle for cannulation. The difficulty arises where there is an acute angle between the renal vein and the IVC. Deep inspiratory maneuvers may help peripheral placement of the Arrows sheath. The Quick-core system can then be advanced and wedged distally while simultaneously withdrawing the Arrows sheath. During biopsy, it is important to keep the system stationary, as the tendency during deployment is to push the entire device forward, which may cause unnecessary renal parenchymal injury. Performing the biopsy peripherally also reduces the chances of damaging a large vessel. The low venous pressure and direction of venous flow also reduce the incidence of severe hemorrhage, unless inadvertent arterial puncture occurs.

The significance of the pathological diagnosis in clinical management has been highlighted by an earlier study, where renal biopsy in all 23 cases of TJRB contributed to the patients' management [8]. Our diagnostic yield of 90% (53/59) is comparable to those of 73%–95% in the aspiration needle [1, 5–7]and 89%–96.5% in the core biopsy [8–11]series. Diagnosis is dependent on adequate cortical sampling, providing a sufficient number of glomeruli. Our experience was based on the initial sample assessment by an on-site pathology technician with the aim to obtain a sufficient number of glomeruli, but this did not prove to improve the diagnostic yield significantly compared to the published results where such a preliminary evaluation was unavailable. The mean number of glomeruli per patient of 10.3 for LM is comparable to the 9.8–10.8 in the aspiration series [1, 5–7]and 9–9.8 reported in the core biopsy series [9,11]. Adequacy for IF studies was a problem with TJRB, with generally inadequate samples. Our study provided sufficient samples for IF/IP studies in 71% of cases, which is an improvement compared to our earlier series [8].

Like most interventional procedures, the number of biopsy attempts is largely dependent on the favorability of the anatomy and operator experience. At our institution, the procedure is performed by a consultant radiologist or a senior radiology trainee (with consultant supervision). The average number of needle passes in our series was 5.3, which is comparable to those of 4 to 5.5 in other studies [9,10]. The mean number of core specimens of 4.3 is also comparable to those in the literature [9, 11]. In the published series using the core biopsy system [8–11],there was no mention of a limit to the number of needle passes. In two published series [1,5]using the aspiration technique, the number of passes was limited to a maximum of three and eight, respectively [1],depending on the patient's risk factors. In our series, the rate of major complications did

not differ between patients who had five or fewer needle passes and patients with more than five passes (Fisher's exact test, $p = 1$), although the result may be related to the small sample size. However, increasing the number of biopsies does not necessarily increase the tissue yield, as cortical tissue (in entirety or mixed with medulla or fat) is more likely to be obtained following first and second needle passes (64.3% and 16.1%, respectively). The yield deteriorated significantly with subsequent needle passes. This suggests that the first needle pass is the most important and that subsequent biopsies may yield fragmented or crushed specimens, making accurate diagnosis more difficult. Therefore, in patients with bleeding diathesis, perhaps it is reasonable to restrict the number of passes to three attempts. Moreover, we have shown that six or more needle passes have a higher incidence of capsular perforation compared to five or fewer passes, although our series failed to correlate this with the incidence of major complications.

There was no significant difference in the mean maximum length of cortical tissue (in entirety or mixed with medulla or fat) between the group of patients with capsular and subcapsular perforation (33 patients; mean, 12.6 mm) and the group without the above (23 patients; mean, 12.2 mm) (Student's *t*-test), although Marchetto et al. obtained better specimens after unintentional capsular perforation [19]. In our study there was also no significant difference in the number of glomeruli obtained in the two groups (Student's *t*-test).

There is no published evidence on the benefit of elective embolization of the biopsy track following capsular perforation. Fine et al. reported that when significant extravasation was noted, follow-up injection was repeated after 5 min to determine if any additional treatment was necessary. In their study, 8 of the 37 patients had extravasation on the initial contrast injection but not on the follow-up injection [10]. Check venography may not necessarily show every case of perforation [13], although occult capsular perforation is usually clinically insignificant. In our study, all five cases of collecting system puncture (one isolated, four also with capsular perforation) were associated with complications requiring invasive intervention in two patients. This may be an indication for elective coil embolization if the catheter is still engaged in the biopsy tract. There should also be a low threshold for prompt arteriography. Patients without noticeable collecting system puncture during the procedure who subsequently develop macrohematuria imply that breaching of the collecting system has occurred and closer observation is required. On the other hand, isolated capsular/subcapsular extravasation is mainly subclinical, and elective embolization of the biopsy track is probably not indicated in the majority of cases, unless the patient is hemodynamically unstable.

The reported rates of major complications (which included the need for postprocedure blood transfusion) using the aspiration biopsy techniques range from 1% to 18% [1, 5–7], compared with 2.7% to 27% [8–11] for the core biopsy system. In our series, there were seven (12.5%) major postprocedural complications, five of whom required only blood transfusion. Compared to the major complication rate of 6.4% in a large series of 750 low-risk patients who underwent percutaneous renal biopsy [4], this seems more acceptable, but could be improved on, with more vigilant correction of coagulation and platelet abnormalities. Contrast-induced renal failure is a theoretical problem, given that many patients already have some degree of renal impairment. However, only a small volume of contrast medium (15–30 ml) is usually required, and this is unlikely to be of significance. Routine postprocedure ultrasonography to detect complication is not necessary, and in our study 11 patients (19%) underwent ultrasonography for persistent severe loin pain, frank hematuria, and clot retention. Other potential but rare complications of the transjugular route include arrhythmias, pneumothorax, and hemothorax.

Both the aspiration and the Quick-core biopsy techniques were derived from the experience with transjugular liver biopsy. The principle of aspiration technique requires insertion of the needle into the renal parenchyma, followed by continuous aspiration with an empty syringe. Such negative suction is not required in the Quick-core biopsy technique. The device has a thinner needle (18 or 19 gauge) with a beveled end, which allows deeper placement for cortical sampling, although this comes with the risk of capsular perforation. It has also been commented that due to the thinner renal cortex compared to the liver, a 20-mm throw length needle will perforate the renal capsule and therefore a 13-mm needle should be used [14]. Indeed an animal study suggested that the use of a side-cutting needle with a shorter (1-cm) throw and a blunt tip reduces the risk of capsular perforation [20]. This was supported by a study of seven patients, using a mean of four needle passes per patient, which resulted in satisfactory specimens for pathological diagnosis with no clinically significant complications [12]. The blunt-tipped needle, in theory, pushes the capsule away rather than perforating it, and therefore it could potentially reduce the risk of capsular perforation. The shorter, 1-cm throw (compared to the usual 2 cm) also reduces the risk of parenchymal and vascular injury. However, it may compromise sampling adequacy when using the transvenous approach. We have experience using a blunt-tipped device (with a 2-cm throw) in a single patient who, following the procedure, had a small subcapsular hematoma without a capsular leak.

Further evaluation, with randomization if feasible, of the new blunt-tipped Tru-cut device versus the beveled-end Quick-core device as well as short- versus long-throw length needle may establish the potential advantages of the blunt-tipped and short-throw needle.

In the liver, a randomized controlled trial demonstrated that the automated biopsy device was more effective in obtaining diagnostic samples than the aspiration needle, with no significant difference in the complication rates [21]. However, a more recent 18-gauge aspiration needle device (Hakko Co. Ltd., Nagano, Japan), used in transjugular liver biopsy, has been shown to provide significantly better tissue adequacy ($p < 0.05$) compared to the Quick-core biopsy needle, with no tissue fragmentation or increased risk of major complications [22]. Its use has not been reported in TJRB but this may be potentially useful to address the current limitations of the Quick-core biopsy device.

The size of the sample is partly dependent on the biopsy device. Comparison of five biopsy devices (16- and 18-gauge Quick-core, 16-gauge Colapinto, Mansfield biopsy forceps, and 16-gauge Flexi-Temno) in transvenous renal biopsies performed in an ex vivo swine kidney model demonstrated that the 16- and 18-gauge Quick-core side-cutting biopsy devices are the most efficacious in obtaining diagnostic quality specimens, and the 16-gauge needle yielded a greater number of glomeruli [19].

In summary, TJRB is recognized as an alternative, safe, and effective technique in patients with renal parenchymal disease when contraindications to the percutaneous approach exist. In addition, we have expanded the potential use for TJRB to include biopsy via a transfemoral approach. In this cohort, a consistently high diagnostic yield has been obtained, without an excessive risk of major complications. The best tissue yields are obtained with the first two needle passes. In patients with a bleeding diathesis it seems prudent to limit the number of needle passes to no more than three. Inadvertent collecting system puncture (± concurrent capsular puncture) is associated with major complications and elective biopsy track embolization should be considered. Prompt arteriography is essential in symptomatic (gross hematuria or falling Hb) or hemodynamically unstable patients. Patient selection and optimization are critical to avoid major complications. Future adaptations to the design of the biopsy needle may further improve sample adequacy and reduce complications, aiding the safer provision of diagnostic and prognostic information, critical to the management of this high-risk patient group.

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