Research article

# Transjugular renal biopsy in high-risk patients: an American case series

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## Abstract

**Background:** In the United States, transjugular renal biopsies using the Quickcore™ side cut needle system have previously been described primarily for transjugular renal biopsy in patients with concurrent liver and kidney disease.

**Methods:** We describe transjugular renal biopsy with the Quickcore™ system in 9 patients with nephrotic syndrome and contraindications to percutaneous renal biopsy, who underwent biopsy between 23 October 1996 and 12 April 2001. The most common contraindication was oral anticoagulation with coumadin (40%). Other contraindications included horseshoe kidney, severe renal failure, and spontaneous coagulopathy. A 62 cm straight catheter and 60 cm side-cut Quickcore™ biopsy needle were used to obtain cortical tissue. Packing of the biopsy tract with Gelfoam™ was used for venographically identified capsular perforation.

**Results:** Ten procedures were performed on 9 patients with one requiring re-biopsy (5% of all renal biopsies performed at our institution). There were 9 transjugular renal biopsy and one combined liver-kidney biopsy. A mean of $4 \pm 2$ passes were made, with a mean of $3 \pm 1$ cores obtained per procedure. Histologic diagnosis was made in 90% of biopsies and in 100% of patients. Two patients developed transient hydronephrosis associated with gross hematuria; both required transfusion. Capsular perforation occurred in 90%. One patient died of bacterial sepsis, unrelated to the biopsy, several days after the procedure.

**Conclusions:** Transjugular renal biopsy appears to be efficacious in high-risk patients, for whom the percutaneous approach is contraindicated, including patients on oral anticoagulation. The transfusion rate in the present study was similar to other American reports using this technique.

## Background

The number of patients who are not suitable candidates for percutaneous renal biopsy (PRB) may increase in the future because of increasing prevalence of bleeding diatheses, both spontaneous and due to wider use of anticoagulation for thrombotic disorders and dysrythmias. [1] The most common indication for renal biopsy in the United States is the nephrotic syndrome. [2] This condition has been associated with an increased risk of thromboembolism, particularly in patients with membranous nephropathy [3] or systemic lupus erythematosus, [4] and such patients may thus also require anticoagulation. Several alternative techniques have developed over the last decade for those who have contraindications to PRB. Of these, the most widely used are the various methods of endovascular biopsy. The current status of transjugular renal biopsy (TJRB) has been reviewed recently. [1] Most reports and the largest series, in a broad array of settings, have come from Europe. [5–7] In the United States, the only reports of experience with TJRB have been in patients with concurrent liver and kidney disease. [8]

Since the seminal report of Mal, et al [5], an even larger TJRB series has been reported by Cluzel, et al [6]. Four hundred patients undergoing TJRB were compared to 400 patients undergoing PRB, using the modified Colapinto™ aspiration needle system. Diagnostic tissue adequacy was 95.8%, with a major complication rate of 1%. Although excellent results were obtained, this technique appears to require a steep "learning curve," according to the authors. The endovascular automated side-cut core biopsy sets such as the Quick-Core™ (Cook, Bloomington, IN) may allow even higher yields of diagnostic tissue with possibly less operator-dependence. In addition, biopsy tract embolization to reduce bleeding risk post-biopsy is possible using this system. So far no American center has reported results on the use of the Quick-Core™ biopsy set in patients with contraindications to PRB (other than combined liver and kidney disease) referred for TJRB. We report our experience with this technique at our institution from October 1996–April 2001.

## Materials and Methods

Data on 9 of 10 patients undergoing TJRB at Walter Reed Army Medical Center (WRAMC) from 23 October 1996 to 30 April 2001, including demographics, indications, technical details, and complications, were recorded and analyzed. The starting date reflects the time at which all TJRB began to be tracked by both Nephrology and Interventional Radiology at WRAMC. The protocol (WU # 1186) was submitted to the WRAMC institutional review board and approved in May 1997. Seven patients with biopsies performed between October 1996 and May 1997 were analyzed retrospectively. Data on 3 of 4 subsequent biopsies were obtained prospectively. (One patient declined consent, and thus no clinical data is available regarding the biopsy). Six different interventional radiologists performed the biopsies over the course of the study.

All biopsies were performed in the interventional radiology suite with biplane or single-plane anteroposterior and lateral fluoroscopic capabilities. Biopsy was performed only if patient blood pressure was <140/90 mm Hg. In most patients, a previous abdominal sonogram was available. Prothrombin time, partial thromboplastin time, INR (where indicated), platelet count, and serum creatinine level were obtained before each procedure. No patient had significant thrombocytopenia. Management of patients on anticoagulation was per the recommendations of Kearon, et al [9]. No patient was given fresh frozen plasma or cryoprecipitate, before or after the procedure. No bleeding times were performed. Patients were given prebiopsy DDAVP or estrogen if the serum creatinine was ≥ 3 mg/dl or the creatinine clearance by the Cockcroft-Gault formula was ≤ 30 cc/min, as previously described (N = 5) [10]. No patients were dialysis-dependent, either acutely or chronically.

All biopsies were performed with the transjugular Quick-Core™ needle biopsy system (Cook, Bloomington, IN), which consists of a 7 F, 50.5-cm transjugular sheath with a 14 G inner-stiffening cannula; a 5 F, 80-cm multipurpose curved catheter; and a 60-cm biopsy needle with a 2-cm throw length. Biopsy was performed preferentially on the right kidney because the right renal vein is shorter than the left, and provides a better angle for access to the kidney. Biopsy specimens were obtained with the 60-cm biopsy needle oriented in a posterolateral direction to avoid inadvertent puncture of the colon.

The right neck was prepared and draped in sterile fashion. A guide wire was advanced through the distal lumen of 9F catheter into the inferior vena cava and the 9F catheter removed. This was replaced with a 14F short vascular sheath.

For the one patient who underwent a combined liver and kidney biopsy, a 5F angled multipurpose catheter was advanced through this sheath, over a wire, to the inferior vena cava and used to selectively cannulate the right hepatic vein. The catheter was passed distally into the hepatic vein. Hepatic wedge venography with carbon dioxide (because of the patient's renal insufficiency) was performed. An Amplatz™ (Cook, Bloomington, IN) wire was then placed and the catheter removed. Over the Amplatz™ wire the Cook Quick-Core™ biopsy sheath was advanced without difficulty into the proximal hepatic vein. The wire was removed and a 20-gauge Quick-Core™ biopsy needle used to obtain core biopsy specimens. The sheath was then removed over a wire.

For patients undergoing renal biopsy (either combined or separate), after cannulation of the right internal jugular vein, the multipurpose catheter was advanced and used to engage the right renal vein. Over a hydrophilic wire, the catheter was advanced until it wedged within the right lower pole of the kidney. This was verified by injection of 3 cc of contrast material. The guiding sheath was then angled posteriorly (to avoid inadvertent colonic puncture) and biopsy specimens obtained with the 18-gauge Quick Core™ needle as described for liver biopsy. Extravasation of contrast post venography through the sheath was taken as evidence of capsular perforation. If extravasation of contrast was seen, the tract was selected using a Terumo wire and the small catheter included in the liver access set. A Gelfoam™ (Pharmacia, Upjohn Inc., Peapack, New Jersey) pledget was then placed at the far aspect of this tract near the capsule until no further extravasation of contrast was demonstrated. The collecting system was assessed for free drainage of contrast or development of caliectasis. No further filling of the tract was demonstrated after the embolization. All biopsy devices were then removed. The catheter, its stiffeners, and sheath were all removed and hemostasis obtained with manual compression. For patients previously on oral coumadin, depending on the indication (as per Kearon, et al [9]), intravenous heparin was restarted in as soon as two hours (no bolus, maintenance infusion only). Oral coumadin was generally started the same night.

For the patient with the horseshoe kidney, access to the right internal jugular vein and inferior vena cava was as above. A wedged venogram with a very small amount of contrast material demonstrated some cortical staining. The Rosen guide wire was reintroduced and the catheter was exchanged for the 8-French vascular sheath with a stiffener. The guide wire was removed, and a small amount of contrast material again demonstrated intravascular placement of the sheath.

There was transgression of the collecting system with the first biopsy specimen; however, there was no filling of the collecting system following the introduction of a single pledget of GelfoamTM. After completion of the procedure, there was no evidence of intraluminal filling defect within the right renal collecting system (i.e., no significant thrombus within the collecting system). The extracapsular contrast collection was approximately 2 cm × 2 cm and was not observed to expand over the final 10 minutes of the procedure.

The length of core samples obtained was generally 10–14 mm, maximally 18–20 mm. Tissue for hematoxylin and eosin, periodic acid-Schiff and other special stains, as well as electron microscopy was fixed in 2% glutaraldehyde solution. Tissue for immunofluorescence was preserved in Michel's Fixative (Poly Scientific, Bay Shore, NY). Paraffin sections were used for light microscopy. Specimens were processed for immunofluorescence and electron microscopy in standard fashion. All specimens were examined by a single nephropathologist at the Armed Forces Institute of Pathology.

After biopsy, outpatients were admitted to a 23-hour recovery unit, and remained in bed for at least 12 hours, with frequent observation of vital signs. Hematocrit was assessed 4–6 hours post biopsy. Serial urines were collected to assess for hematuria. All but two of the patients in whom TJRB was performed as an outpatient procedure were discharged the next day. The patient found to have systemic amyloidosis was already an inpatient for clinical reasons.

## Results

Patient characteristics, contraindications to conventional PRB, and outcomes are shown in Table 1 (see additional file 1). Ten biopsies were performed in 9 patients (1 patient had a successful repeat TJRB one month after the first attempt yielded inadequate tissue). No patient required open surgical biopsy. Mean age was $58 \pm 21$ years. Six were Caucasian; 2 African-American, and 1 Asian-American. There were 4 males and 5 females.

Four of 9 patients had substantial renal failure, i.e., serum creatinine $\geq 3$ mg%, which constituted a relative contraindication. No patient was referred for morbid obesity. The most common contraindication to PRB was bleeding diathesis (5/9), either due to coumadin anticoagulation (2 with history of deep vein thrombosis, 1 with history of pulmonary embolus, and 1 with anti-cardiolipin antibody syndrome with associated deep vein thrombosis) or spontaneous coagulopathy. No patient had a platelet count < 100,000 cells/mm3. Mean INR (international normalized ratio) at the time of biopsy in these 5 patients was $1.4 \pm 0.3$. Two patients proved to have membranous glomerulonephritis, and were on coumadin prior to biopsy. Proteinuria had preceded thromboembolic events in these patients.

Tissue was adequate for diagnosis in 9/10 biopsies, and in all patients (due to successful re-biopsy). The mean number of passes was $4 \pm 2$, yielding $3 \pm 1$ biopsy cores, with a mean glomerular number of $9 \pm 8$. Capsular perforation occurred in 9/10 biopsies, but gross hematuria occurred in 6/10 biopsies-1 of which occurred in the only patient without capsular perforation. The biopsy that produced inadequate tissue was the only one in which capsular perforation did not occur. The hematocrit declined $\geq 4$ % after biopsy in 3/10 biopsies. Transfusion was needed in only 2 patients; these two also developed hydronephrosis due to collecting system bleeding, which resolved

without further intervention. One had horseshoe kidney, and the other was on coumadin for anti-cardiolipin antibody syndrome. She resumed intravenous heparin and coumadin the day of the biopsy due to high thrombosis risk. Only one other of the 4 patients on oral anticoagulants had intravenous heparin restarted the same day; the other two began oral coumadin that night. One patient died of bacterial sepsis (presumed due to line infection) several days after biopsy (an 88-year-old man with liver and renal amyloidosis). No patient developed significant renal failure after the procedure (defined as a serum creatinine level elevation ≥ 1.5 mg/dl or requirement for dialysis).

## Discussion

Recent series have shown that tissue adequacy with TJRB is excellent (>95%) 5,7 and comparable to PRB [5]. The tissue adequacy of 90% for procedures and 100% for patients in our study is comparable to that in other reports. The mean number of glomeruli obtained by Sam, et al [8] was higher than in our series. This may be due to their routine use of pathology review during biopsy, which was not feasible at our institution.

Biopsy influenced management in all cases, except for Patient 9, who was diagnosed with amyloidosis, and who died from sepsis. Subsequent to biopsy, patients 1 and 2 were treated with chlorambucil and methylprednisolone [11]. Patient 7, who presented with heavy proteinuria and nephritic urinary sediment, proved to have mesangial lupus nephritis. Without renal biopsy, which excluded diffuse proliferative lupus nephritis, she might have been reasonably treated empirically with cyclophosphamide [12]. Patient 8 had minimal change nephropathy. While this 22-year-old patient might have been treated empirically with prednisone, his presentation was also consistent with focal segmental glomerulosclerosis, which would have been treated differently [13].

Although large series of TJRB using the modified Colapinto™ aspiration needle system have been reported [5–7], the largest series on the use of 18-g automated biopsy needle is that of Sam, et al, [8] which reported on 29 TJRB. In the series reported by Cluzel, et al [6], 8 of 400 TJRB were done with Quick Core™ automated systems. They commented that the stiffness of the Quick Core™ system virtually precludes a left jugular approach, but because of its thinness, allows deeper placement in the renal parenchyma. The Colapinto™ device appears to require more training to deploy properly, because of its flexibility and the requirement for manual aspiration of samples. In a randomized, unblinded study of liver biopsies, the time required for training, procedure time, and tissue adequacy were superior for automated biopsies vs. aspiration biop-

sies, with similar complication rates [14]. No such comparisons exist for TJRB.

During the same time period as this series, we performed 192 native PRB. There were no laparoscopic or open surgical biopsies. Thus, only 5% of biopsies at WRAMC were deemed "contraindicated" by the percutaneous approach, and all were able to be done using TJRB. Therefore, TJRB, at least in our practice setting, is unlikely to become a "high-volume" procedure, but despite this, is able to be effectively and safely done by interventional radiologists with transjugular liver biopsy experience and equipment, i.e., the Quick Core™ automated system. Transjugular liver biopsy is generally a more common procedure, and was performed 12–14 times a year at our institution during the time of the study.

In our series, 5/9 patients had a coagulopathy, either spontaneous or due to coumadin. Two (22%) had an INR > 1.5 at the time of biopsy, in comparison to 39% in the series of Sam, et al [8], whose patients had advanced chronic liver disease. They attempted to correct coagulopathy in all patients, although the details of correction were not specified. In contrast, because of the different etiology of coagulopathy in most of our patients, we performed TJRB through a heparin window as per Kearon, et al [9]. Theoretically, the same could be done for PRB, although bleeding risk would typically persist for six weeks, and the percutaneous tract would be associated with a greater bleeding risk than with TJRB, even given capsular perforation.

The issue of capsular perforation is also relevant to tissue adequacy. In animal models, better specimens with more glomeruli were obtained after unintentional capsular perforation, presumably due to more distal positioning of the biopsy needle [15]. The high rate of capsular perforation in our study was not associated with a high complication rate, given the high risk of the population. The transfusion rate of 20% is lower than the 29% rate of Sam, et al [8]. The use of a side-cut needle with a shorter (1 cm) throw and a blunt-tipped end to reduce the risk of capsular perforation and other organ damage 16 has been successful in animal models, but has not been reported in humans.

Cluzel, et al [6] reported low transfusion rates (about 1%) after TJRB. However, the population studied is not comparable to ours or that of Sam, et al [8]. Possibly the most common indication for TJRB in the Cluzel study was an elevated bleeding time, even with a normal creatinine or absent bleeding history. It was largely on this basis that 76% of the patients in the study were said to have had a "bleeding abnormality." In many centers, particularly in the United States, such patients are likely to be treated

with DDAVP or conjugated estrogen before PRB [1]. In our study, only one patient with a "coagulopathy" required transfusion. The other transfusion was required by the patient with a horseshoe kidney, who had no other risk factors for bleeding, and is, to our knowledge, the first such patient to undergo TJRB.

The two cases of bleeding-associated hydronephrosis, one of which was in the patient with horseshoe kidney, were the result of a communication with the urinary tract. In the horseshoe kidney, this could have been due to aberrant location of the collecting system. In fact, contrast extravasation into the collecting system was observed during the procedure. In the other case, caliectasis was noted during the procedure, which was initially attributed to the pressure of injection. This patient had been on coumadin anticoagulation, although the INR at the time of biopsy was 1.2. She was restarted on heparin and coumadin the day of the biopsy because of high risk of thrombosis. The use of Gelfoam™ embolization did not prevent significant bleeding in these two patients, possibly because the tracts could not be exactly approximated, or the Gelfoam™ pledget became displaced. It is noteworthy that both transfusion and Gelfoam™ failure were associated with urinary tract perforation, because Gelfoam™ embolization is less likely to be successful in preventing bleeding in this setting. Gross hematuria, without the need for transfusion, has not been reported specifically as a complication after TJRB. Therefore, our gross hematuria rate of 60% cannot be compared with other studies. However, we speculate that in the process of obtaining a core specimen, adjacent vessels were disrupted and could have led to introduction of blood into the renal tubules, especially in patients with disturbed hemostasis.

The one death in our series was due to sepsis in a patient with systemic amyloidosis, unrelated to the biopsy. The patient's hematocrit declined only 1.4% post-procedure, despite a spontaneous coagulopathy.

The generalizability of our series is limited by its small size. Because none of the patients were obese, no conclusions about the safety of TJRB in obese patients can be drawn. As technology improves, the cost and complexity of TJRB is likely to decrease. In fact, the cost of TJRB at "experienced" institutions is less than twice that of PRB, and the technique is particularly advantageous in combined liver-kidney biopsy [5–8]. Given the "user-friendly" characteristics of the Quick Core™ transjugular biopsy set, interventional radiologists throughout the world with transjugular liver biopsy experience can reasonably apply this technique. The most common contraindications to PRB are likely to be maintenance anticoagulation or bleeding diathesis (due in some cases to acute or chronic renal failure), perhaps followed by congenital abnormalities. The present study shows that the transjugular technique can obtain diagnostic renal tissue in these circumstances. The safety of this procedure in high-risk populations is still uncertain due to the small numbers of patients studied with the equipment used in the present study. Due to the low volume of procedures, it is unusual to find institutions with experience in multiple methods of high-risk renal biopsy (ie, both TJRB and Laparoscopic renal biopsy). Because TJRB is considered only when conventional PRB is contraindicated, comparison with PRB is not possible. Future studies are suggested to determine the best method of embolizing the biopsy tract in TJRB, given the results of the present study.

## Competing Interests
None declared.

## Author's contributions
Dr. Abbott assumed the role of primary investigator for the research protocol after the departure of Dr. Musio, and was responsible for data collection, analysis, and manuscript preparation.

Dr. Musio originally submitted the research protocol, and as the first primary investigator, was responsible for submission of the initial abstract, which was presented a poster at the 1997 American Society of Nephrology meeting and published in the Journal of the American Society of Nephrology in 1997.

Dr. Chung was responsible for performance of the transjugular renal biopsy in the patient with the horseshoe kidney and was responsible for the diagnostic and therapeutic planning and description of the case, as part of the overall manuscript.

Dr. Lomis was responsible for the performance of the combined transjugular renal and hepatic biopsy, the first performed at Walter Reed Army Medical center, and was responsible for the diagnostic and therapeutic planning and description of the case, as part of the overall manuscript.

Dr. Lane was responsible for two of the transjugular renal biopsies and contributed to the development and description of the technique, as well as provided comparisons with other techniques of transjugular biopsies in the literature. Dr. Lane assisted in all aspects of manuscript preparation and data analysis.

Dr. Yuan was an associate investigator on the original protocol and assisted in all aspects of manuscript preparation and data analysis.

All authors read and approved the final manuscript.

## Additional material

**Additional File 1**

*Table1*

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[http://www.biomedcentral.com/content/supplementary/1471-2369-3-5-S1.doc]

## Acknowledgements

## References

1.  Stiles KP, Yuan CM, Chung EM, Lyon RD, Lane JD, Abbott KC: **Renal biopsy in high-risk patients with medical diseases of the kidney.** *Am J Kidney Dis* 2000, **36:**419-433
2.  Haas M, Meehan SM, Karrison TG, Spargo BH: **Changing etiologies of unexplained adult nephrotic syndrome: a comparison of renal biopsy findings from 1976–1979 and 1995–1997.** *Am J Kidney Dis* 1997, **30:**621-631
3.  Bellomo R, Atkins RC: **Membranous nephropathy and thromboembolism: is prophylactic anticoagulation warranted?** *Nephron* 1993, **63:**249-254
4.  Arnout J: **Antiphospholipid syndrome: diagnostic aspects of lupus anticoagulants.** *Thromb Haemost* 2001, **86:**83-91
5.  Mal F, Meyrier A, Callard P, Kleinknecht D, Altmann JJ, Beaugrand M: **The diagnostic yield of transjugular renal biopsy. Experience in 200 cases.** *Kidney Int* 1992, **41:**445-449
6.  Cluzel P, Martinez F, Bellin MF, Michalik Y, Beaufils H, Jouanneau C, Lucidarme O, Deray G, Grenier PA: **Transjugular versus percutaneous renal biopsy for the diagnosis of parenchymal disease: comparison of sampling effectiveness and complications.** *Radiology* 2000, **215:**689-693
7.  Jouet P, Meyrier A, Mal F, Callard P, Guettier C, Stordeur D, Trinchet JC, Beaugrand M: **Transjugular renal biopsy in the treatment of patients with cirrhosis and renal abnormalities.** *Hepatology* 1996, **24:**1143-1147
8.  Sam R, Leehey DJ, Picken MM, Borge MA, Yetter EM, Ing TS, Van Thiel DH: **Transjugular renal biopsy in patients with liver disease.** *Am J Kidney Dis* 2001, **37:**1144-1151
9.  Kearon D, Hirsh J: **Current concepts: Management of anticoagulation before and after elective surgery.** *N Engl J Med* 1997, **336:**1506-1511
10. Stiles KP, Hill C, Lebrun CJ, Reinmuth B, Yuan CM, Abbott KC: **The Impact of Performing Bleeding Time Determinations Prior to Percutaneous Real-time Ultrasound-Guided Renal Biopsies on Major Complication Rates.** *J Nephrol* 2001, **4:**275-279
11. Ponticelli C, Zucchelli P, Passerinie P, Cagnoli L, Cesana B, Possi C, Pasquali S, Imbasciati E, Gassi C, Redaelli B, Sasdelli M, Locatelli F: **A randomized trial of methylprednisolone and chlorambucil in idiopathic membranous nephropathy.** *N Engl J Med.* 1989, **320:**8-13
12. Rose BD: **Uptodate in Medicine,** *BDRinc, Wellesley, MA* 2001
13. Stiles KP, Abbott KC, Welch PG, Yuan CM: **Effects of angiotensin-converting enzyme inhibitor and steroid therapy on proteinuria in FSGS: a retrospective study in a single clinic.** *Clin Nephrol* 2001, **56:**89-95
14. Banares R, Alonso S, Catalina MV, Casado M, Rincon D, Salcedo M, Alvarez E, Guerrero C, Echenagusia A, Camunez F, Simo G: **Randomized controlled trial of aspiration needle versus automated biopsy device for transjugular liver biopsy.** *J Vasc Interv Radiol.* 2001, **12:**583-587
15. Marchetto BE, Meglin AJ, Chiricosta FM, Temo JA, Duhan JL: **Transvenous renal biopsy in an ex vivo swine kidney model: comparison of five devices.** *J Vasc Interv Radiol* 1997, **8:**831-834
16. Lakin PC, Pavcnik D, Bloch RD, Uchida BT, Corless CL, Timmermans HA, Kubota Y: **Percutaneous transjugular kidney biopsy in swine with use of a side-cutting needle with a blunt-tipped stylet.** *J Vasc Interv Radiol.* 1999, **10:**1229-1232

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