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Clinical Relevance of Kidney Biopsy in Patients Qualified for Liver Transplantation and After This Procedure in the Model for End-stage Liver Disease (MELD) Era: Where Are We Today?

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Statistical Analysis C
Data Interpretation D
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Chronic kidney disease (CKD) has been recognized as an increasingly common complication of liver transplantation (OLTx). Post-transplant renal dysfunction contributes to long-term morbidity and mortality following OLTx and is a very important issue in the management of liver transplant recipients. Its etiology is multifactorial and can be determined by kidney biopsy, which is too rarely done in this patient group. In the clinical context of patients with liver cirrhosis, accurate and reliable evaluation of the renal injury is crucial.

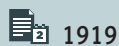
We performed a review of kidney biopsies in patients with symptoms of CKD (proteinuria/hematuria/elevated creatinine) before and after liver transplantation in the published literature.

Kidney biopsies were performed either before or after liver transplantation using percutaneous technique. There are few reports on transjugular kidney biopsy. Biopsy results prevented unnecessary modification of immunosuppressive therapy or selection of candidates for liver transplantation.

In our opinion, kidney biopsy is a clinically relevant diagnostic approach to recognize kidney disease before and after liver transplantation, it also helps with the management of kidney disease in this population, and it is safe. Kidney biopsy should be offered more often in liver transplant patients to ensure appropriate therapy in concomitant CKD in this population. Our decisions today will impact clinical outcomes in the future.

MeSH Keywords: Biopsy • Liver Transplantation • Renal Insufficiency, Chronic

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Background

Chronic kidney disease (CKD) is the most common kidney problem in the general population, and, in advanced stages, patients need dialysis treatment. CKD is also a huge problem in special patient groups, such as patients with end-stage liver disease (ESLD).

The number of patients with concomitant renal dysfunction qualified for liver transplantation (OLTx) and after this procedure has recently further increased due to the implementation of MELD (Model for End-stage Liver Disease) score-based allograft allocation. About 30–80% of patients develop CKD, with a cumulative risk of ESRD (End-Stage Renal Disease) requiring renal replacement therapy consisting of either maintenance dialysis or renal transplantation [1,2]. Although chronic kidney disease (CKD) is a common problem in these patients, kidney biopsy is rarely performed because of its invasive nature and potential complications, and therapeutic decisions are made solely on the basis of biochemical tests. There is no criterion standard diagnostic assessment used in most transplant centers, and data on histological changes and complications in patients with CKD in ESLD patients are scarce. The prevalence of CKD in patients qualified to OLTx and after this procedure has not been precisely defined, but it is known to affect the long-term results of liver transplant recipients. Several large studies have shown that pretransplant CKD in patients with a stage higher than 1 (especially with elevated creatinine), presence of hepatorenal syndrome before transplantation, or requirement of renal replacement therapy early after transplantation have an increased risk of post-transplant ESRD [3–6]. Chronic renal dysfunction has also been shown to have a significant association with cardiovascular events in clinical analyses [7]. These findings confirm retrospective evidence that the risk of major cardiac events increases with deteriorating renal function in liver recipients. At present, the decision is made on a case-by-case basis and there is no guideline regarding the role of renal biopsy in the setting of kidney injury in liver transplant patients [8].

We conducted a literature review of kidney biopsy performed in patients before and after liver transplantation, including percutaneous and transjugular procedures. We performed a search in Medline, PubMed, and Embase using the keywords: kidney biopsy, kidney impairment, kidney failure, CKD, liver transplantation, ESLD, and liver cirrhosis. We limited our search to adult patients and publications in English and Polish between 1995 and 2020. We found 2306 articles, but only 23 articles were analyzed due to lack of information about histological changes in kidneys, lack of full clinical data, and availability of abstracts only.

Pretransplant Kidney Biopsy and OLTx

Assessment of kidney function before liver transplantation is important because the presence of impaired kidney function before transplantation, particularly the presence of hepatorenal syndrome, is a significant predictor of post-transplant CKD or even requirement for renal replacement therapy [9,10]. Approximately 25% of patients qualified for OLTx have some renal function damage. Cirrhotic patients have specific disturbances that affect the serum creatinine value; therefore, this endogenous marker remains an imperfect parameter of renal function in this clinical setting [11]. In patients with glomerulonephritis, it is particularly important in regard to treatment and outcome, especially when there is co-existing hepatitis B and/or C [12]. Published studies have not established the correlation between kidney disease progression after transplantation and renal histological damage, kidney function, or clinical picture [12–14]. The role of pretransplant kidney biopsy in liver transplant candidates has not been established. Kidney biopsy findings are not included in the 2016 OPTN/UNOS criteria for selection of patients for simultaneous liver-kidney transplantation [15,16], although only kidney biopsy can differentiate the type and severity of kidney injury and provide information about reversibility or irreversibility of renal damage (excluding obvious cases like cystic disease or atrophy). A pre-liver transplant kidney biopsy can help make the decision and establish the cause of kidney disease. In addition, kidney biopsy can be helpful to determine chronicity, treatability, and likelihood of future progression or reversibility. A few published studies on pretransplant kidney biopsy and evaluation for potential simultaneous liver-kidney transplantation suggest performing dual transplantation in a case of glomerulosclerosis exceeding 40% and interstitial fibrosis exceeding 30% [5,6,17], but these studies are limited by the small number of biopsies performed. However, a study reported avoidance of dual transplantation in 70% of patients on the basis of biopsy [6]. In these patients, the extent of glomerulosclerosis was a predictor of eGFR reduction over the first 12 months after liver transplantation [6]. Wadei et al. [18] reported that 22% of liver transplant recipients with pretransplant kidney biopsies showing reversible histology were evaluated for kidney transplantation by 12 months after liver transplant [18]. Therefore, more studies are needed to determine whether pretransplant kidney biopsies can predict long-term kidney outcomes after liver transplantation. A summary of studies on pretransplant kidney biopsy with clinical relevance is presented in Table 1.

Post-Transplant Kidney Biopsy and OLTx

The etiology of CKD after liver transplantation may be multifactorial. The disease may result from treatment (e.g., early renal dysfunction after LT has been associated with the use of

Table 1. Kidney biopsy before liver transplantation.

First author/ number/study period	Number of patients	The most common causes of ESLD	Renal biopsy indication	Renal biopsy results	Clinical implication
Axelsen et al. [20] 1989–1990	23	PSC/PBC	Scr 80–180 µmol/L Proteinuria <200–450 mg/24h	Minor glomerular abnormalities n=9 IgA GN n=2 Mesangiocapillary GN type I n=1 Hepatic glomerulosclerosis n=8	All biopsies showed glomerular abnormalities, which may contribute to the occurrence of post-transplant renal dysfunction.
McGuire et al. [12] 2006	30	HCV	NA	25 patients had immune-complex glomerulonephritis: MPGN type 1 n=12 IgAN n=7, and mesangial glomerulonephritis n=6	Immune-complex glomerulonephritis was common in patients with end-stage HCV-induced cirrhosis and was often clinically silent. Its potential to cause renal failure after liver transplantation may be underappreciated. Of these patients, 10 had normal serum creatinine levels, normal urinalysis results, and normal quantitative proteinuria. For 5 others, the only renal abnormality was an increased serum creatinine level.
Wadei et al. [14] 2005–2008	44	HCV	GFR <40 mL/min (n=37), proteinuria and/or hematuria	IgAN n=20 ATN n=13 MPGN n=5 DN n=5 FSGS n=4 Advanced IF n=12 Advanced gGS n=7 Minimal changes n=11	Renal biopsy is feasible in liver transplant candidates with moderate to severe renal failure and provides histological data that does not relate to the pretransplant clinical data. RB could be useful in selecting SLK candidates.
Calmus et al. [38] 2003–2005	60	ALD HCV+HBV	Unselected patient with ESLD undergoing screening for LTx	25 pts had a morphological diagnosis of renal disease: IgA GN n=12 DN n=10 IgA GN+DN n=3 Normal n=21	In patients with ESLD, IgA nephropathy and diabetic lesions were frequently found despite the absence of renal impairment and/or urinalysis abnormalities. These results strongly suggest that severe renal failure develops preferentially in liver transplant recipients with DM or carbohydrate intolerance, and that pre-existing arterial lesions may favor the nephrotoxicity of CNIs.
Pichler et al. [6] 2000–2018	59	HCV ALD	Liver transplant candidate with renal impairment of unclear etiology referred for SLK vs. LTx	MPGN 23% patients FSGS 11% IgAN 19% ATN 19% Ischemic glomerulopathy 8.5% DN 8.5% Normal histology 8.5% TMA 4%	Renal biopsy can be relatively safe in this high-risk population, may help diagnose the etiology of renal disease, may predict post-transplant kidney function, and can be useful in kidney allocation for liver transplant candidates. The best histological predictor for post-transplant GFR in LTx group was the extent of global glomerulosclerosis.

Table 1 continued. Kidney biopsy before liver transplantation.

First author/ reference number/study period	Number of patients	The most common causes of ESLD	Renal biopsy indication	Renal biopsy results	Clinical implication
Singh et al. [41] 2005–2016	11	HCV ALD NALD PSC Alpha 1 deficiency	Liver transplant candidate with renal impairment of unclear etiology referred for SLK vs. LTX (eGFR \leq 40 ml/min)	Minimal changes n=8 DM n=2 MPGN n=1	LTX n=8 SLKT n=3 The level or duration of decreased e-GFR before LTX is insufficient to predict the irreversibility of post- transplant kidney function.
Wadei et al. [43] 2002–2014	128	HCV NALD Cryptogenic Primary biliary cirrhosis	Liver transplant candidate with renal impairment of unclear etiology referred for SLK vs. LTX (IGFR \leq 40 ml/min or proteinuria $>$ 500 mg/d, or hematuria)	Normal n=13 ATN n=25 MPGN n=19 Minimal changes n=24 Advanced interstitial fibrosis and GS n=47	MELD score, serum creatinine, urinary sodium excretion, and renal size did not correlate with biopsy diagnosis; only SBP at the time of LTX evaluation correlates with renal histology.

AKI – acute kidney injury; ATN – acute tubular necrosis; CKD – chronic kidney disease; CNI – calcineurin inhibitor; CsA – cyclosporine A; DM – diabetes mellitus; DN – diabetic nephropathy; ESLD – end-stage liver disease; FSGS – focal segmental glomerulosclerosis; GN – glomerulonephritis; GS – glomerulosclerosis; HGS – hepatic glomerulosclerosis; HP – hypertension; iGFR – iothalamate glomerular filtration rate; IF – interstitial fibrosis; IgA – immunoglobulin A; HBV – hepatitis B virus; HCV – hepatitis C virus; ALD – alcoholic liver disease; IFTA – interstitial fibrosis and tubular atrophy; LAT – alone liver transplantation, LTX liver transplantation; MGA – minor glomerular abnormalities; MPGN – membranoproliferative glomerulonephritis; NA – not available; NALD – nonalcoholic liver disease; NASH – nonalcoholic steatohepatitis; NRSOT – nonrenal solid organ transplantation; PSC – primary sclerosing cholangitis; RB – renal biopsy; RRT – renal replacement therapy; SBP – systolic blood pressure; SLK – tx simultaneous-liver-kidney transplantation; TA – tubular atrophy; TAC – tacrolimus; TMA – thrombotic microangiopathy; TDV tenofovir associated nephrotoxicity.

the calcineurin inhibitors [CNI] approved to prevent liver graft rejection in all immunosuppression regimens), with complications after transplantation (e.g., post-transplant diabetes or hypertension), may appear *de novo*, or can be an unrecognized pre-LTx disease [19]. Beyond the evaluation of CKD, a biopsy can reveal additional, sometimes unsuspected, pathology, as several studies have reported frequent glomerular abnormalities [12,20]. The best approach to a more appropriate diagnosis of kidney disease and thus reversibility of renal dysfunction, especially in patients after LTX, is performing native kidney biopsy in these patients. Modification of treatment without histological confirmation can harm the patient, and the existence of concurrent specific renal disease and the chance to administer specific treatment options to preserve or improve of renal function may be missed. Kidney biopsy is very useful, and, in the general population, is the standard procedure for diagnosis of kidney disease and is often necessary to make the right therapeutic decision. It is performed in native and transplanted kidneys and is generally considered a safe procedure. The most common indications for kidney biopsy are: proteinuria (especially nephrotic range), nephritic syndrome, and unknown acute kidney injury with rapid deterioration of kidney function. Figure 1 provides indications for kidney

biopsy after liver transplantation and a short algorithm. The procedure is usually performed with a percutaneous access with the use of real-time ultrasound and automated needles, and over 99% of biopsies are diagnostic. A summary of studies on post-transplant kidney biopsy with clinical relevance is presented in Table 2. In special cases, such as in patients with a high risk of bleeding or with extreme obesity, transjugular access or computed tomography, respectively, are also used. A summary of studies on post-transplant transjugular kidney biopsy with clinical relevance is presented in Table 3. The success of the procedure is defined by the ability to obtain adequate tissue for diagnosis and, equally important, by the safety profile. The most frequent complications after percutaneous kidney biopsy are hematuria, hematoma around the kidney, arteriovenous fistula, and pain, and are usually not dangerous. Major complications, including death and the need for nephrectomy, are extremely rare. Life-threatening complications occur in $<$ 0.1% of biopsies and appear during the first 24 h after the procedure in most cases. The standard of care after kidney biopsy has included bed rest with 24-h observation [21]. Biopsy risk in the OLTx patient population is definitely higher and several studies have shown lower bleeding risk when the transjugular approach to kidney biopsy is used

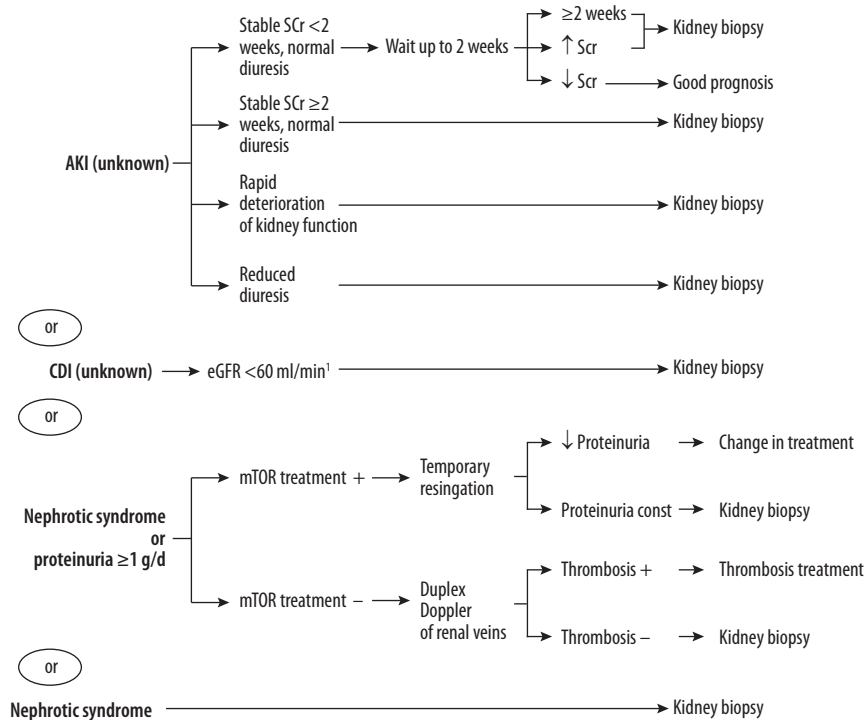


Figure 1. Indications for kidney biopsy after liver transplantation and a short algorithm. (AKI/ CKD “unknown” after exclusion: dehydration, renal arterial stenosis/thrombosis, kidney infection, heart failure, CNI overdosage, rhabdomyolysis, use of nephrotoxic drugs).

in the presence of cirrhosis [22,23]. Unfortunately, the availability of transjugular kidney biopsy is lower than that of percutaneous biopsy. The correct diagnosis of kidney disease is the key to optimal treatment in all such patients, especially in cases where all potential causes are likely to exist. The etiological spectrum of kidney disease in patients after liver transplantation is very broad, ranging from diseases that can damage both the liver and kidneys, to those with procedure- and treatment-related complications, from mild and stable CKD, to rapid deterioration of renal function [24,25]. At present, kidney biopsy is the most reliable examination for diagnosing kidney disease. Although many liver recipients have some signs of potential kidney disease that may be important for kidney and liver function, kidney biopsy is performed too rarely and data about histological changes and complications in patients with CKD after liver transplantation are scarce [6,26–28]. Our histological results showed the discordance between clinical, laboratory, and ultrasound information. In 1 case, histological findings demonstrated typical changes for end-stage disease, even though the deterioration of kidney function was acute and suggested acute kidney injury. In other cases, kidney biopsy has prevented unnecessary modifications of immunosuppression [29]. Percutaneous kidney biopsy is a very good method for sampling the kidney tissue and is associated with

bleeding risk in 3–13% of cases, with 6.4% of complications requiring intervention and/or blood transfusion in the general population [21]. Similar native kidney biopsy studies documented a 2.3-fold increased risk of bleeding after kidney biopsy in patients with a low eGFR [21, 30]. Wadei et al. [14,18] found a 30% rate of kidney biopsy complications in patients with renal failure qualified for liver transplantation, with major complications occurring in 18% and INR (international normalized ratio) ≥ 1.5 was the single predictor of post-biopsy bleeding. In the study by Welker et al. [31], 4/14 patients (29%) had peri-renal hematoma, all without subsequent interventions. In our study, kidney biopsy complications were documented in all our patients (4/4), but the patients had slightly higher creatinine concentration at the time of the study (2.39 vs. 1.83 mg/dl) [29]. This group was too small for statistical analysis, but our study also showed that complications in this group are not life-threatening and do not cause hemodynamic changes. Our results, similar to other studies, highlight the discordance between clinical information and histological findings, and suggest that percutaneous kidney biopsy is safe and helpful in avoiding unnecessary immunosuppression treatment modifications [30,31]. Histopathological analysis may have diagnostic and prognostic implications, allowing individualized management protocols aimed at renal protection

Table 2. Kidney biopsy after liver transplantation.

First author/ reference number/ study period	The mean time until biopsy after LTx	Number of patients	The most common causes of ESLD	Renal biopsy indication	Renal biopsy results	Clinical implication
Neau-Cransac et al. [33] 1989–2000	72 (1–108) months	9	ALD HCV	Scr >200 µmol/L	Chronic CNI-related nephrotoxicity	Cyclosporine and tacrolimus withdrawal. Despite this modification, there was no significant renal function improvement.
Pillebout et al. [28] 1999–2003	4.8 years (0.5–11.6)	26	HCV ALD	CKD Isolated proteinuria 1.2 g/24 h	45±3% of sclerotic glomeruli 45±4%, associated with marked vascular lesions n=17 TMA n=13; CNI nephrotoxicity n=12 DKD n=9 FSGS n=9	CKD in LTx recipients is more complex than originally thought histologic lesions suggesting the interplay of multiple factors in renal destruction and should not be classified as anti-calceineurin nephrotoxicity without further investigations, including renal histology.
Kim et al. [34] 2002–2008	4.89 years	81	HCV	Scr ≥1.5 mg/dl or new proteinuria	Arterionephrosclerosis: mild n=61 moderate n=20 Tubulointerstitial abnormalities n=53, mild tubular atrophy n=45 Podocyte effacement n=65 GBM widening n=52 HGS n=30 FSGS n=21 CNI toxicity n=13	All biopsies demonstrated universal glomerular abnormalities in kidney biopsies after LTx. Only 16% showed evidence of CNI toxicity.
Kamar et al. [35] 2006–2007	60±48 months	99	HCV	eGFR ≥15 ml/min.	Only 5 patients had features of a specific kidney disease: IgA nephropathy, cryoglobulinemic membranoproliferative glomerulonephritis, nephroangiosclerosis, signs of TMA, and tubulointerstitial nephritis.	In the setting of liver transplantation, this is the largest kidney-histology study to confirm that histological kidney lesions are complex, multiple, and interrelated. 13 pts converted from CNIs to rapamycin but with no significant improvement in eGFR. Kidney function at 6 months post-transplant can predict long-term kidney function and histology.
Kubal et al. [36] Since 1999	4years (0.3–15.9)	62 NRSOT 31 pts post LTx	NA	Liver, heart, lung, and heart- lung transplant recipients who underwent a renal biopsy at least 3 months post-transplant as a part of work up for deteriorating renal function.	35.5% CNI chronic nephrotoxicity (50% also hypertensive nephropathy). Of the remaining 40 biopsies, 27 showed HN with no or minimal arteriolar hyalinosis, ATN (5), MPGN (2), DN (1), postinfectious GN (1), and membranous nephropathy (12)	Many patients do not have overt histological evidence of CNI toxicity. Quantitative parameters of chronic damage can stratify renal prognosis.
Lee JH et al. [27] 1999–2012	24.5 months (3–66)	10	HBV ALD	Unexplained increase of serum creatinine, newly developed proteinuria with microscopic hematuria.	IgA GN (4); Mesangial proliferative GN (1) CNI-induced nephrotoxicity (3) GS in 90% of cases; IF in 80% of cases TA in 80% of cases	Kidney biopsy is safe and effective method after LTx. Management of patients based on the result of kidney biopsy can improve renal outcome.

Table 2 continued. Kidney biopsy after liver transplantation.

First author/ reference number/ study period	The mean time until biopsy after LTx	Number of patients	The most common causes of ESLD	Renal biopsy indication	Renal biopsy results	Clinical implication
Chan et al. [37] 2002–2010	1590 days (102–3699)	10	HBV	Proteinuria (>1 g/24h) (in 7 pts in the nephrotic range) or >20% increase in serum creatinine level from baseline on at least 2 occasions.	DN n=6 IgA GN n=4. Only one patient had chronic CNI- nephrotoxicity.	Most biopsies showed complex renal lesions while CNI nephrotoxicity was rare.
Fujinaga et al. [26] 2002–2008	20–76 months	4	HCV	Regardless of serum creatinine level, unexplained progressive renal failure, proteinuria, persistent glomerular hematuria and systemic disease with renal involvement.	Only one patient had HCV related membranous proliferative nephritis, DN n=1 Tacrolimus toxicity n=2.	Although HCV and hypertension were determined to be independent risk factors for late renal disease, a renal biopsy should be performed when clinical symptoms develop regardless of creatinine levels to provide appropriate treatment.
Welker et al. [31] 2011–2015	3 years (0.2–12)	14	HCV ALD	Severe renal impairment with progressive deterioration of renal function, overt proteinuria 0.2–8.6 g/24 h	IgA GN n=4 MPGN type I n=1 Membranous GN n=1 Nephrosclerosis n=5 TDF n=1 DN/CNI toxicity n=1 AA amyloidosis n=1 IFTA was present in all biopsies ranging from 5–70%	Renal biopsy in patients with CKD after LTx seems safe and may offer specific therapeutic options. Unnecessary changes of immunosuppression can be avoided in a considerable number of patients.
Tsapenko et al. [32] 1988–2008 (retrospective analysis)	6.9 years (4.6 months– 16.2 years)	23/1698 (23 RB from 1698 pts after OLTx)	Different	Proteinuria, progressive CKD, hematuria	Focal and global GS n=8 (30.4%) FSGS n= 2 (8.7%) IgAN n=2 (8.7%) MPGN n=2 (8.7%) Nonspecific GN n=1 (4.3%) CNI toxicity n=2 (8.7%) DN n=2 (8.7%) ATN n=1 (4.3%) Nonspecific n=3 (13%)	Immunosuppression was modified in 8 pts; RAAS blockade was initiated in 6 pts;
Lee JP et al. [39] 1997–2008 (retrospective analysis)	NA	9/431	HBV (80%) HCV HCC	Proteinuria >1g/d, Persistent microscopic hematuria, Progressive deterioration of renal function.	Global GS n=9 (100%; 3.7– 93.5%) Segmental GS n=4 (44.4%) Fibrosis n=9 (100%) Arteriopathy 6 (66.7%) Arteriopathy 8 (88.9%) DN n=0 Chronic CNI toxicity n=0	CNI withdrawal in 7 pts with improvement of kidney function; ARB addition in 2 pts.
Schwartz et al. [40] 2009 (retrospective analysis); 105 KB in nonrenal transplant recipients)	35 months	39 (41 biopsies)	HBV HCV ALD Cystic fibrosis Malformation of the biliary duct	AKI n=5 (12%) Creatinine increases n=33 (80.5%) Heavy proteinuria n=12 (29.3%) Renal insufficiency before re-Tx n=3 (7.3%).	IgAN n=6 Minimal changes n=1 MPGN n=3 TMA n=5 Iron overload n=2 CNI toxicity n=25 (64%) HP n=16 (41%) AT injury n=19 (49%)	CNI terminated in TMA and CNI toxicity.

Table 2 continued. Kidney biopsy after liver transplantation.

First author/ reference number/ study period	The mean time until biopsy after LTx	Number of patients	The most common causes of ESLD	Renal biopsy indication	Renal biopsy results	Clinical implication
Hiesse et al. [42] 1990–1994	NA	9	NA	Significant proteinuria Renal function impairment	MPGN with immunodeposits n=4 MN n=1 DN n=2 Interstitial nephritis n=2	All underwent liver transplantation followed by kidney transplantation.

AKI – acute kidney injury; ATN – acute tubular necrosis; CKD – chronic kidney disease; CNI – calcineurin inhibitor; CsA – cyclosporine A; DM – diabetes mellitus; DN – diabetic nephropathy; ESLD – end-stage liver disease; FSGS – focal segmental glomerulosclerosis; GN – glomerulonephritis; GS glomerulosclerosis; HCC – hepatocellular carcinoma; HGS – hepatic glomerulosclerosis; HP – hypertension IF interstitial fibrosis; IgA - immunoglobulin A; HBV – hepatitis B virus; HCV – hepatitis C virus; ALD – alcoholic liver disease; IFTA – interstitial fibrosis and tubular atrophy; LAT – alone liver transplantation, LTx – liver transplantation; MGA – minor glomerular abnormalities; MPGN – membranoproliferative glomerulonephritis; NA – not available; NASH – nonalcoholic steatohepatitis, NRSOT – nonrenal solid organ transplantation; RAAS – renin-angiotensin-aldosterone system; RB – renal biopsy; RRT – renal replacement therapy; SLK – tx simultaneous-liver-kidney transplantation; TA – tubular atrophy; TAC – tacrolimus; TMA – thrombotic microangiopathy; TDV – tenofovir-associated nephrotoxicity.

Table 3. Transjugular kidney biopsy in liver transplant recipients.

First author/ reference number/ study period	Number of patients	The most common causes of ESLD	Renal biopsy indication	Renal biopsy results	Clinical implication
Jouet et al. [22] 1996 1987–1994	55	ALD	Patients considered for LTx	Glomerular lesions Interstitial abnormalities End-stage kidney Normal histology	The transjugular biopsy may be a useful procedure in patients with cirrhosis and clotting disorders. This approach may influence treatment decisions in patients proposed for liver transplantation.
Sam et al. [23] 2001	29		No data	Tubular injury MPGN Nephrosclerosis Minimal change disease ESRD GS Nonspecific changes No abnormality in 4 cases	Irrespective of urine or blood findings, glomerular, and tubular abnormalities are relatively common in the setting of advanced liver disease.
Abbott et al. [30] 2002 1996–2001	9		No data	–	Transjugular biopsy appears to be efficacious in high-risk patients for whom percutaneous procedure is contraindicated.

AKI – acute kidney injury; ATN – acute tubular necrosis; CKD – chronic kidney disease; CNI – calcineurin inhibitor; CsA – cyclosporine A; DM – diabetes mellitus; DN – diabetic nephropathy; ESLD – end-stage liver disease; FSGS – focal segmental glomerulosclerosis; GN – glomerulonephritis; GS – glomerulosclerosis; HGS – hepatic glomerulosclerosis; HP – hypertension IF interstitial fibrosis; IgA – immunoglobulin A; HBV – hepatitis B virus; HCV – hepatitis C virus; ALD – alcoholic liver disease; IFTA – interstitial fibrosis and tubular atrophy; LAT – alone liver transplantation; LTx – liver transplantation; MGA – minor glomerular abnormalities; MPGN – membranoproliferative glomerulonephritis; NA – not available; NASH – nonalcoholic steatohepatitis; NRSOT – nonrenal solid organ transplantation; RB – renal biopsy; RRT – renal replacement therapy; SLK – tx simultaneous-liver-kidney transplantation; TA – tubular atrophy; TAC – tacrolimus; TMA – thrombotic microangiopathy; TDV – tenofovir-associated nephrotoxicity.

among liver transplant recipients. Transjugular kidney biopsy is an alternative method for sampling kidney tissue, especially in patients with advanced liver disease. Complications after this procedure are rare (about 4%), but up to 30% of patients do not provide adequate diagnostic samples and some of these patients need a repeat biopsy. We do not have experience with transjugular kidney biopsy, but this is certainly an interesting diagnostic option for patients with high bleeding risk, such as patients with liver diseases.

Conclusions

Kidney biopsy is very useful in diagnosing kidney damage and assessing prognosis in liver transplant recipients. The procedure is safe, but is rarely performed. The data on pre- and post-transplant kidney biopsy are very scarce. Kidney damage

occurring in approximately 25% of patients qualified for OLTx is often irreversible, and predicting renal recovery after OLTx, without knowledge of histological changes in the kidneys, is imperfect and challenging. In some studies, the incidence of kidney biopsies was about 1-2% [32]. It would be helpful to know if a patient has a chance to improve kidney function after OLTx or should be qualified for simultaneous transplantation (SLKT). On the other hand, immunosuppressive treatment after OLTx with a CNI reduction can improve kidney function, but studies show that CNI toxicity accounts for only a small percentage of complications. Performing a kidney biopsy in such a situation may reduce unnecessary discontinuation of immunosuppression. We suggest that kidney biopsy in patients qualified for OLTx and after transplantation should be done more often, as it can help in the treatment and prognosis of CKD in this vulnerable population.

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