REVIEW ARTICLE

The Role of Gastroenterologists in Preoperative Assessment and Management of Prospective Renal Transplantation Candidates

Suprabhat Giri[1], Kumar Avijeet Dash[2], Jijo Varghese[3], Shivaraj Afzalpurkar[4]

Received on: 12 May 2023; *Accepted on:* 26 June 2023; *Published on:* 03 August 2023

Abstract

Renal transplant is the most common organ transplant worldwide, accounting for 65% of the total number of transplants. End-stage renal disease (ESRD) often has multiple significant comorbidities. Among the gastrointestinal (GI) disorders, peptic ulcer disease (PUD), cholelithiasis, and colon and liver diseases increase the risk of posttransplant morbidity. Potential renal transplantation (RT) candidates need a multidisciplinary assessment of coexisting illnesses, which may affect the perioperative risk and survival after transplantation. Successful outcome of RT depends on careful selection of the recipients by a thorough medical evaluation and screening. This review summarizes the role of gastroenterologists and hepatologists in preoperative assessment and management of renal transplant recipients.

Keywords: Cholelithiasis, Hepatitis B virus, Hepatitis C virus, Inflammatory bowel disease, Renal transplant.

Euroasian Journal of Hepato-Gastroenterology (2023): 10.5005/jp-journals-10018-1390

Introduction

Renal transplantation (RT) is the most preferred treatment option for end-stage renal disease (ESRD) patients. Compared with hemodialysis (HD), it offers a significantly better quality of life and outcome for patient.[1] As per the World Health Organization (WHO) 2019 data, renal transplant is the most common organ transplant worldwide, accounting for 65% of the total number of transplants, with a 4.8% increase in the rate of renal RT compared to the previous year.[2] Patients with ESRD often have multiple significant comorbidities.[3] Among the gastrointestinal (GI) disorders that increase the posttransplant morbidity risk are peptic ulcer disease (PUD), cholelithiasis, and diseases of the colon and liver (Fig. 1).[4]

Apart from these, patients on maintenance HD have an increased risk of acquisition of blood-borne infections such as hepatitis B virus (HBV) and hepatitis C virus (HCV).[5] Increased vaccination rates and improved infection control measures have led to a decrease in transmission of HBV and HCV in the West.[6] At the same time, the prevalence of HBV and HCV in patients with HD continues to be high in Asia and Africa.[5,7] The routine tests used for the screening of HBV and HCV may not be sufficient for patients of ESRD on HD. In a study from Egypt, the false-negativity rate of anti-HCV was found to be 17.9%.[8] Also, the occult HBV infection rate is higher in HD patients than in the general population.[9] Failure to identify these infections prior to RT may lead to reactivation or flare with the use of immunosuppression after RT, which will adversely affect the outcome of RT.

Hence, the potential RT candidates need a multidisciplinary assessment of coexisting illnesses, which may affect the perioperative risk and survival after transplantation. Successful outcome of RT depends on careful selection of the recipients by a thorough medical evaluation and screening. Presently there is a paucity of evidence for assessing a prospective RT candidate referred to a gastroenterologists for fitness. Hence, this review article summarizes the current evidence on preoperative assessment and management of GI and hepatic diseases in potential RT candidates.

[1]Department of Gastroenterology, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India

[2]Department of Nephrology, Kalinga Institute of Medical Sciences, Bhubaneswar, India

[3]Department of Gastroenterology, KM Cherian Institute of Medical Sciences, Kallissery, India

[4]Department of Gastroenterology, Nanjappa Multi-Speciality Hospitals, Davanagere, Karnataka, India

Corresponding Author: Shivaraj Afzalpurkar, Department of Gastroenterology, Nanjappa Multi-Speciality Hospitals, Davanagere, Karnataka, India, Phone: +91 7038578275, e-mail: drshivaraj62@gmail.com

How to cite this article: Giri S, Dash KA, Varghese J, *et al*. The Role of Gastroenterologists in Preoperative Assessment and Management of Prospective Renal Transplantation Candidates. Euroasian J Hepato-Gastroenterol 2023;13(1):18–25.

Source of support: Nil

Conflict of interest: None

Pretransplant Assessment

Gastrointestinal Pathologies

Peptic Ulcer Disease and Helicobacter pylori Infection

Patients with chronic kidney disease (CKD) experience upper GI symptoms at a higher rate compared to those without CKD. In a long-term population-based study from Taiwan over 10 years it was found that the incidence of PUD was 10–12 times higher in patients with CKD. Patients on maintenance HD had a significantly higher risk of PUD [adjusted odds ratio (OR), 9.74; 95% confidence interval (CI), 7.11–13.31].[10] However, this increased risk of PUD in CKD may not be attributed to *Helicobacter pylori* (Hp) infection, as the prevalence of Hp infection in patients with CKD is significantly lower in a meta-analysis (OR, 0.64; 95% CI, 0.52–0.79).[11] In the posttransplant period, PUD is the most common GI complication

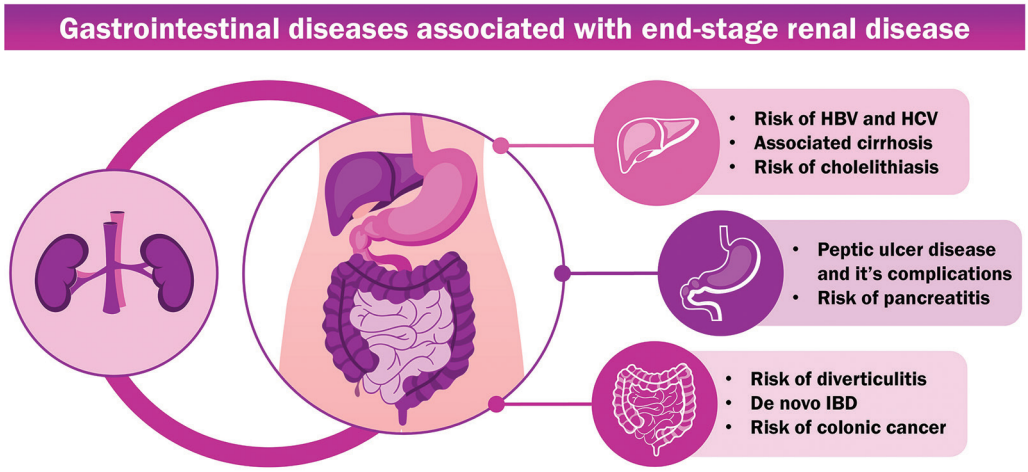

Fig. 1: The GI diseases associated with ESRD

occurring at a higher rate compared to the general population.[12,13] The majority of PUD in the posttransplant period occurs within the first 3 months, and mycophenolate mofetil has been found to have a significant association.[13]

The rate of complications with PUD is also high in CKD, with one study reporting the rate of bleeding and perforation as 28% and 5.2%, respectively.[12] Due to this high rate of PUD in CKD with an increased risk of complications in the posttransplant period, Kidney Disease: Improving Global Outcomes (KDIGO) recommends esophagogastroduodenoscopy (EGD) and Hp testing only for prospective RT candidates with symptoms suggestive of active PUD.[14] However, studies suggest that most patients with CKD and PUD were asymptomatic.[15,16] Hence, prospective large-scale studies are needed to assess the benefit of pretransplant EGD for all patients irrespective of symptoms. Furthermore, RT in patients with active PUD should be delayed until resolution, but a prior history of PUD should not serve as an exclusion criterion for RT.

Colorectal Cancer and Colonic Polyps

The presence of adenomatous polyps is not a contraindication for RT. Still, colorectal cancer (CRC) excludes the patients from the transplant list for a period of 2–5 years from disease control based on Duke's staging.[14] At present, in potential transplant candidates recommendations for CRC screening is the same as the general population,[14] with 2-yearly fecal immunochemical testing (FIT) for age above or equal to 50 years and colonoscopy for those with positive FIT.[17,18] However, in a meta-analysis of patients with CKD, a significantly increased risk of CRC was observed in patients without [pooled standardized incidence rate (SIR), 1.18; 95% CI, 1.01–1.37) or with transplant (pooled SIR, 1.40; 95% CI, 1.15–1.71).[19] Meta-regression analysis showed a positive correlation between CRC risk and the proportions of males, increasing age, and follow-up duration.[19] Thus, patients with CKD have a significantly increased risk of CRC regardless of a history of RT. In a retrospective analysis evaluating the utility of colonoscopy as a part of pretransplant workup, 75.6% of patients were found to have pathologies. Polyps were seen in 30.7%, while advanced adenomas were seen in 10.2% of cases.[20] This calls for the inclusion of baseline colonoscopy in the pretransplant workup of prospective RT patients, regardless of age, although further large-scale future studies are needed.

Diverticular Disease

Post-RT immunosuppression may mask the symptoms of diverticulitis and is associated with an increased risk of colonic perforation.[21] Subsequently, a systematic review reported a very low pooled incidence of post-RT diverticulitis (0.8%) and complicated diverticulitis (1%).[22] Hence, diverticulosis screening in prospective RT candidates is not justifiable based on these incidence rates. The KDIGO guidelines recommend delaying RT in ESRD patients with active diverticulitis until the resolution of symptoms. Patients with asymptomatic diverticulosis and a prior history of diverticulitis neither need prophylactic colectomy nor to be excluded from the transplant list.[14] However, patients with autosomal dominant polycystic kidney disease (ADPKD) undergoing RT have a higher risk of colonic diverticulosis and its complications.[23–25] Hence, this subgroup of patients may require a pre-RT colonoscopy, and ADPKD patients with a history of one or more episodes of acute diverticulitis should be considered for colonic resection.[23]

Inflammatory Bowel Disease

Renal involvement in the form of calculi and tubular damage is considered one of the extraintestinal manifestations of inflammatory bowel disease (IBD) but is uncommon. Nephrolithiasis, tubulointerstitial nephritis, glomerulonephritis, amyloidosis, and drug-induced nephrotoxicity are the most common renal involvements in patients with IBD and IgA nephropathy being the commonest form of glomerulonephritis.[26] The data on renal transplant outcomes in patients with IBD is scarce, with only a few case reports and series. Patients with IBD undergoing RT have a lower 5-year survival and higher risk of hospitalization due to infections than patients without IBD,[27] and up to one-third of patients may have a disease flare after RT.[28] Patients in remission prior to RT usually maintain remission in the posttransplant period,[27] while liver transplant studies have shown active IBD at transplant to be a predictor of posttransplant flare.[29] Hence, pre-RT assessment of IBD disease activity with colonoscopy or radiological modalities is essential, and RT in patients with active IBD should be postponed until remission.[14] Screening for CRC in patients with IBD is the same as per the surveillance for colorectal endoscopic neoplasia detection and management in inflammatory bowel disease patients: international consensus (SCENIC) guidelines.[30]

Pancreatic Diseases

Patients with ESRD are at a higher risk of acute pancreatitis (AP),[31,32] with peritoneal dialysis contributing to greater risk compared to HD.[31,32] Hypercalcemia is an important cause of AP in ESRD irrespective of dialysis requirement.[33] Mortality and morbidity associated with AP are also higher in patients with ESRD and post-RT.[31,33] Hence, patients with prior history of AP should be evaluated for risk factors and managed prior to RT.[14] However, there is no evidence to support routine pre-RT evaluation of the pancreas in asymptomatic patients.

Acute pancreatitis is a known risk factor for poor surgical outcomes in liver transplantation patients. Preoperative pancreatitis (within 30 days preoperatively or postoperatively) has been associated with early graft failure and patient mortality.[34] In the absence of similar data for RT, this data can be extrapolated to prospective RT candidates, and RT may be delayed for 3–6 months after an episode of AP to prevent an early recurrence.[14,35]

Chronic uremia is a known risk factor for the development of chronic pancreatitis (CP).[36] The presence of CP is not a contraindication for RT, and the management of patients with exocrine and endocrine insufficiency in these patients is similar to those without ESRD. The CP patients with severe endocrine insufficiency requiring insulin with resultant ESRD are candidates for simultaneous pancreas–kidney transplantation and should be evaluated for the same.[37]

Hepatobiliary Pathologies

Cholelithiasis and Cholecystitis

There is no definite evidence whether patients with ESRD have a higher prevalence of cholelithiasis, with some studies showing a higher prevalence[38,39] and others showing no association.[40] Hence, there has been no consensus on the screening of asymptomatic renal transplant candidates for cholelithiasis. However, for patients with a history of cholecystitis and diabetes screening is warranted. No definite benefit of elective, pretransplant cholecystectomy has been observed with respect to posttransplant morbidity or mortality.[41,42] Transplantation should be delayed in patients with complicated gallstone disease until resolution.[14] Pretransplant cholecystectomy is recommended for ERSD patients with symptomatic cholelithiasis due to the increased risk of life-threatening cholecystitis after transplantation.[43]

Active Hepatitis

There is no specific data on the outcome of RT in patients with active hepatitis. However, patients with acute hepatitis of any etiology (viral, alcohol, ischemia, toxic, thrombosis, or drugs) have an increased operative risk, and hence, active hepatitis is a contraindication for elective surgeries.[44] This inference is based on data from older studies, reporting a mortality rate of 10–13% in patients undergoing laparotomy in the presence of acute hepatitis.[45] The majority of acute viral hepatitis cases are self-limited, and hence, RT can be planned after clinical and biochemical improvement. However, acute viral hepatitis due to hepatitis E virus (HEV) infection deserves special mention as it has a risk of progression to chronicity with immunosuppression.[46] Furthermore, HEV RNA usually becomes undetectable within 3 weeks after the onset of symptoms in most cases but can persist for 100 days.[47] Hence, it seems prudent to delay the RT in patients with HEV-related acute viral hepatitis to prevent the development of chronic hepatitis and cirrhosis associated with HEV infection.

The outcome of surgery for alcoholic hepatitis is still worse compared to viral hepatitis. Alcoholic hepatitis has been shown to increase perioperative mortality after urgent surgery and is also a contraindication to elective surgery.[48] Thus, patients with acute alcoholic hepatitis should wait until the clinical and biochemical resolution of hepatitis before undergoing surgery.

Hepatitis-B Virus Infection

Clinical outcomes in kidney allograft recipients can be negatively impacted by chronic HBV infection. The requirement for immunosuppression in the posttransplant period puts the patient with HBV infection at risk for liver injury. The goal of management is to prevent HBV reactivation or flare in recipients with chronic or prior HBV infection and prevent *de novo* infection in patients without HBV infection receiving a kidney from a donor with chronic or prior HBV infection.

The recommended screening of the recipient included testing for hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), and hepatitis B core antibody (anti-HBc).[14,49] The need for vaccination or additional tests will be determined based on the result of these tests. Patients with evidence of chronic infection should also be evaluated for the stage of liver disease and managed accordingly. Potential kidney donors (living and deceased) screening involves testing for HBsAg, anti-HBc, and HBV DNA nucleic acid testing (NAT).[49] The optimal timing of testing of donor for both HBV and HCV markers before organ procurement is as follows: (A) Within 28 days for a living donor and (B) within 96 hours for a deceased donor.[49] For patients from hepatitis D virus endemic areas, KDIGO recommends screening HDV serology in HBsAg or anti-HBc positive.[14]

Table 1 summarizes the management algorithm depending on the donor and recipient HBV status.

Preferred regimen and duration of therapy: Current guidelines recommend tenofovir and entecavir as the antiviral therapy of choice for prophylaxis or treatment in patients undergoing solid organ transplants due to their high barrier to resistance.[50,51] Entecavir and tenofovir alafenamide (TAF) are preferred for patients with CKD because of their lower risk of nephrotoxicity than tenofovir disoproxil fumarate (TDF). While entecavir requires dose modification as per the creatinine clearance, TAF does not require any dose modification for patients on HD, and on HD days, it should be administered after HD.[51] Pegylated interferon alfa may precipitate acute allograft rejection and should not be used in kidney transplant recipients.[52] For HBsAg-negative, anti-HBc-positive recipients, the duration of antiviral therapy should be a minimum of 6–12 months (period of maximal immunosuppression).

Monitoring: In patients receiving antiviral therapy to prevent *de novo* infection, HBsAg, anti-HBc, and HBV DNA should be monitored every 3 months. Antiviral treatment can be safely discontinued if the above parameters remain negative for 1 year. Checking the anti-HBs titer before drug discontinuation and administering a booster dose of vaccine if the titer is below 10 mIU/mL reduces the risk of *de novo* infection. After discontinuation of therapy, the frequency of monitoring can be prolonged to an annual interval. Recipients receiving antiviral therapy to prevent reactivation or flare should have serum aminotransferases and HBV DNA monitored every 6 months or more frequently as indicated. If antiviral therapy is discontinued in recipients with prior HBV infection (anti-HBc positive) after immunosuppression is decreased, liver chemistries,

Table 1: Management based on transplant donor–recipient HBV status

Donor status	*Recipient status*	*Management*
HBsAg(+)	HBsAg(+)	Lifelong antiviral treatment
	HBsAg(–), Anti-HBc(+)	Lifelong antiviral treatment
	Anti-HBs titer ≥10 mIU/mL	One booster vaccination dose combined with HBIG just before transplantation, 12 months of antiviral therapy after transplantation
	Anti-HBs titer <10 mIU/mL	Avoid elective transplant, give booster vaccination dose, and repeat titer after 1 month If transplant is urgent, HBIG in addition to antiviral therapy (12 months) to prevent *de novo* infection, recipient vaccination after transplant
HBsAg(–), Anti-HBc (+)	HBsAg (+)	Lifelong antiviral treatment
	HBsAg (–), Anti-HBc (+)	Lifelong antiviral treatment
	Anti-HBs titer ≥10 mIU/mL	No therapy required unless donor has detectable HBV viral load
	Anti-HBs titer <10 mIU/mL	Booster dose and repeat titer after 1 month No therapy unless donor has detectable HBV viral load
HBsAg(–), Anti-HBc(–)	HBsAg(+)	Lifelong antiviral treatment
	HBsAg(–), Anti-HBc(+)	Antiviral therapy, usually for the initial 12 months after which immunosuppression is reduced to low-dose maintenance level (may consider for lifelong therapy)

HBV DNA, and HBsAg need to be monitored at least once every 3 months for 1 year.

Hepatitis C Virus Infection

All prospective RT candidates should undergo screening for HCV infection, with HCV antibody testing being the initial test.[14,49] A negative antibody test is likely enough to rule out HCV infection in dialysis centers or countries with a low HCV prevalence.[14] However, transplant candidates should be screened by HCV RNA testing in high prevalence areas due to the high false-negativity rates of HCV antibody tests.[8] Patients with positive antibody tests and those treated prior to HCV infection should undergo HCV RNA testing.

Staging of liver disease: Patients with ESRD and HCV infection need further evaluation for the staging of liver disease for fibrosis and the presence of portal hypertension, which would help in prognostication, selection of regimen for HCV treatment, and the decision on kidney versus simultaneous liver-kidney transplantation (SLKT). Initial assessment of fibrosis should be done by non-invasive methods, which include liver stiffness measurement by transient elastography (TE), and serum biomarkers [aspartate aminotransferase (AST)-to-platelet ratio index (APRI), fibrosis-4 (FIB-4) index].[53] As liver stiffness measurements have been shown to decrease significantly after HD, TE should only be performed after a dialysis session.[54] With the improvements in non-invasive methods, the use of liver biopsy has reduced, and presently it is reserved for patients with discordant results of non-invasive tests, potential additional etiologies, and in patients who have achieved sustained viral response (SVR) after antiviral therapy for HCV.[53] Dedicated biomarker panels such as Fibrotest® and ActiTest® are not reliable markers for fibrosis assessment in ESRD patients with HCV on HD.[55] Patients with cirrhosis detected clinically or on staging tests should be evaluated for portal hypertension. The approach to RT in patients with cirrhosis is discussed in the next section.

Use of kidneys from HCV-seropositive donors: Transplanting kidneys from a donor with chronic HCV infection will reduce the waiting time on the transplant list and improve long-term outcomes. However, organ transplants from HCV-positive donors are associated with a substantial risk of transmission of the infection. Hence, the KDIGO guidelines recommend that kidneys from HCV-RNA-positive donors should only be given to HCV RNA-positive recipients with the posttransplant treatment of HCV.[14] However, with the advent of direct-acting antiviral (DAA) leading to a high cure rate of HCV, studies have evaluated the allocation of kidneys from HCV RNA-positive donors to HCV RNA-negative patients followed by DAAs with excellent allograft function.[56,57] More extensive studies are needed before recommending RT from HCV RNA-positive donors to HCV RNA-negative patients.

Timing of HCV antiviral treatment: The decision regarding the timing of antiviral therapy (before or after transplantation) depends on multiple factors, including the severity of liver disease, donor type (living vs. deceased donor), and estimated waiting time on the kidney transplant list.[14] The HCV-infected candidates should not be excluded from kidney transplantation as safe and effective posttransplantation DAA therapy. Figure 2 summarizes the approach to the management of HCV in prospective renal transplant candidates and the timing of HCV therapy.

Selection of drugs for HCV treatment: The choice of pretransplant antiviral regimen in HCV-infected RT candidates depends on genotype, the extent of underlying liver disease, comedication, and antiviral treatment history. The commonly used pan-genotypic regimens include glecaprevir–pibrentasvir and sofosbuvir–velpatasvir. Ledipasvir–sofosbuvir is another option for genotype 1, 4, 5, and 6 infections.

Renal clearance is the major elimination pathway for GS-331007, the dephosphorylation-derived nucleoside metabolite of sofosbuvir, and was initially not recommended for patients with severe renal impairment (eGFR <30 mL/minute/1.73 m^2) or ESRD. However, two meta-analyses of studies on the outcome of the sofosbuvir-based regimen in stage 4–5 CKD[58,59] showed a pooled SVR12 rate of 97% with an 11–12% average pooled incidence of adverse effects. Thus, dialysis and advanced renal disease do not require a dose adjustment of DAAs.[53] However, the sofosbuvir-containing regimens are cleared by dialysis and should be given after the

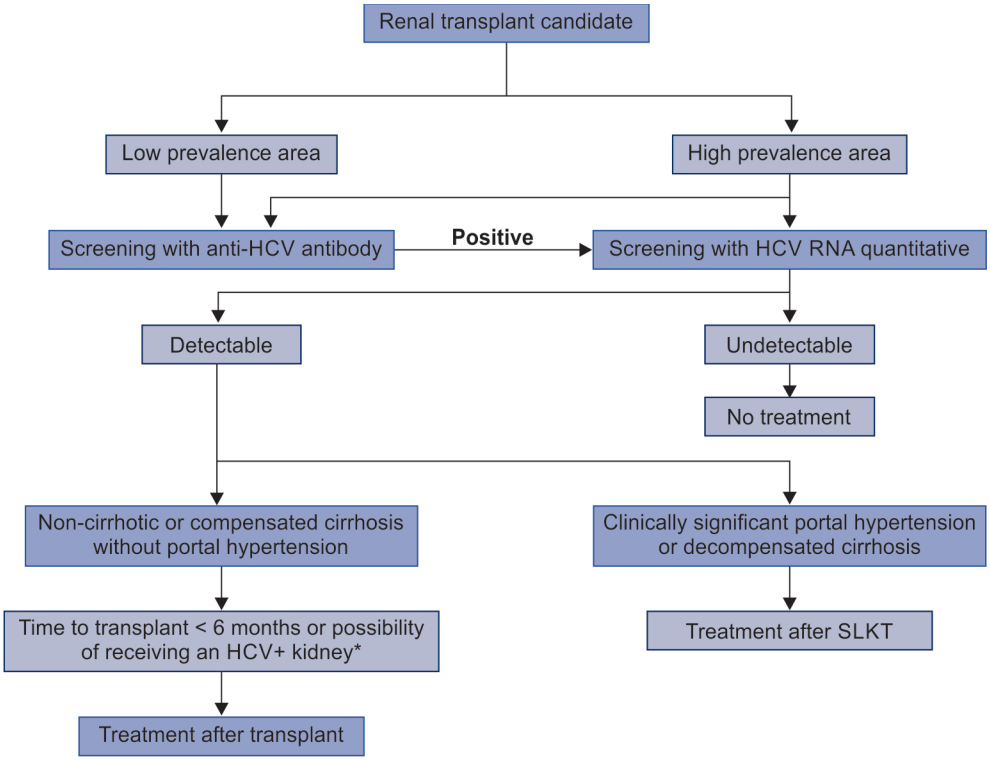

Fig. 2: Flowchart showing evaluation and treatment of patients with HCB infection awaiting renal transplant

session on HD days. The duration of DAA is 3 months for non-cirrhotic and compensated cirrhosis patients and 6 months for decompensated cirrhotics.[53]

Figure 2 provides the algorithm for the diagnosis and treatment of HCV in kidney transplant candidates.

Non-alcoholic Fatty Liver Disease

Non-alcoholic fatty liver disease (NAFLD) has a pooled global prevalence of 29.8% and is emerging as the most common cause of chronic liver disease worldwide.[60] The trend analysis showed an increase in prevalence from 21.9% in 1991 to 37.3% in 2019 (a yearly increase of 0.7%, $p < 0.0001$).[60] In a large-scale study from the UK,[61] the prevalence of NAFLD based on USG was 17.9% in patients with CKD, being much higher (30.7%) in diabetics. A previous smaller study reported a NAFLD prevalence of 85.5% in patients with CKD.[62] However, the later study utilized TE for diagnosis of NAFLD which may have led to a higher prevalence. Any patient diagnosed with NAFLD should undergo assessment for liver fibrosis preferably by a non-invasive method.[63] The risk for cardiovascular diseases and mortality increases in patients having both NAFLD and CKD.[61] However, the effect of NAFLD on post-RT outcomes has not been studied. The presence of NAFLD is not a contraindication for RT and patients on waiting list should be counseled for lifestyle interventions.

Chronic Liver Disease and Cirrhosis

The data on renal transplant outcomes in patients with compensated cirrhosis is limited. In two previous studies, the 1-year and 3-year graft and patient survival were similar between patients with HCV-related cirrhosis[64,65] and no cirrhosis, while a subsequent study showed a lower 3-year survival for patients with cirrhosis.[66] Patients

Table 2: Recommended investigations for assessment of GI and hepatic pathologies in patients being evaluated for renal transplant

Investigations	*Indications in prospective renal transplant candidate*
Liver function test	For all patients
Hepatitis B virus serology	HBsAg, Anti-HBs titer and Anti-HBc total to be done for all HBV DNA quantitative for patients with positive HBsAg or anti-HBc total
Hepatitis C virus serology	Anti-HCV for all patients HCV RNA quantitative for patients from high prevalence areas
Ultrasound of abdomen	Recommended for patients with diabetics, or patients with a history of biliary type pain or prior history of cholecystitis Can be considered for all patients for assessment of other conditions like non-alcoholic fatty liver disease
EGD	Recommended for patients with dyspepsia or prior history of PUD Can be considered for all patients, as majority of patients with PUD are asymptomatic
Colonoscopy	Patients with history of colonic polyp and prior colorectal cancer, one or more attack of colonic diverticulitis, and those with inflammatory bowel disease

with ESRD and compensated cirrhosis with clinically significant portal hypertension (hepatic venous wedge pressure > 10 mm Hg) or decompensated cirrhosis or associated acute or acute-on-chronic liver failure are candidates for SLKT.[14] For evaluation, these patients should be referred to centers with expertise in combined liver–kidney transplantation. In a recent multicentric study of patients undergoing SLKT, the 1-year survival has shown a significant improvement, being 89% in 2002 to 96% in 2017 ($p < 0.001$).[67]

Table 2 summarizes the recommended investigations for the assessment of GI and hepatic pathologies in patients being evaluated for renal transplant.

Conclusion

Patients with ESRD are at risk of multiple GI comorbidities, increasing the risk of complications in the posttransplant period. Screening and effective management of these comorbidities can help improve renal transplant outcomes.

Summary

- Esophagogastroduodenoscopy and Hp testing is recommended for prospective RT candidates and RT should be delayed until resolution in patients with symptoms suggestive of active PUD. However, a prior history of PUD should not serve as an exclusion criterion for RT.
- Baseline colonoscopy should be included in the pretransplant workup of prospective RT patients, regardless of age, especially in regions with a high prevalence of CRC, although further large-scale future studies are needed.
- Delaying RT in ESRD patients with active diverticulitis until resolution of symptoms is recommended. ADPKD undergoing RT have a higher risk of colonic diverticulosis and hence may require a pre-RT colonoscopy.
- Pre-RT assessment of IBD disease activity with colonoscopy or radiological modalities is essential, and RT in patients with active IBD should be postponed until remission.
- Patients with prior history of AP should be evaluated for risk factors and managed prior to RT. Also, CP patients with severe endocrine insufficiency requiring insulin with resultant ESRD are candidates for SLKT.
- Transplant should be delayed in patients with complicated gallstone disease until resolution and pretransplant cholecystectomy is recommended for ERSD patients in symptomatic cholelithiasis.
- Active hepatitis is a contraindication for elective surgeries due to increased operative risk. RT should be delayed in patients with HEV-related acute viral hepatitis to prevent the development of chronic hepatitis and cirrhosis associated with HEV infection.
- It is recommended to screen the recipients for hepatitis B and hepatitis C infection with tests such as HBsAg, anti-HBs, anti-HBc, and anti-HCV. The HDV serology and HCV RNA should be done in high-prevalence areas.
- Initial assessment of fibrosis should be done by non-invasive methods such as liver stiffness measurement by TE and serum biomarkers [aspartate aminotransferase (AST)-to-platelet ratio index (APRI), fibrosis-4 (FIB-4) index]. Also, TE should only be performed after a dialysis session.
- More extensive studies are needed before recommending RT from HCV RNA-positive donors to HCV RNA-negative patients.
- Presence of NAFLD is not a contraindication for RT and patients on waiting list should be counseled for lifestyle interventions.
- Patients with ESRD and compensated cirrhosis with clinically significant portal hypertension (hepatic venous wedge pressure >10 mm Hg) or decompensated cirrhosis or associated acute or acute-on-chronic liver failure are candidates for SLKT.

Orcid

Suprabhat Giri https://orcid.org/0000-0002-9626-5243
Jijo Varghese https://orcid.org/0000-0002-9794-9188
Shivaraj Afzalpurkar https://orcid.org/0000-0002-4810-5165

References

1. Abecassis M, Bartlett ST, Collins AJ, et al. Kidney transplantation as primary therapy for end-stage renal disease: a National Kidney Foundation/Kidney Disease Outcomes Quality Initiative (NKF/KDOQITM) Conference. Clin J Am Soc Nephrol 2008;3(2):471–480. DOI: 10.2215/CJN.05021107.
2. Global Observatory on Donation and Transplantation. Available at: http://www.transplant-observatory.org. Accessed on: 2 August 2022.
3. Miskulin D, Bragg–Gresham J, Gillespie BW, et al. Key comorbid conditions that are predictive of survival among hemodialysis patients. Clin J Am Soc Nephrol 2009;4(11):1818–1826. DOI: 10.2215/CJN.00640109.
4. Bouthot BA. Gastrointestinal evaluation in renal transplant candidates. Sem Col Rect Surg 2002;13(3):197–201. DOI: 10.1053/scrs.2002.127393.
5. Rinonce HT, Yano Y, Utsumi T, et al. Hepatitis B and C virus infection among hemodialysis patients in Yogyakarta, Indonesia: Prevalence and molecular evidence for nosocomial transmission. J Med Virol 2013;85(8):1348–1361. DOI: 10.1002/jmv.23581.
6. Garthwaite E, Reddy V, Douthwaite S, et al. Clinical practice guideline management of blood borne viruses within the haemodialysis unit. BMC Nephrol 2019;20:388. DOI: 10.1186/s12882-019-1529-1.
7. Adane T, Getawa S. The prevalence and associated factors of hepatitis B and C virus in hemodialysis patients in Africa: A systematic review and meta-analysis. PLoS One 2021;16(6):e0251570. DOI: 10.1371/journal.pone.0251570.
8. El-Sherif A, Elbahrawy A, Aboelfotoh A, et al. High false-negative rate of anti-HCV among Egyptian patients on regular hemodialysis. Hemodial Int 2012;16(3):420–427. DOI: 10.1111/j.1542-4758.2011.00662.x.
9. Makvandi M. Update on occult hepatitis B virus infection. World J Gastroenterol 2016;22(39):8720–8734. DOI: 10.3748/wjg.v22.i39.8720.
10. Liang CC, Muo CH, Wang IK, et al. Peptic ulcer disease risk in chronic kidney disease: Ten-year incidence, ulcer location, and ulcerogenic effect of medications. PLoS One 2014;9(2):e87952. DOI: 10.1371/journal.pone.0087952.
11. Shin SP, Bang CS, Lee JJ, et al. Helicobacter pylori infection in patients with chronic kidney disease: A systematic review and meta-analysis. Gut Liver 2019;13(6):628–641. DOI: 10.5009/gnl18517.
12. Sarkio S, Halme L, Kyllönen L, et al. Severe gastrointestinal complications after 1,515 adult kidney transplantations. Transpl Int 2004;17(9):505–510. DOI: 10.1007/s00147-004-0748-x.
13. Telkes G, Peter A, Tulassay Z, et al. High frequency of ulcers, not associated with *Helicobacter pylori*, in the stomach in the first year after kidney transplantation. Nephrol Dial Transplant 2011;26(2):727–732. DOI: 10.1093/ndt/gfq401.
14. Chadban SJ, Ahn C, Axelrod DA, et al. KDIGO clinical practice guideline on the evaluation and management of candidates for kidney transplantation. Transplantation 2020;104(4S.1 Suppl. 1):S11–S103. DOI: 10.1097/TP.0000000000003136.
15. Sotoudehmanesh R, Ali Asgari A, Ansari R, et al. Endoscopic findings in end-stage renal disease. Endoscopy 2003;35(6):502–505. DOI: 10.1055/s-2003-39672.

16. Netto JPH, Pinheiro JPS, Ferrari ML, et al. Upper gastrointestinal alterations in kidney transplant candidates. J Bras Nefrol 2018;40(3):266–272. DOI: 10.1590/2175-8239-JBN-3829.
17. Bibbins–Domingo K, Grossman DC, Curry SJ, et al. Screening for colorectal cancer: US preventive services task force recommendation statement. JAMA 2016;315(23):2564–2575. DOI: 10.1001/jama.2016.5989.
18. Wong G, Hope RL, Howard K, et al. One-time fecal immunochemical screening for advanced colorectal neoplasia in patients with CKD (DETECT study). J Am Soc Nephrol 2019;30(6):1061–1072. DOI: 10.1681/ASN.2018121232.
19. Komaki Y, Komaki F, Micic D, et al. Risk of colorectal cancer in chronic kidney disease: A systematic review and meta-analysis. J Clin Gastroenterol 2018;52(9):796–804. DOI: 10.1097/MCG.0000000000000880.
20. Kobiela J, Dobrzycka M, Danielewicz R, et al. Colonoscopy as part of pre-transplant work-up in successful kidney transplant candidates: Single-center experience and review of literature. Ann Transplant 2018;23:782–788. DOI: 10.12659/AOT.910658.
21. Coccolini F, Catena F, Di Saverio S, et al. Colonic perforation after renal transplantation: Risk factor analysis. Transplant Proc 2009;41(4):1189–1190. DOI: 10.1016/j.transproceed.2009.02.064.
22. Oor JE, Atema JJ, Boermeester MA, et al. A systematic review of complicated diverticulitis in post-transplant patients. J Gastrointest Surg 2014;18(11):2038–2046. DOI: 10.1007/s11605-014-2593-2.
23. Scotti A, Santangelo M, Federico S, et al. Complicated diverticulitis in kidney transplanted patients: analysis of 717 cases. Transplant Proc 2014;46(7):2247–2250. DOI: 10.1016/j.transproceed.2014.07.044.
24. Rencuzogullari A, Ozuner G, Binboga S, et al. Colonic diverticulosis and diverticulitis in renal transplant recipients: Management and long-term outcomes. Am Surg 2017;83(3):303–307. PMID: 28316316.
25. Pourfarziani V, Mousavi–Nayeeni SM, Ghaheri H, et al. The outcome of diverticulosis in kidney recipients with polycystic kidney disease. Transplant Proc 2007;39(4):1054–1056. DOI: 10.1016/j.transproceed.2007.02.007.
26. Corica D, Romano C. Renal involvement in inflammatory bowel diseases. J Crohns Colitis 2016;10(2):226–235. DOI: 10.1093/ecco-jcc/jjv138.
27. Grupper A, Schwartz D, Baruch R, et al. Kidney transplantation in patients with inflammatory bowel diseases (IBD): Analysis of transplantation outcome and IBD activity. Transpl Int 2019;32(7):730–738. DOI: 10.1111/tri.13415.
28. Schnitzler F, Friedrich M, Stallhofer J, et al. Solid organ transplantation in patients with inflammatory bowel diseases (IBD): Analysis of transplantation outcome and IBD activity in a large single center cohort. PLoS One 2015;10(8):e0135807. DOI: 10.1371/journal.pone.0135807.
29. Verdonk RC, Dijkstra G, Haagsma EB, et al. Inflammatory bowel disease after liver transplantation: Risk factors for recurrence and *de novo* disease. Am J Transplant 2006;6(6):1422–1429. DOI: 10.1111/j.1600-6143.2006.01333.x.
30. Laine L, Kaltenbach T, Barkun A, et al. SCENIC guideline development panel. SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease. Gastroenterology 2015;148(3):639–651.e28. DOI: 10.1053/j.gastro.2015.01.031.
31. Chen HJ, Wang JJ, Tsay WI, et al. Epidemiology and outcome of acute pancreatitis in end-stage renal disease dialysis patients: A 10-year national cohort study. Nephrol Dial Transplant 2017;32(10):1731–1736. DOI: 10.1093/ndt/gfw400.
32. Wang IK, Lai SW, Lai HC, et al. Risk of and fatality from acute pancreatitis in long-term hemodialysis and peritoneal dialysis patients. Perit Dial Int 2018;38(1):30–36. DOI: 10.3747/pdi.2016.00313.
33. Kroner PT, Mareth K, Raimondo M, et al. Acute pancreatitis in advanced chronic kidney disease and kidney transplant recipients: Results of a US nationwide analysis. Mayo Clin Proc Innov Qual Outcomes 2019;3(2):160–168. DOI: 10.1016/j.mayocpiqo.2019.03.006.
34. Russell TA, Park S, Agopian VG, et al. Peritransplant pancreatitis: A marker of high mortality and graft failure in liver transplant patients. Liver Transpl 2017;23:925–932. DOI: 10.1002/lt.24760.
35. Knoll G, Cockfield S, Blydt–Hansen T, et al. Canadian Society of Transplantation consensus guidelines on eligibility for kidney transplantation. CMAJ 2005;173(10):1181–1184. DOI: 10.1503/cmaj.051291.
36. Barry K. Chronic pancreatitis: Diagnosis and treatment. Am Fam Physician 2018;97(6):385–393. PMID: 29671537.
37. Jiang AT, BHSc, Rowe N, et al. Simultaneous pancreas–kidney transplantation: The role in the treatment of type 1 diabetes and end-stage renal disease. Can Urol Assoc J 2014;8(3–4):135–138. DOI: 10.5489/cuaj.1597.
38. Lai SW, Liao KF, Lai HC, et al. The prevalence of gallbladder stones is higher among patients with chronic kidney disease in Taiwan. Medicine (Baltimore) 2009;88:46–51. DOI: 10.1097/MD.0b013e318194183f.
39. Kazama JJ, Kazama S, Koda R, et al. The risk of gallbladder stone formation is increased in patients with predialysis chronic kidney disease but not those undergoing chronic hemodialysis therapy. Nephron Clin Pract 2009;111(3):c167–c172. DOI: 10.1159/000199456.
40. Tsai CH, Wu JS, Chang YF, et al. The number of metabolic abnormalities associated with the risk of gallstones in a non-diabetic population. PLoS One 2014;9(3):e90310. DOI: 10.1371/journal.pone.0090310.
41. Melvin WS, Meier DJ, Elkhammas EA, et al. Prophylactic cholecystectomy is not indicated following renal transplantation. Am J Surg 1998;175(4):317–319. DOI: 10.1016/s0002-9610(98)00009-9.
42. Jackson T, Treleaven D, Arlen D, et al. Management of asymptomatic cholelithiasis for patients awaiting renal transplantation. Surg Endosc 2005;19(4):510–513. DOI: 10.1007/s00464-004-8817-x.
43. Pham PT, Pham SV, Pham PA, et al. Medical evaluation of the adult kidney transplant candidate. In: Current Issues and Future Direction in Kidney Transplantation, Thomas Rath, editor. IntechOpen 2013. DOI: 10.5772/54736.
44. Friedman LS. The risk of surgery in patients with liver disease. Hepatology 1999;29(6):1617–1623. DOI: 10.1002/hep.510290639.
45. Harville DD, Summerskill WH. Surgery in acute hepatitis. Causes and effects. JAMA 1963;184:257–261. DOI: 10.1001/jama.1963.03700170049006.
46. Murali AR, Kotwal V, Chawla S. Chronic hepatitis E: A brief review. World J Hepatol 2015;7(19):2194–2201. DOI: 10.4254/wjh.v7.i19.2194.
47. Kraef C, Schlein C, Hiller J, et al. Course of HEV viremia and anti-HEV IgM/IgG response in asymptomatic blood donors. J Clin Virol 2018;105:26–30. DOI: 10.1016/j.jcv.2018.05.013.
48. Powell–Jackson P, Greenway B, Williams R. Adverse effects of exploratory laparotomy in patients with unsuspected liver disease. Br J Surg 1982;69(8):449–451. DOI: 10.1002/bjs.1800690805.
49. Jones JM, Kracalik I, Levi ME, et al. Assessing solid organ donors and monitoring transplant recipients for human immunodeficiency virus, hepatitis B virus, and hepatitis C virus infection: U.S. Public Health Service Guideline, 2020. MMWR Recomm Rep 2020;69(4):1–16. DOI: 10.15585/mmwr.rr6904a1.
50. Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology 2018;67(4):1560–1599. DOI: 10.1002/hep.29800.
51. European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol 2017;67(2):370–398. DOI: 10.1016/j.jhep.2017.03.021.
52. Rostaing L, Modesto A, Baron E, et al. Acute renal failure in kidney transplant patients treated with interferon alpha 2b for chronic hepatitis C. Nephron 1996;74(3):512–516. DOI: 10.1159/000189444.
53. European Association for the Study of the Liver, Clinical Practice Guidelines Panel, EASL Governing Board representative. EASL recommendations on treatment of hepatitis C: Final update of the series. J Hepatol 2020;73(5):1170–1218. DOI: 10.1016/j.jhep.2020.08.018.

54. Taneja S, Borkakoty A, Rathi S, et al. Assessment of liver fibrosis by transient elastography should be done after hemodialysis in end stage renal disease patients with liver disease. Dig Dis Sci 2017;62(11):3186–3192. DOI: 10.1007/s10620-017-4777-6.
55. Arrayhani M, Sqalli T, Tazi N, et al. Non invasive assessment of liver fibrosis in chronic hemodialysis patients with viral hepatitis C. Pan Afr Med J 2015;22:273. DOI: 10.11604/pamj.2015.22.273.2311.
56. Goldberg DS, Abt PL, Blumberg EA, et al. Trial of transplantation of HCV-infected kidneys into uninfected recipients. N Engl J Med 2017;376(24):2394–2395. DOI: 10.1056/NEJMc1705221.
57. Jandovitz N, Nair V, Grodstein E, et al. Hepatitis C-positive donor to negative recipient kidney transplantation: A real-world experience. Transpl Infect Dis 2021;23(3):e13540. DOI: 10.1111/tid.13540.
58. Li M, Chen J, Fang Z, et al. Sofosbuvir-based regimen is safe and effective for hepatitis C infected patients with stage 4–5 chronic kidney disease: A systematic review and meta-analysis. Virol J 2019;16(1):34. DOI: 10.1186/s12985-019-1140-x.
59. Jabbari SM, Maajani K, Merat S, et al. An updated systematic review and meta-analysis on efficacy of Sofosbuvir in treating hepatitis C-infected patients with advanced chronic kidney disease. PLoS One 2021;16(2):e0246594. DOI: 10.1371/journal.pone.0246594.
60. Le MH, Yeo YH, Li X, et al. 2019 Global NAFLD prevalence: A systematic review and meta-analysis. Clin Gastroenterol Hepatol 2021:20(12):2809–2817.e28. DOI: 10.1016/j.cgh.2021.12.002.
61. Chinnadurai R, Ritchie J, Green D, et al. Non-alcoholic fatty liver disease and clinical outcomes in chronic kidney disease. Nephrol Dial Transpl 2019;34(3):449–457. DOI: 10.1093/ndt/gfx381.
62. Mikolasevic I, Racki S, Bubic I, et al. Chronic kidney disease and nonalcoholic fatty liver disease proven by transient elastography. Kidney Blood Press Res 2013;37(4–5):305–310. DOI: 10.1159/000350158.
63. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology 2018;67(1):328–357. DOI: 10.1002/hep.29367.
64. Paramesh AS, Davis JY, Mallikarjun C, et al. Kidney transplantation alone in ESRD patients with hepatitis C cirrhosis. Transplantation 2012;94(3):250–254. DOI: 10.1097/TP.0b013e318255f890.
65. Parsikia A, Campos S, Khanmoradi K, et al. Equal 3-year outcomes for kidney transplantation alone in HCV-positive patients with cirrhosis. Int Surg 2015;100(1):142–154. DOI: 10.9738/INTSURG-D-13-00231.1.
66. Patel A, Harrison S, Rudraraju M. Graft outcomes in kidney transplantation alone with concomitant cirrhosis. Jour Gastro Hepat Res 2016;5(2):2001–2004. DOI: 10.17554/j.issn.2224-3992.2016.05.471.
67. Cullaro G, Sharma P, Jo J, et al. Temporal trends and evolving outcomes after simultaneous liver–kidney transplantation: Results from the US SLKT Consortium. Liver Transpl 2021;27(11):1613–1622. DOI: 10.1002/lt.26232.