Non-alcoholic fatty liver disease and liver transplantation: Outcomes and advances

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Abstract
Non-alcoholic fatty liver disease (NAFLD) is one of the most prevalent causes of chronic liver disease worldwide. In the last decade it has become the third most common indication for liver transplantation in the United States. Increasing prevalence of NAFLD in the general population also poses a risk to organ donation, as allograft steatosis can be associated with non-function of the graft. Post-transplant survival is comparable between NAFLD and non-NAFLD causes of liver disease, although long term outcomes beyond 10 year are lacking. NAFLD can recur in the allograft frequently although thus far post transplant survival has not been impacted. De novo NAFLD can also occur in the allograft of patients transplanted for non-NAFLD liver disease. Predictors for NAFLD post-transplant recurrence include obesity, hyperlipidemia and diabetes as well as steroid dose after liver transplantation. A polymorphism in PNPLA3 that mediates triglyceride hydrolysis and is linked to pre-transplant risk of obesity and NAFLD has also been linked to post transplant NAFLD risk. Although immunosuppression side effects potentiate obesity and the metabolic syndrome, studies of immunosuppression modulation and trials of specific immunosuppression regimens post-transplant are lacking in this patient population. Based on pre-transplant data, sustained weight loss through diet and exercise is the most effective therapy for NAFLD. Other agents occasionally utilized in NAFLD prior to transplantation include vitamin E and insulin-sensitizing agents. Studies of these therapies are lacking in the post-transplant population. A multimodality and multidisciplinary approach to treatment should be utilized in management of post-transplant NAFLD.

Core tip: Non-alcoholic fatty liver disease (NAFLD) is a prevalent indication for liver transplantation. It also poses a risk to organ donation, with decreasing rates of suitable allografts. NAFLD frequently recurs in the allograft or develops de novo. Post-transplant recurrence is related to obesity and immunosuppression associated metabolic derangements. A polymorphism in PNPLA3 also increases recurrence risk. Pre-transplant data favors sustained weight loss through diet and exercise as the most effective therapy for NAFLD. Vitamin E and insulin-sensitizing agents are occasionally used. Trials on immune-suppression regimens in this population are sorely needed. A multimodality approach to treatment should be utilized in management of post-transplant NAFLD.

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EPIDEMIOLOGY OF NON-ALKOHOLIC FATTY LIVER DISEASE AND ASSOCIATED ADVANCED LIVER DISEASE

Non-alcoholic fatty liver disease (NAFLD) is the most prevalent chronic liver disease in the developed world with a prevalence averaging 20% in the ulcerative colitis[1,3]. Its incidence in the developing world is also increasing sharply[8]. Prevalent in adults, it has also become the most common chronic liver disease in children[9]. Mirroring the epidemic of obesity, it is closely related to the metabolic syndrome particularly diabetes and dyslipidemia in association with truncal obesity[10]. Prior to the widespread recognition of NAFLD which was first described as a separate clinic-pathologic entity in 1980[4], many cases of NAFLD were likely classified as cryptogenic liver disease and cryptogenic cirrhosis (CRC). In a study where 39 liver transplant candidates diagnosed with CRC were carefully re-evaluated, 44% had prior biopsy consistent with NAFLD or clinical features of the metabolic syndrome[5]. Although NAFLD has been associated with excess mortality compared to the general population (Hazard ratio 1.34)[5], the natural history of NAFLD is often one of slow progression. In patients with isolated steatosis (fatty liver) the course of liver disease can be frequently benign[7,10]. The progressive form of NAFLD known as Non-alcoholic steatohepatitis (NASH) is associated with hepatocyte damage and consequently can lead to fibrosis as well as cirrhosis and end-stage liver disease[5]. Recently data about the natural history of NAFLD related cirrhosis was reported from four international referral centers. In this study, patients with NAFLD or hepatitis C virus (HCV) associated compensated (Childs A) cirrhosis were enrolled. Over the long term (mean follow up 86 mo for NAFLD and 75 mo for HCV), the incidence of liver related complications and hepatocellular carcinoma (HCC) was lower for NAFLD than for HCV. The probability of remaining free of cancer related destruction was 81.5% in the NAFLD cohort and 76.5% in the HCV cohort at 120 mo of follow up with a higher incidence of complications in HCV when adjusted for age, sex, body mass index and diabetes (P = 0.03). The incidence of HCC over follow up was 2.4% in the NAFLD cohort and 6.8% in HCV. Despite these differences, the incidence of cardiovascular disease and overall mortality were similar between NAFLD and HCV patients (82% survival at 120 mo in both cohorts)[5].

LIVER TRANSPLANTATION INCIDENCE FOR NAFLD

The incidence of liver transplantation related to NAFLD has exploded in the last decade[8]. Although some of the reported increase in incidence of NAFLD related liver transplantation is due to increased recognition of patients previously classified as CRC, the increased incidence of NAFLD related liver transplantation is real. Even if the majority of CRC related liver transplants in prior eras were due to unrecognized NAFLD, the magnitude of increase in transplants for NAFLD far outweighs any classification bias[5]. In an audit of United States national transplant data (SRTR), liver transplants attributed to NAFLD related liver disease increased from 1.2% in 2001 to 9.7% by 2009 and this is now the third most common indication for liver transplantation in the United States[13]. In this study patients with NAFLD receiving a liver transplant were older, more likely to be females, had higher body mass index (BMI) and were less likely to have HCC at transplant compared to all other recipients.

There have been concerns about bias in transplant evaluation and listing of patients with NAFLD related cirrhosis. NAFLD patients are on average older at presentation and have higher rates of obesity and metabolic syndrome raising concerns about worse outcomes of transplant in these patients including increased risks of cardiovascular disease and chronic kidney disease. In a study from a single liver transplant center, the cohort of NAFLD patients with MELD less than 15 at listing were found to progress more slowly compared to patients with HCV and were more likely to die on the waiting list or be taken off the transplant list due to becoming “too sick”[14]. However for patients who were listed with MELD scores over 15 there were no differences in rate of progression of end-stage liver disease, listing rate and receipt of liver transplantation. In another study, patients with NAFLD were equally likely than non-NAFLD patients to undergo liver transplant evaluation, listing and transplantation. In this single center study, NASH patients were older, had similar rates of HCC but increased rates of other prior cancers by history. In addition diabetes and complications of metabolic syndrome were more prevalent in NASH patients. NAFLD patients also had higher creatinine levels at transplant listing than non-NAFLD patients[15]. Routine audits of multicenter and national data will have to be done to see if NAFLD patients are indeed at a disadvantage for evaluation and listing due to these concerns.

OUTCOMES AFTER LIVER TRANSPLANTATION FOR NAFLD

Survival after liver transplantation for NAFLD
Outcomes after liver transplantation in patients with NAFLD have been reported in both large national database audits as well as from single center studies. These studies have been restricted to adult recipients (> 18 years) of liver transplants. In the pediatric population although NAFLD is common, it is a rare indication for liver transplantation[16] (Table 1).

The national databases (UNOS and SRTR) studies have looked at outcomes at 1 year and beyond after liver transplantation (Table 1). Overall 1-year, 3-year and 5-year survival has been comparable between NAFLD and non-NAFLD recipients[13]. In more specific sub-analyses of the same databases post-transplant survival for NAFLD...
| Table 1  Liver transplantation for non-alcoholic fatty liver disease |
|----------------------------------|
| **Ref.** | **Patient** | **Population** | **Follow up** | **Graft survival** | **Patient survival** | **NAFLD recurrence in graft** | **Predictors of NAFLD recurrence** | **Predictors of survival** |
| National registry data | | | | | | | | |
| Charlton et al[13] | 35781 adults, adult liver transplant recipient | SIRTR (US national data) of liver transplant recipients from 2001 to 2009 Included NASH plus 50% of CRC and NASH plus CRC with BMI > 30 kg/m² | 3 yr post-transplant survival reported | NASH 3-yr survival 76% (similar to other indications) | NASH 1-yr survival 84% and 3-yr 78% CRC 1-yr survival 86% and 3-yr 79% Other Diagnoses 1-yr survival 87% and 3-yr 78% (P = 0.67) | Not reported | Not reported | Not reported |
| Singal et al[18] | 5467 adult liver transplant recipient | UNOS adult liver transplant recipients from 1994 to 2009 | 10-yr survival reported | 1-yr, 3-yr, 5-yr and 10-yr survival NASH 86%, 82%, 80% and 80% NAFLD post-transplant survival similar to cholestatic liver disease, HBV and better than ALD, CRC, HCV and HCC | Not reported | Not reported | For all recipients, age of recipient, male recipient black race, ventilator support pre-transplant and MELD score as well as donor risk index associated with worse patient survival |
| Afzali et al[17] | 5378 adult liver transplant recipients | UNOS adult liver transplant recipients from 1997 to 2010 | 5-yr survival reported | Not reported | 1-yr, 3-yr and 5-yr survival NASH: 88%, 82% and 77% Overall adjusted HR for NASH post-transplant mortality compared to other etiologies was 0.75 (95%CI: 0.66-0.85) Adjusted survival was better for NASH than for ALD, HCV, and HCC. NASH survival was worse than cholestatic liver disease, AIH, HBV | Not reported | Not reported | Not specified- although state survival adjusted for several donor, recipient characteristics (individual Hazards ratios not reported) |
| Single center studies | | | | | | | | |
| Tanaka et al[57] | 7 patient with NAFLD (425 total LDLT recipients) | Patients with NAFLD that underwent Live donor liver transplant at a single center in Japan between 1996 and 2013 | Median follow up 5.3 yr | 100% at last follow up | 1/7 (14%) had recurrent NASH | Not reported | Not reported | Not reported |
| El Atrache et al[27] | 83 recipients, NAFLD and CRC[46] | Liver transplant recipients at a single US center between 1996 and 2008 | Mean follow up 46 mo | 12/83 underwent re-transplantation | 12 recipients died. Overall survival not reported | NAFLD recurrence in 20/83 recipients Predictors of recurrence were metabolic syndrome, hypertension and insulin use as well as hyperlipidemia after transplant | Five year survival worse for those with metabolic syndrome, hypertension and insulin use as well as hyperlipidemia after transplant | No difference in survival between those with NASH recurrence and those without |
| Authors          | Number of Recipients | Description of NAFLD | Follow-up Time | Survival Details | Disease Recurrence | Survival Compared to Non-NAFLD | Associated Factors |
|------------------|----------------------|----------------------|----------------|------------------|--------------------|-------------------------------|--------------------|
| Dureja et al.    | 88                   | Liver transplant recipients at a single US center between 1995 and 2007 | Mean follow up 82 mo | Not reported | 5-yr patient survival similar between those with NAFLD recurrence and those without NAFLD recurrence (P = 0.78) | NAFLD Disease Recurrence in 34/88 (39%) | Pre and post-transplant survival was worse in NAFLD patients with higher triglyceride levels and prednisone dose was post-transplant cardiac disease (HR 3.2, 95%CI: 1.3-7.7) |
| Agopian et al.   | 144 (total 1294 transplants) | Liver transplant recipients at a single US center between 1995 and 2011 | Mean follow up 2.3 yr | Graft survival similar between NAFLD and non NAFLD (90 d survival 86% for NASH) and lower only than PBC/PSC (90 d graft survival of 94%) | Patient survival similar between NASH and non-NASH. 90 d survival 90% for NASH. 5-yr patient survival for NASH (70%) similar to ALD, HBV, CC and PSC/PSC but better than HCV | NASH recurrence in 23 (16%) | Not reported |
| Kennedy et al.   | 129                   | Liver transplant recipients at a single US center between 1999 and 2009 | 5-yr survival reported | Graft survival not reported | 1-yr, 3-yr, and 5-yr survival NASH: 90%, 88% and 85% Non-NASH: 92%, 86% and 80% (P = NS) | Not reported |
| Barritt et al.   | 21                   | Liver transplant recipients at a single US center between 2004 and 2007 | 3-yr survival reported | 30-d graft survival worse in NAFLD (81%) vs non-NAFLD (85%), P = 0.02 | 30-d patient survival worse in NAFLD (81%) vs non-NAFLD (97%), (81% vs 97%, P = 0.001) | Not reported |
| Yalamanchili et al. | 40                | Liver transplant recipients at a single German center between 2007 and 2011 | 1-yr survival reported | Not reported | 30-d mortality for NAFLD patients was 25% and 1-yr mortality was 35% | Not reported | Patients with BMI > 35 kg/m² had worse graft survival (1-yr graft failure 55%) than those with lower BMI |
was better as compared to HCV, alcohol, CRC, and HCC related liver disease. When compared to primary biliary cirrhosis (PBC) one study showed similar survival and an other study showed worse survival for NAFLD. In single center studies, post transplantation outcomes were also similar between NAFLD and non-NAFLD patients. Survival at 1, 3, 5 and 10-year was reported as similar in the studies, although some have demonstrated higher early mortality (30 d) after transplantation in NAFLD than in non-NAFLD patients. Kennedy et al reported a twofold higher mortality for NAFLD patients at 4 mo after transplantation than for non-NAFLD patients (8.5% mortality vs 4.2% for others). The commonest causes of mortality in NAFLD patients were infectious and cardiac disease. Another study confirmed higher 30-d mortality and 1-year mortality in NAFLD patients, although by 3 years survival were comparable in NAFLD and non-NAFLD patients. In this study infections accounted for the majority of deaths. Factors associated with decreased survival in the cohort of NAFLD patients have included age of recipient post-transplant, diabetes, obesity and post-transplant metabolic syndrome, and post-transplant cardiovascular disease. Close monitoring and critical analysis of early and late outcomes after liver transplantation for NAFLD is thus necessary to further refine criteria and improve outcomes for liver transplantation in NAFLD.
NAFLD recurrence after liver transplantation

Recurrent NAFLD is common\cite{22,26,27}. The recurrence rate depends to some extent on the method chosen for detection, (i.e., evaluation of abnormal liver enzymes, liver biopsy, imaging techniques). Use of liver enzymes alone is fairly insensitive as a significant proportion of patients with NAFLD recurrence have normal liver enzymes.

Metabolic syndrome including obesity, diabetes, hyperlipidemia and hypertension are all increased in prevalence after transplantation linked largely to immunosuppression use, particularly steroid use and calcineurin inhibitors. Other factors include post-transplant weight gain due to reduced mobility, at least in the early period and these factors all contribute to recurrence of NAFLD in the allograft\cite{38}.

In some studies the risk of allograft steatosis was increased by the presence of the rs738409 single nucleotide polymorphism (SNP) in the PNPLA-3 gene in the recipient\cite{29} as well as post-transplant obesity and diabetes\cite{28}. This polymorphism (rs738409:1448M) in PNPLA-3 has been associated with reduced triglyceride hydrolysis in the adipocyte and increases the risk of developing NAFLD and NASH in the general population\cite{34}. The presence of this SNP in PNPLA-3 in the donor has not been associated with development of allograft steatosis, obesity and diabetes. Thus the role of peripherally mediated triglyceride hydrolysis (in extrahepatic adipose tissue) seems to account for risk of NAFLD recurrence rather than liver related triglyceride hydrolysis, at least in post-transplant NAFLD\cite{26,28}.

In a study that systematically re-examined post-transplant biopsies and imaging, recurrent NAFLD was seen in 39\% (34/88), with NASH in 25 and isolated steatosis in 9 of these 34 patients within 5 years post-transplant. Severe recurrence (NAS score \( \geq 5 \)) or advanced fibrosis was seen in 6 of the 34 with recurrent NAFLD\cite{26}. NAFLD recurrence was correlated with pre and post-transplant BMI and post-transplant triglyceride levels and prednisone dose at 6 mo post-transplant. In this study post-transplant survival was similar between those with NAFLD recurrence vs those without.

Other studies have showed similar rates of NAFLD recurrence with one study showing recurrent NAFLD in 20 of 83 (24\%). The metabolic syndrome and insulin use were linked to recurrent NAFLD in this study\cite{27}.

Yalamanchili et al\cite{23} reported long term outcomes with post-transplant NAFLD recurrence. In this study, recurrent steatosis was reported in 45\% of NAFLD transplant recipients and NASH was less common occurring in 4\%. Advanced allograft fibrosis or cirrhosis was reported in 5\% by 5 years and 10\% by 10 years post transplantation and was more common in those with recurrent NAS (31\%) vs those with steatosis alone (6\%) or no steatosis (3\%). In this study survival was similar at 1, 5 and 10 years in those with NAFLD and those with other liver diseases at transplant. Death from cardiovascular disease was more common than due to recurrent liver disease attesting to the strong link between the factors that predict development of NAFLD (Metabolic syndrome) and cardiac disease\cite{26}.

Other studies have also not shown reduced survival with NAFLD recurrence so far\cite{37}, although studies have been limited by a dearth of long term follow up (10 years or more) for large number of patients.

In patients transplanted for CRC, NAFLD has been reported to occur post transplantation and may be due to recurrent disease in a significant number of these patients who likely had undiagnosed NAFLD prior to transplantation. In one study steatosis alone developed in 25\% and NASH in 16\% of patients transplanted for CRC\cite{31}. Predictors for post-transplant NAFLD in this population include pre or post-transplant diabetes, hypertriglyceridemia and higher BMI. In another study of thirty CRC patients who had the NAFLD phenotype (metabolic syndrome) prior to liver transplantation, recurrent steatosis was seen in 100\% by 5 years post-transplant. Steroid dose was correlated with development of post-transplant NAFLD\cite{34}.

Very few if any data exist on risk of HCC in NAFLD and outcomes for these patients after transplantation. In a single center study, 17\% of NASH cirrhosis patients referred for liver transplantation had HCC (6 noted incidentally on explant) which was higher than the number of patients with PBC/PSC with HCC and similar to ALD and HCV with HCC. Survival in NASH and HCC patients was good after liver transplant with 88\% survival at a mean follow-up of 2.5 years\cite{33}.

DEVELOPMENT OF DE NOVO NAFLD AFTER LIVER TRANSPLANTATION

De novo NAFLD has been reported after liver transplantation in recipients who did not carry the diagnosis of NAFLD prior to liver transplantation. The incidence of de novo NAFLD after liver transplantation has ranged from 18\% to 33\%\cite{34,36} with the progressive form NASH reported in 9\% in one report\cite{34}. In a study with liver biopsies done as protocol at 1, 5 and 10 years post-transplantation, as well as for clinical indications, the incidence of de novo NAFLD (defined as steatosis greater than 5\% after more than 6 mo post liver transplantation) was 31\% in 599 recipients with an average follow up of 40 mo. Histological NASH was present in only 3.8\%, but perisinusoidal fibrosis was present in 29\% and advanced fibrosis/cirrhosis in 2.25\%\cite{37}. The increased incidence of perisinusoidal fibrosis without steatohepatitis has not been well described in non-transplant populations and may represent a modified presentation in immunosuppressed individuals who may not present with brisk inflammatory response. In addition 51\% of the recipients with de novo NAFLD had normal liver enzymes in this study attesting to the importance of liver biopsies and possibly imaging in accurately diagnosing NAFLD.

Factors associated with de novo NAFLD include post-transplant obesity, post-transplant diabetes, hyperlipidemia and hypertension\cite{37}. In addition tacrolimus was also associated with recurrent NAFLD and this drug has
been well described as having an increased risk for developing diabetes. In addition to this, a pretransplant diagnosis of alcoholic cirrhosis was associated with an increased risk of de novo NAFLD. In this study, patients with recurrent alcoholism and recurrent hepatitis C or hepatitis B were excluded from the analysis as these conditions can lead to steatosis. The increased risk of de novo NAFLD in patients with prior ALD may reflect an underlying predisposition to NAFLD that could not be diagnosed prior to transplantation due to the concomitant alcoholic steatohepatitis. Donor allograft steatosis was also more prevalent in the group that developed de novo NAFLD (30%) as compared to the group that did not develop NAFLD (12.6%). This study did not quantify the degree of hepatic steatosis and nor were any genetic polymorphisms tested for in the donor. Other studies have suggested that donor polymorphisms that regulate cytokine release, inflammation and microsomal triglyceride transfer may be important in risk of developing NAFLD. Protective factors against de novo NAFLD may include use of Angiotensin converting enzyme inhibitors, although this approach has not been tested in a trial.

The consequences of de novo NAFLD are not well known. In the study mentioned above complete regression occurred in 13% (all with grade 1 steatosis initially), reduction of steatosis was seen in 35%, stability in 22%, and exacerbation in 30%. Higher prevalence of obesity was present in those with progression of histological liver disease.

In patients with hepatitis C the risk of developing de novo NAFLD is higher and can be linked to recurrence of hepatitis C. Development of de novo NAFLD in the allograft can reduce the response rate to current antiviral therapy for hepatitis C and thus impact graft and patient outcomes.

**MANAGEMENT OF NAFLD AFTER LIVER TRANSPLANTATION**

There have been no published trials of pharmacotherapy specifically for post-transplant NAFLD. Analysis of the predictors of post-transplant NAFLD recurrence and data from non-transplant therapeutic studies on NAFLD suggest that sustained weight loss through a combination of dietary changes and exercise are most successful in reversing the histological findings of NAFLD, and improving biochemical and metabolic parameters including liver enzymes, insulin resistance, lipid levels and blood pressure in this condition.

Studies on pharmacotherapeutic agents in non-transplant patients suggest a role for vitamin E in selected individuals. In non-diabetics a large randomized controlled trial over 48 wk improved the histological features and liver enzymes in NAFLD. Recent concerns about risk of prostate cancer and risk of cardiac disease in susceptible individuals, as well as lack of long term data on sustained efficacy and safety may limit its usefulness in the post-transplant population.

The use of PPAR-gamma agonists (e.g., Pioglitazone) improves insulin resistance and has shown some promise in reversing NAFLD in non-transplant patients. In a large randomized controlled trial however it was not superior to placebo and inferior to vitamin E in reversing NAFLD. This class of agents is also associated with weight gain and this also limits its utility in treatment of NAFLD.

Pharmacologic treatment of clinically overt diabetes, dyslipidemia and hypertension should be carried out as per best practice guidelines for managing these conditions and in multidisciplinary teams involving the transplant team, primary care providers, diabetes specialists and preventive cardiologists.

Given that to a large extent immune-suppression exacerbates or promotes the development of the metabolic syndrome, immunosuppression modulation should be considered in patients with recurrent NAFLD or at risk of developing recurrent or de novo NAFLD. In particular minimization or avoidance of steroids, minimization of calcineurin inhibitor dose and levels and avoiding sirolimus in patients with hyperlipidemia is important in the management of NAFLD, obesity and metabolic syndrome post liver transplantation.

Bariatric surgery for obesity and morbid obesity has shown promising results in non-transplant patients and can reverse some of the metabolic consequences related to obesity such as diabetes. Limited series have reported successful bariatric surgery specifically in patients with NAFLD, and in case reports in patients with NAFLD with compensated cirrhosis.

For NAFLD patients undergoing liver transplantation there are limited case reports of the utility of bariatric surgery after recurrence of NAFLD post transplantation. There are also risks of exacerbation of NASH after bariatric surgery due to excessive weight loss as well as risks of impaired drug absorption and bacterial overgrowth that can impact post-transplant outcomes. At this point more evidence is needed before advocating bariatric surgery in transplant recipients.

**DONORS WITH NAFLD**

An adverse consequence of the epidemic of obesity and fatty liver in the population is the impact on suitable donors for liver transplantation. There is an increased risk of primary non-function of the allograft with fatty donors. This data suggest that greater than 30% steatosis in the donor organ increases the risk of primary non-function. As NAFLD in the populations increases, the pool of potentially suitable organs for liver transplantation may diminish as a consequence.

In a Korean paper that evaluated steatosis in potential donors over a year, NAFLD (> 5% steatosis) was present in 51% and greater than 30% steatosis was present in 10.4% with NASH in 2.2%. The prevalence of steatosis was higher in donor over the age of 30, and those donor...
with obesity and elevated triglyceride levels. In this study ultrasonography and CT both had limitations in diagnosis of NAFLD (> 30% steatosis in donors) with sensitivity of 92% for ultrasound but positive predictive value of only 34.5% and for CT a sensitivity of 64% and PPV of 45%. More recently the use of MRI Quantification methods for steatosis have been developed and validated independently against liver biopsy showing excellent correlation with histological steatosis grading. 5,25,34. Although donor biopsies should still be considered before excluding donors as unsuitable due to steatosis, utilization of MRI, particularly for liver donors may in the near future supplant the need for liver biopsies. 55.

Although patient and graft survival can be diminished due to use of steatotic grafts, this is possibly not a risk factor for diminished graft survival if it exists in isolation. 56. Selection bias also confounds the picture as grafts that are not utilized due to steatosis may have different outcomes than steatotic grafts that are transplanted. 57.

FUTURE DIRECTIONS

With increasing numbers of transplants in patients with NAFLD, current data support a careful audit of both short and long term post-transplant outcomes. Rigorous studies on immune-suppression regimens designed to decrease the incidence of metabolic complications for this population are needed. In addition post-transplant therapy for NAFLD including diet and exercise regimens, pharmacologic agents and bariatric surgery all warrant further study. With increasing numbers of donors with fatty livers, outcomes with these grafts should be tracked in prospective databases that include both donor and recipient variables.

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