Published in final edited form as:

Clin Transplant. 2017 September ; 31(9): . doi:10.1111/ctr.13032.

Resolution of donor non-alcoholic fatty liver disease following liver transplantation

Andrew D. Posner¹, Samuel T. Sultan^{2,iD}, Norann A. Zaghloul¹, William S. Twaddell¹, David A. Bruno², Steven I. Hanish², William R. Hutson¹, Laci Hebert², Rolf N. Barth², and John C. LaMattina^{2,iD}

¹University of Maryland School of Medicine, Baltimore, MD, USA

²Division of Transplantation, University of Maryland School of Medicine, Baltimore, MD, USA

Abstract

Introduction—Transplant surgeons conventionally select against livers displaying high degrees (>30%) of macrosteatosis (MaS), out of concern for primary non-function or severe graft dysfunction. As such, there is relatively limited experience with such livers, and the natural history remains incompletely characterized. We present our experience of transplanted livers with high degrees of MaS and microsteatosis (MiS), with a focus on the histopathologic and clinical outcomes.

Methods—Twenty-nine cases were identified with liver biopsies available from both the donor and the corresponding liver transplant recipient. Donor liver biopsies displayed either MaS or MiS 15%, while all recipients received postoperative liver biopsies for cause.

Results—The mean donor MaS and MiS were 15.6% (range 0%–60%) and 41.3% (7.5%–97.5%), respectively. MaS decreased significantly from donor ($M=15.6\%$) to recipient postoperative biopsies ($M=0.86\%$), $P<.001$. Similarly, MiS decreased significantly from donor biopsies ($M=41.3\%$) to recipient postoperative biopsies ($M=1.8\%$), $P<.001$. At a median of 68 days postoperatively (range 4–384), full resolution of MaS and MiS was observed in 27 of 29 recipients.

Conclusions—High degrees of MaS and MiS in donor livers resolve in recipients following liver transplantation. Further insight into the mechanisms responsible for treating fatty liver diseases could translate into therapeutic targets.

Keywords

biopsy; donors and donation; extended criteria; liver allograft function/dysfunction

Correspondence. John C. LaMattina, Division of Transplantation, University of Maryland School of Medicine, Baltimore, MD, USA. JLaMattina@som.umaryland.edu.

Samuel T. Sultan <http://orcid.org/0000-0002-5575-9693>

John C. LaMattina <http://orcid.org/0000-0001-7016-0382>

CONFLICT OF INTEREST

None.

1 | INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a wide spectrum of non-alcohol-related, fatty liver disorders, which range from bland steatosis (NAFL, non-alcoholic fatty liver) to severe non-alcoholic steatohepatitis (NASH).¹ NAFL is characterized by hepatocyte steatosis and is considered a benign condition. In contrast, NASH is characterized by hepatocyte damage and inflammation, and has the potential to progress to advanced fibrosis and cirrhosis.² NAFLD is associated with obesity, diabetes, dyslipidemia, and metabolic syndrome. Almost all patients with NAFLD are insulin-resistant, and it is believed that NAFLD is the hepatic manifestation of insulin resistance.^{3,4}

The obesity epidemic and the increasing concomitant prevalence of both metabolic syndrome and insulin resistance have resulted in increasing rates of NAFLD worldwide.⁵ Studies indicate that the prevalence of NAFLD in the adult US population is 30%–40%, and it is estimated that 15%–20% of those NAFLD patients have NASH.⁶ As a result, millions of patients are at risk of their liver disease progressing to cirrhosis and potentially requiring liver transplantation (LT).^{7,8} In fact, NAFLD is expected to become the leading indication for LT within the next 10–20 years.¹

The increased prevalence of NAFLD in the population also affects the quality and quantity of donor livers available for LT.⁹ Currently, more than 15 000 patients are waiting for LT, but only 6000 liver transplants are performed annually across the United States. As a result, about 1500 patients a year die waiting for a liver, making the mortality on the liver transplant waiting list between 5% and 10% per year.¹⁰ In response to the shortage of donor livers, transplant centers have increasingly attempted to maximize the supply of livers, by utilizing extended criteria and high-risk donors.¹¹

Donor hepatic steatosis is one of the many factors believed to be related to increased risk. Nonetheless, in response to the organ shortage, transplant centers have begun to examine the actual degree of risk that steatotic grafts impart on the recipient.^{12,13} Historically, graft steatosis has been associated with primary graft non-function, dysfunction, delayed function, and poor outcomes.^{14,15} However, recent studies have demonstrated that livers with moderate steatosis can be transplanted safely without affecting long-term patient outcome or organ survival, despite impaired primary postoperative liver function.^{11,16} In fact, Wong et al. recently reported their experience of excellent outcomes with the use of severely steatotic grafts.¹⁷ Further research evaluating the composition of steatosis has indicated that although MaS and MiS are commonly found together, MaS has a stronger correlation with negative outcomes.¹⁸ Studies have demonstrated that the relative composition of steatosis and the percent MaS, as opposed to percent MiS or total steatosis (MaS+MiS), characterizes the largest risk of poor outcomes following LT.¹⁹ Here, we report our finding that donor steatosis resolves following transplantation and discuss some of the clinical considerations in using such livers for transplant.

2 | MATERIALS AND METHODS

2.1 | Study population

All adult liver transplant recipients performed from 2007 to 2014 at the University of Maryland Medical Center (UMMC) were identified after obtaining IRB approval (IRB: HP-00063670). Recipients whose donors underwent preoperative liver biopsy showing 15% or greater MaS or MiS were included in this study. A retrospective analysis of the UMMC prospectively collected database was performed.

2.2 | Donor data

One hundred and seven (15.8%) of all donors underwent liver biopsy based on the discretion of the procuring surgeon (visual appearance, donor BMI, and donor past medical history), as it is not our practice to routinely biopsy all donor livers. Of those 107 donor biopsies, 47 (43.9%) had 15% or greater MaS or MiS. Donor variables included degrees of MaS and MiS, demographics (age, gender, ethnicity), BMI, and cause of death. Thirty-six donor organ procurements occurred in the local donor-specific area while 11 occurred regionally.

2.3 | Recipient data

Of the 47 recipients of steatotic grafts, 29 (62%) underwent postoperative biopsies for cause. Overall graft and patient survival data, including 30-day survival and 1-year survival, were collected for all 47 recipients. The sample size was too small to include and statistically analyze 3-year survival. The 29 patients who underwent postoperative biopsies constituted our primary study group. Data collected on that group included biopsy report data (degree MaS and MiS, date, indication for biopsy, biopsy results), demographics, BMI, indication for transplant, past medical history, MELD, and operative characteristics (cold ischemia time [CIT], days to discharge post-LT, intra-operative blood loss, and intra-operative units of packed red blood cells [RBC] received). Postoperative outcomes and liver allograft function were evaluated through alanine aminotransferase (ALT), aspartate aminotransferase (AST), post-transplant complications, and survival.

Biopsy reports with qualitative descriptions were assigned numerical steatosis percentage values as follows: 0%, 15%, and 45%, for statements of no steatosis, mild steatosis, and moderate steatosis, respectively. These numbers were chosen to reflect an averaging effect of the categorization defined by Verran et al.,²⁰ with 0%–30% being considered mild and 30%–60% being moderate. If a patient had more than one postoperative biopsy, all biopsy information was recorded, and the date from the earliest biopsy which demonstrated resolution of MaS and MiS was included in this study. Recipients received tacrolimus, mycophenolate mofetil or mycophenolic acid, and steroids in the perioperative period, and were typically maintained without steroids.

2.4 | Histological examination

Donor biopsy samples used in this study were generally both core needle and wedge liver biopsy samples obtained at the time of procurement. Postoperative recipient biopsies were either percutaneous or transjugular. Steatosis was categorized into MaS, characterized by one large fat droplet displacing the nucleus to the cytoplasmic border, and MiS,

characterized by multiple small vacuoles surrounding a central nucleus.¹⁹ Percent MaS or MiS indicates the percent of MaS or MiS involvement in the specimen. The donor biopsies were reported by the local pathologist, whereas all postoperative biopsies were reported by a single pathologist at our institution.

2.5 | Statistical analysis

All missing data for each variable were noted. Continuous data are presented as median (range) or mean±standard deviation (SD). Paired-samples *t* tests were conducted to compare degrees of MaS, MiS, and total steatosis (MaS+MiS) in donor and recipient biopsies. A Pearson product-moment correlation coefficient was used to assess relationship between continuous variables, and a two-tailed test was used to determine significance. The continuous variables were donor and recipient age, BMI, MaS, MiS; recipient MELD; days to resolution of steatosis post-LT, peak-ALT, peak-AST, CIT, days to discharge post-LT, blood loss, and packed RBCs received. A *P* value <.05 was considered statistically significant in all tests. SPSS version 19 software was used for statistical analysis.

3 | RESULTS

3.1 | Donor and recipient demographics

Demographics of the 29 donors are presented in Table 1. There was a statistically significant inverse relationship between donor age and donor MiS in our sample (*P*=.003). There was no significant relationship between donor BMI and either donor MaS or MiS. Demographics of the 29 recipients who received postoperative biopsies are presented in Table 2. There were statistically significant inverse relationships between recipient age and MELD (*P*=.049), and also between recipient age and peak AST following LT (*P*=.045).

3.2 | Biopsy data

The breakdown of steatosis on preoperative biopsy is shown in Table 3. The mean donor MaS and MiS were 15.6% (range 0%–60%) and 41.3% (7.5%–97.5%), respectively. MaS decreased significantly from donor (*M*=15.6%) to recipient postoperative biopsies (*M*=0.86%), *P*<.001. Similarly, MiS decreased significantly from donor biopsies (*M*=41.3%) to recipient postoperative biopsies (*M*=1.8%), *P*<.001. Figure 1 demonstrates a representative patient showing the resolution of steatosis.

Biopsies were performed for cause, typically for elevated liver function tests, to rule out rejection and/or hepatitis C recurrence. The median number of days postoperatively that recipient biopsies were obtained demonstrating resolution of MaS and MiS was 68 days (range 4–384). Full resolution of MaS and MiS was observed in all but two recipients, who had biopsies only on postoperative day 3 and day 14, respectively. These two recipients did not undergo subsequent biopsy.

3.3 | Survival data

The 30-day survival and 1-year survival of all 47 patients receiving liver transplants with greater than 15% MaS or MiS were stratified by those who did or did not undergo postoperative biopsies, as shown in Table 4.

3.4 | Operative variables and complications

Operative characteristics are included in Table 5. There was a statistically significant relationship between donor MaS and postoperative peaks in AST ($P=.045$) but not with ALT ($P>.05$). There were also statistically significant relationships between CIT and postoperative peaks in AST ($P=.04$) and ALT ($P<.001$), and units of packed RBCs received ($P=.01$). There was also a statistically significant relationship between recipient MELD and the days to discharge postoperatively ($P=.03$).

3.5 | Postoperative interventions and complications

Postoperative interventions and complications for the primary study group of 29 patients are included in Table 6, delineating the 12 patients who underwent ERCP and the 13 patients who required reoperation. Thirty-day survival for those who underwent ERCP was 100%, but 1-year survival for those with biliary complications (stricture or leak) was 66.7%. In total, 18 patients (62.1%) underwent ERCP and/or reoperation, and there was significant overlap between those two groups. Seven patients (24.1%) underwent both ERCP and reoperation, five patients (17.2%) underwent ERCP only, and six patients (20.7%) underwent reoperation only.

4 | DISCUSSION

Transplant surgeons generally select against livers displaying high degrees ($>30\%$) of MaS, out of concerns for primary non-function or severe graft dysfunction. As such, there is relatively limited experience with transplanting such livers, and the natural history remains incompletely characterized. This study presents statistically significant evidence that high degrees of MaS, MiS, and total steatosis in donor livers resolve in recipients following LT. Full resolution of MaS and MiS was observed in 93% of recipients. MaS and MiS failed to resolve in two recipients, who had biopsies only on postoperative day 3 and day 14, respectively. In patient #1, MiS decreased from 97.5% to 45% in 3 days postoperatively, while MaS was 0% in both the donor and recipient biopsies. In patient #2, MaS decreased from 60% to 25% in 14 days postoperatively. Subsequent biopsies from these two recipients were not available, thus preventing the confirmation of the complete resolution of steatosis; however, there is clear evidence on the available biopsies that percent steatosis in both patients was significantly decreased. It is reasonable to project that steatosis would have been shown to fully resolve on subsequent biopsies from those two recipients, had later biopsies been available. Histological changes in our study demonstrating the resolution of steatosis were similar to those presented by Marsman et al., Li et al., and McCormack et al.^{15,21,22} In addition to the initial resolution, we also observed that there was no evidence of recurrent steatosis in the longer term biopsies, which may relate to the fact that none of the recipients in the study group originally had NASH.

The recipient biopsies were obtained at a median of 68 days postoperative (range 4–384 days). Biopsies were taken for cause, and not at standardized intervals, which accounts for the wide range and precludes the ability to accurately comment on the length of time for steatosis to resolve, although it appears to generally occur within the first 3 months following transplantation.

In our study, there was no statistical relationship between any recipient, donor, or operative characteristics with either the absolute resolution of steatosis or the time to resolution of steatosis. Notably, donor steatosis resolves in patients irrespective of their MELD at transplant and their indication for transplant. While none of the recipients in the primary study group were formally diagnosed with NASH cirrhosis, this was not by design, as we do not intentionally avoid using steatotic grafts for recipients with NASH; moreover, given the high prevalence of hypertension (62.1%) and diabetes (37.9%), it is possible that some of the patients had at least a component of NASH, although it was not the diagnosed primary cause of their liver disease. This theory may lead to the conclusion that intra-operative and/or postoperative factors are responsible for the subsequent resolution of steatosis. These factors are currently unknown but may be iatrogenic, immunologic, metabolic, or genetic, among other possible explanations. The near universal resolution of fat is a very encouraging finding and supports the notion that steatosis is highly reversible with robust mechanisms for therapeutic targets. Investigations into the mechanisms responsible for this phenomenon have been initiated.²³ In an in vitro model, for example, Nativ et al.²⁴ have demonstrated the effect of hypoxia/reoxygenation on lipid droplets in hepatocytes, as a representation of the ischemia/ reperfusion process in transplantation. A potential treatment to reverse obesity-related disease, such as NAFLD, may also be applicable to medical fields outside of liver transplantation and could have a substantial effect on public health.

We were surprised to find that there was no significant relationship between donor BMI and either donor MaS or MiS. This suggests that potential donors with even markedly elevated BMI should not be prematurely disregarded on the presumption of severe hepatic steatosis. Conversely, procuring surgeons must be prepared to encounter donors with regular BMI yet substantial steatosis.

One-year patient survival (92.9%) for all recipients of fatty livers in our study was superior to the nationwide average reported by Scientific Registry of Transplant Recipients (88.8%), or our center's outcomes for all LT.¹⁰ Such favorable outcomes may be due, at least in part, to the fact that the average MELD for the study recipients (22.9) was lower than our overall average, which reflects an intentional selection practice, as we generally try to avoid using such grafts for the highest MELD recipients. When our survival data are stratified into the groups with and without postoperative biopsies, 1-year survival was 88.5% and 100%, respectively. Patients received postoperative biopsies for cause; thus, it is reasonable that the individuals who were biopsied were experiencing complications and/or graft injury, and therefore had inferior survival.

One notable factor that may relate to our center's favorable patient survival when compared to nationwide data is the length of CIT. In the study group, the median CIT was 4.53 hours, compared to 7.3 hours reported by Spitzer et al. when analyzing 21 777 transplants.²⁵ Further Scientific Registry of Transplant Recipients analysis supports this advantage: At our center, 94.4% of local liver transplants have CIT between 0 and 5 hours while nationally, only 54.3% are between 0 and 5 hours.¹⁰ Our group has taken a number of steps to minimize CIT, including starting the recipient operation prior to the donor liver arrival at our center. Furthermore, this study demonstrates a direct relationship between CIT and ALT and AST, which are proven indicators of graft function. Our data may support the growing field of

literature, which indicates that, when CIT is minimized, grafts with mild steatosis and moderate steatosis perhaps with other contraindications being absent can be safely utilized in transplantation.^{16,22} With the current shortage of liver donors, utilization of these extended criteria grafts appears justified.

An important observation was the elevated number of patients who experienced postoperative complications. In our study, 41.4% of the study group underwent ERCP, which is higher than that reported in the literature. McElroy et al. reported the estimated mean incidence of biliary strictures as 12.5%, while Kochhar et al. reported a range of 5%–15%.^{26,27} Our reported value of 27.6% exceeded both of these estimates. The pathogenesis of anastomotic strictures at the site of biliary anastomosis can be attributed to surgical technique, local tissue ischemia, and fibrosis related to healing.²⁸ Steatosis is known to decrease the liver's ability to cope with ischemia/reperfusion injury, which may suggest that steatosis can predispose grafts to biliary stricture.²⁹ Baccarani et al.³⁰ reported that correlation directly, identifying graft MaS as an independent risk factor for biliary complications. Our study supports that notion and further suggests that donor graft steatosis is correlated with postoperative biliary stricture. In addition, in our study, 1-year survival for patients with biliary stricture was 75%, which was inferior to both the national average for LTs and the average within our study. As the utilization of extended criteria donor continues, steatosis must be recognized as a risk factor for biliary strictures, which in turn may be associated with inferior patient outcomes.

Three patients who underwent ERCP were found to have a normal radiographic appearance of the biliary system. The established pathophysiology regarding bilirubin and the utilization of steatotic grafts may play a role in this outcome. Following ischemia, bilirubin levels tend to lag behind AST/ALT, being slower to both increase and decrease. Steatosis accentuates this lag in bilirubin, which may unnecessarily prompt ERCP. Awareness of this lag in bilirubin may help to possibly avoid unnecessary procedures.

In total, 44.8% of patients required reoperation within 90 days. Ninety-day reoperation rate following LT has been reported in the literature as 29.3%.³¹ In our study, it is very important to differentiate between the indications for reoperation. The single most common indication for reoperation in our study was planned delayed closure for size mismatch, which permitted edema to decrease and for the liver mass to shrink before closing the abdominal wall. Many of the steatotic livers are procured from higher BMI donors, and are overall larger in size, and although we generally consider the size matching of the donor and recipient, we prioritize additional variables in the selection process. Only one patient required planned closure for pack removal following coagulopathy, demonstrating that organ dysfunction was only a minor cause of reoperation. Importantly, 1-year survival was 100% for patients who underwent planned delayed closure, showing the safety and efficacy of this approach. As the utilization of large steatotic grafts increases, it is important to be prepared for a substantial size discrepancy and recognize that planned delayed closure is a favorable surgical solution with excellent patient outcomes.

We acknowledge several limitations to this study, most importantly that it is retrospective and with a relatively small sample size. The donor biopsies were reported by a local

pathologist, and we no longer have the slides to be able to have them reviewed by a single experienced pathologist. Postoperative biopsies were performed only for cause, and so the timing and performance of such biopsies are inconsistent. Additionally, longer follow-up may be valuable. Nonetheless, we believe that our initial experience has been insightful, and we plan to build on this experience, as we work collaboratively toward a more optimal utilization of steatotic grafts.

5 | CONCLUSION

High degrees of MaS, MiS, and total steatosis in donor livers resolve in recipients following LT. Future investigations are necessary to identify the mechanisms responsible for the marked resolution of hepatic steatosis following transplantation. Insight into the mechanisms responsible for the resolution of donor NAFLD following LT could lead to therapeutic targets for treating NAFLD. In addition, our study demonstrates that carefully selected and managed steatotic donor grafts can be safely used in LT, particularly when CIT is minimized; however, an elevated incidence of postoperative complications should be expected, primarily biliary strictures and planned delayed closure for size mismatch. And ultimately, in the setting of a major organ shortage, the degree of acceptable steatosis should be reconsidered in donor selection.

Acknowledgments

Funding information Mid-Atlantic Nutrition Obesity Research Center, Grant/Award Number: P30DK072488

References

1. Zezos P, Renner E. Liver transplantation and non-alcoholic fatty liver disease. *World J Gastroenterol.* 2014; 20:15532–15538. [PubMed: 25400437]
2. Angulo P. Nonalcoholic fatty liver disease and liver transplantation. *Liver Transpl.* 2006; 12:523–534. [PubMed: 16555318]
3. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. *Hepatology.* 2012; 55:2005–2023. [PubMed: 22488764]
4. Lazo M, Clark JM. The epidemiology of nonalcoholic fatty liver disease: a global perspective. *Semin Liver Dis.* 2008; 28:339–350. [PubMed: 18956290]
5. Angulo P. Nonalcoholic fatty liver disease. *N Engl J Med.* 2002; 346:1221–1231. [PubMed: 11961152]
6. Vernon G, Baranova A, Younossi ZM. Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. *Aliment Pharmacol Ther.* 2011; 34:274–285. [PubMed: 21623852]
7. McCullough AJ. Pathophysiology of nonalcoholic steatohepatitis. *J Clin Gastroenterol.* 2006; 40(Suppl 1):S17–S29. [PubMed: 16540762]
8. Williams CD, Stengel J, Asike MI, et al. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: a prospective study. *Gastroenterology.* 2011; 140:124–131. [PubMed: 20858492]
9. McCormack L, Dutkowski P, El-Badry AM, Clavien PA. Liver transplantation using fatty livers: always feasible? *J Hepatol.* 2011; 54:1055–1062. [PubMed: 21145846]
10. [Accessed March 4, 2016] Program-Specific Report: University of Maryland Medical System. Scientific Registry of Transplant Recipients. www.srtr.org

11. Angele MK, Rentsch M, Hartl WH, et al. Effect of graft steatosis on liver function and organ survival after liver transplantation. *Am J Surg*. 2008; 195:214–220. [PubMed: 18154767]
12. Gastaca M. Extended criteria donors in liver transplantation: adapting donor quality and recipient. *Transplant Proc*. 2009; 41:975–979. [PubMed: 19376402]
13. Westerkamp AC, de Boer MT, van den Berg AP, Gouw AS, Porte RJ. Similar outcome after transplantation of moderate macrovesicular steatotic and nonsteatotic livers when the cold ischemia time is kept very short. *Transpl Int*. 2015; 28:319–329. [PubMed: 25545740]
14. Imber CJ, St Peter SD, Handa A, et al. Hepatic steatosis and its relationship to transplantation. *Liver Transpl*. 2002; 8:415–423. [PubMed: 12004340]
15. Marsman WA, Wiesner RH, Rodriguez L, et al. Use of fatty donor liver is associated with diminished early patient and graft survival. *Transplantation*. 1996; 62:1246–1251. [PubMed: 8932265]
16. Goldaracena N, Quiñonez E, Méndez P, et al. Extremely marginal liver grafts from deceased donors have outcome similar to ideal grafts. *Transplant Proc*. 2012; 44:2219–2222. [PubMed: 22974958]
17. Wong TC, Fung JY, Chok KS, et al. Excellent outcomes of liver transplantation using severely steatotic grafts from brain-dead donors. *Liver Transpl*. 2016; 22:226–236. [PubMed: 26359934]
18. Han S, Ha SY, Park CK, et al. Microsteatosis may not interact with macrosteatosis in living donor liver transplantation. *J Hepatol*. 2015; 62:556–562. [PubMed: 25450710]
19. Crowley H, Lewis WD, Gordon F, Jenkins R, Khettry U. Steatosis in donor and transplant liver biopsies. *Hum Pathol*. 2000; 31:1209–1213. [PubMed: 11070113]
20. Verran D, Kusyk T, Painter D, et al. Clinical experience gained from the use of 120 steatotic donor livers for orthotopic liver transplantation. *Liver Transpl*. 2003; 9:500–505. [PubMed: 12740794]
21. Li J, Liu B, Yan LN, et al. Reversal of graft steatosis after liver transplantation: prospective study. *Transplant Proc*. 2009; 41:3560–3563. [PubMed: 19917344]
22. McCormack L, Petrowsky H, Jochum W, Mullhaupt B, Weber M, Clavien PA. Use of severely steatotic grafts in liver transplantation: a matched case-control study. *Ann Surg*. 2007; 246:940–948. [PubMed: 18043095]
23. Nativ NI, Maguire TJ, Yarmush G, et al. Liver defatting: an alternative approach to enable steatotic liver transplantation. *Am J Transplant*. 2012; 12:3176–3183. [PubMed: 23057797]
24. Nativ NI, Yarmush G, So A, et al. Elevated sensitivity of macrosteatotic hepatocytes to hypoxia/reoxygenation stress is reversed by a novel defatting protocol. *Liver Transpl*. 2014; 20:1000–1011. [PubMed: 24802973]
25. Spitzer AL, Lao OB, Dick AA, et al. The biopsied donor liver: incorporating macrosteatosis into high-risk donor assessment. *Liver Transpl*. 2010; 16:874–884. [PubMed: 20583086]
26. McElroy LM, Daud A, Davis AE, et al. A meta-analysis of complications following deceased donor liver transplant. *Am J Surg*. 2014; 208:605–618. [PubMed: 25118164]
27. Kochhar G, Parungao JM, Hanouneh IA, Parsi M. Biliary complications following liver transplantation. *World J Gastroenterol*. 2013; 19:2841–2846. [PubMed: 23704818]
28. Verdonk RC, Buis CI, Porte RJ, et al. Anastomotic biliary strictures after liver transplantation: causes and consequences. *Liver Transpl*. 2006; 12:726–735. [PubMed: 16628689]
29. Han S, Choi GS, Kim JM, et al. Macrosteatotic and nonmacrosteatotic grafts respond differently to intermittent hepatic inflow occlusion: comparison of recipient survival. *Liver Transpl*. 2015; 21:644–651. [PubMed: 25690881]
30. Baccarani U, Isola M, Adani GL, et al. Steatosis of the hepatic graft as a risk factor for post-transplant biliary complications. *Clin Transplant*. 2010; 24:631–635. [PubMed: 19878512]
31. Ertel AE, Wima K, Chang AL, et al. Risk of reoperation within 90 days of liver transplantation: a necessary evil? *J Am Coll Surg*. 2016; 222:419–428. [PubMed: 26905185]

FIGURE 1.

Photographs of sequential biopsies from a representative patient. Biopsies are from the donor (A), showing a mix of moderate micro-and macrosteatosis; post-transplant on postoperative day 2 (B), and postoperative day 5 (C), demonstrating the progressively resolving steatosis

TABLE 1

Donor demographics

Donor factors	Value
Age: Mean±SD (Range)	49±13.9 (21–72)
Gender: Female, n (%)	16 (55.2)
Ethnicity: n (%)	
White	22 (75.9)
African American	5 (17.2)
Not reported	2 (6.9)
BMI: Mean±SD (Range)	33.12±6.88 (21.5–50.31)
Cause of Death: n (%)	
Anoxia	14 (48.3)
Cerebrovascular accident/stroke	9 (31.0)
Head trauma	5 (17.2)
Not reported	1 (3.4)

TABLE 2

Recipient demographics

Recipient factors	Value
Age: Mean±SD (Range)	55.6±10.8 (20–71)
Gender: male, n (%)	21 (72.4)
Ethnicity: n (%)	
White	16 (55.2)
African American	10 (34.5)
Asian	1 (3.4)
Hispanic	1 (3.4)
East Indian	1 (3.4)
BMI (kg/m ²) at listing: Mean±SD (Range)	25.91±5.31 (18.0–38.0)
Indication for transplantation: n (%)	
Hepatitis C	15 (51.7)
Alcoholic cirrhosis	10 (34.5)
Primary sclerosing cholangitis	1 (3.4)
Primary biliary cirrhosis	1 (3.4)
Cryptogenic cirrhosis	1 (3.4)
Fulminant hepatic failure	1 (3.4)
Underlying HCC	10 (34.5)
Past medical history: n (%)	
Hypertension	18 (62.1)
Diabetes mellitus	11 (37.9)
Hyperlipidemia	3 (10.3)
Coronary artery disease	2 (6.9)
MELD	
Mean±SD (Range)	22.9±9.7 (9–40)
6–14	7 (24.1%)
15–24	11 (38.0%)
25–34	5 (17.2%)
35–39	2 (6.9%)
40+	4 (13.8%)

TABLE 3

Breakdown of steatosis in preoperative biopsies

Steatosis category	Number of donors
Macrosteatosis	
0–9%	11
10–19%	7
20–29%	4
30–39%	4
40–49%	1
50–59%	1
60+	1
Microsteatosis	
0–9%	5
10–19%	4
20–29%	2
30–39%	6
40–49%	1
50–59%	5
60+	6

TABLE 4

Patient and graft survival

Survival	Number	Applicable	Percent survival (%)
Recipients of fatty livers (All)			
30 days	47	47	100
1 y	39	42	92.9
Recipients of fatty livers with postoperative biopsies for cause			
30 days	29	29	100
1 y	23	26	88.5
Recipients of fatty livers without postoperative biopsies			
30 days	18	18	100
1 y	16	16	100

TABLE 5

Perioperative variables

Perioperative variables	Mean±SD (Range)
Peak AST	1776.6±1491.4 (217–6973)
Peak ALT	854.9±745.6 (121–3981)
Cold ischemia time (h)	4.64±1.44 (1.78–8.38)
Days to discharge post-transplant	22.36±16.84 (6–82)
Blood loss in CC	4889.77±5878 (0–22000)
Packed RBC received (units)	11±6.97 (0–26)

TABLE 6

Postoperative interventions and complications

	Number of patients experiencing complication	Percent of patients experiencing complication (%)	30-day Survival (%)	1-y survival (%)
ERCP	12	41.4	100	75
Biliary stricture	8	27.6	100	75
Biliary leak	1	3.4	100	0
Normal ERCP	3	10.3	100	100
Reoperation	13	44.8	100	92.3
Planned delayed closure for size mismatch	5	17.2	100	100
Planned delayed closure for pack removal for coagulopathy	1	3.4	100	100
Re-exploration for bleeding	4	13.8	100	100
Hepatic artery thrombosis	1	3.4	100	0
Drainage of loculated ascites	1	3.4	100	100
Wound dehiscence	1	3.4	100	100