Published in final edited form as:

Dig Dis Sci. 2013 May ; 58(5): 1403–1409. doi:10.1007/s10620-012-2521-9.

Hepatic Preservation Injury: Severity of Hepatitis C Recurrence and Survival after Liver Transplantation

Anthony J. Michaels, M.D.[‡], Renumathy Dhanasekaran, M.D.^{*}, David P. Foley, M.D.[#], Ahmad Alkhasawneh, M.D.[^], Lisa Dixon, M.D.[^], Consuelo Soldevila-Pico, M.D.^{*}, Giuseppe Morelli, M.D.^{*}, Roniel Cabrera, M.D., M.S.^{*}, Virginia C. Clark, M.D., M.S.^{*}, and Roberto J. Firpi, M.D., M.S.^{*}

Anthony J. Michaels: Anthony.Michaels@osumc.edu; Renumathy Dhanasekaran: Renumathyd@gmail.com; David P. Foley: Foley@surgery.wisc.edu; Ahmad Alkhasawneh: ahm0001846@ufl.edu; Lisa Dixon: Dixolr@pathology.ufl.edu; Consuelo Soldevila-Pico: Consuelo.Soldevila@medicine.ufl.edu; Giuseppe Morelli: Giuseppe.Morelli@medicine.ufl.edu; Roniel Cabrera: Roniel.Cabrera@medicine.ufl.edu; Virginia C. Clark: Virginia.Clark@medicine.ufl.edu; Roberto J. Firpi: Roberto.Firpi@medicine.ufl.edu

^{*}Department of Medicine, Division of Gastroenterology, Hepatology and Nutrition Section of Hepatobiliary Diseases and Liver Transplantation, University of Florida, 1600 SW Archer Rd, Gainesville, FL 32610

[^]Department of Pathology, University of Florida, 1600 SW Archer Rd, Gainesville, FL 32610

[‡]Division of Gastroenterology and Hepatology at The Ohio State University Medical Center 395 W 12th Ave, Suite 200, Columbus Ohio 43210

[#]Department of Surgery, University of Wisconsin School of Medicine and Public Health, H4/766 Clinical Science Center 600 Highland Avenue Madison, WI 53792

Abstract

Background—Preservation injury in the HCV liver transplant population has been reported to correlate with poorer survival outcomes compared to preservation injury in the non-HCV liver transplant population. However, determinants of progression to cirrhosis in HCV infection remain poorly defined in this population.

Aim—This study aimed to determine if presence and severity of preservation injury impact the acceleration of HCV recurrence and survival after liver transplant.

Methods—We retrospectively reviewed liver transplant HCV patients over a 10-year period. Biopsies from POD 7 were assessed for preservation injury and 4 and 12-month biopsies were assessed for fibrosis. Patients with Ishak fibrosis > 0.8 units/year were considered rapid fibrosers.

Results—Our study group consisted of 255 patients. The mean age was 49.3 years old, 180 (70.6%) were male and 221 (86.7%) were Caucasian. The incidence of preservation injury on the 7-day biopsy was 69.0%. A strong correlation between postoperative peak AST within the first week and preservation injury was found. The overall prevalence of rapid fibrosers at 4-months, 1-year and 2-years was 47.4%, 75.2%, and 58.9%, respectively. The prevalence of rapid fibrosers at 4 months, 1 and 2 years between patients with or without preservation injury was not statistically significant (p=0.39, p=0.46, and p=0.53, respectively). No differences were seen between patients with and without PI in terms of patient and graft survival.

Conclusion—In this study, the presence and severity of preservation injury were not associated with development of rapid HCV recurrence or worsening in survival.

Keywords

hepatic ischemia; reperfusion injury; liver transplant; hepatitis C; fibrosis

INTRODUCTION

Hepatitis C (HCV) infection is a global burden with an estimated prevalence of two percent in the United States.[1;2] HCV-related end stage liver disease continues to be the leading cause of hepatocellular carcinoma (HCC) and the most common indication for liver transplantation (LT).[3] A number of risk factors for recurrent HCV viremia post-LT have been described including recipient age and race, pre-transplantation HCV-RNA levels, recipient warm ischemia time (WIT), diabetes, HLA haplotype, immunosuppressive regimens, cytomegalovirus infection, donor gender and age, and rejection.[4–10] Similarly, the occurrence of preservation injury (PI) in the HCV LT population has been reported to correlate with poorer survival outcomes compared to PI in the non-HCV LT population or HCV LT population without PI.[11] However, determinants of progression in this HCV population remain poorly defined. Therefore, the aim of this study was to determine if the presence and severity of PI impact the acceleration of HCV recurrence and survival after LT.

In the transplant setting, cold preservation, ischemia, implantation and reperfusion of the allograft lead to the phenomenon of PI. PI can be suspected with postoperative elevation of hepatic transaminases. However, the diagnosis is confirmed based on histological findings of pyknosis, sinusoidal neutrophilia, microvesicular steatosis and hepatocellular cytoaggregation; and late findings of centrilobular necrosis, hepatocyte swelling and cholestasis.[11–13] After the widespread hepatocellular death associated with PI, hepatocyte proliferation occurs and it has been hypothesized that HCV may be able to incorporate itself into these proliferating cells, which could then lead to more rapid HCV recurrence in the graft.[11;14–16] PI has also been associated with increased patient mortality, delayed graft function, primary graft nonfunction, late graft failure by triggering irreversible intrahepatic bile-duct injury or by promoting rejection graft failure, and post LT biliary complications. [11;17–19] In fact, the number of patients listed waiting for LT has dramatically increased leading to a high incentive to use extended criteria donor organs, which include organs with hepatic steatosis, old donor age, prolonged cold ischemia, or donation after cardiac death. Thus, these grafts are inevitably prone to a higher grade of PI.

PATIENTS and METHODS

Study Design & Study Population

We retrospectively reviewed and collected data on all LT performed at the University of Florida for HCV infection (424) between years 1995 and 2005. Our study group consisted of 255 of these patients where post transplant protocol biopsies (7-day, 4-month, 1-year) were available for analysis. Biopsies from postoperative day (POD) 7 were mostly protocol biopsies. A few liver biopsies (18%) on POD 7 later in our study were performed only for elevations in liver function tests due to a change in policy. The liver biopsies were reviewed by one, blinded hepato-pathologist.

The database also included variables that could potentially impact PI such as donor age, gender and ethnicity, recipient age, gender and ethnicity, ABO group, warm ischemia time and cold ischemia time (CIT), HCV genotype, exposure to interferon (IFN), and the

presence of HCC. Laboratory data included peak liver transaminases, total bilirubin, alkaline phosphatase, γ -glutamyl transpeptidase, and INR in the first postoperative week as well as the total bilirubin on the day prior to transplant. The study was approved by the institutional review board at the University of Florida.

Histology

Postoperative protocol biopsies at 7-days, 4-months, 1 year and annually thereafter were available as well as the final outcome of the subjects until the last clinic visit or death. After LT, we have defined two HCV patient populations; rapid fibrosers (RF) who have an accelerated rate of fibrosis of more than 0.8 units/year, and slow fibrosers (SF) with a rate of fibrosis of less than 0.8 units/year.[20] Patients with greater than 0.8 units/year of fibrosis on their four month, one year, or two year protocol biopsy were considered to be RF, and patients with less than 0.8 units/year of fibrosis on their four month, one year and two year protocol biopsy were considered to be SF. Recurrent HCV disease was scored for inflammation and fibrosis, using the modified Knodell scoring system of Ishak et al.[21] At present, since there is no clearly defined grading system for PI severity, a slightly modified scale from Killackey et al. was used to classify the specimens into four categories: negative, mild, moderate or severe.[22] Injury was considered mild when the biopsy showed rare and scattered inflammatory cells in the lobule and minimal canalicular cholestasis. Moderate injury was considered when hepatocyte injury, consisting of feathery degeneration, necrosis and/or drop out was present, but limited to zone 1 (periportal) area with increasing degrees of cholestasis and inflammation. Finally, injury was considered severe when the hepatocyte damage extended into zones 2 (located between the periportal and centrilobular areas) and 3 (centrilobular).

Immunosuppression

The immunosuppression consisted of cyclosporine in combination with prednisone + Imuran prior to 1997. Tacrolimus became the primary calcineurin inhibitor for immunosuppression after 1997. The immunosuppression was tapered to tacrolimus or cyclosporine monotherapy within four to six months of LT. Sirolimus was used as part of a renal-sparing regimen as necessary when chronic renal insufficiency occurred during prolonged follow-up after transplantation. Combination therapy with IFN and ribavirin was initiated once patients developed significant fibrosis (Ishak fibrosis stage > 2) on liver biopsy. The duration of treatment was 48 weeks for genotype 1 and 24 weeks for genotype 2 and 3, if tolerated.

Statistical Analysis

The data was analyzed to see if there was an association with PI and accelerated HCV recurrence. Statistical analysis also was performed to see if an association of PI existed with any other variables recorded in the database using patients without PI in the study as the comparison group. Chi square test was used to compare categorical variables and student t tests were used to compare continuous variables. Survival time is defined as the time from the time of transplant to the date of death or the date of last follow up. Survival analysis was performed using Kaplan Meier Estimator method. Survival estimates were compared with log rank test in the Kaplan Meier estimator method. SPSS Graduate version 16.0 (SPSS Inc., Chicago, IL) was used for all statistical computations.

RESULTS

Patient Characteristics

A total of 932 adult LT were performed at the University of Florida from 1995–2005. Of the 424 patients that were transplanted for HCV, liver biopsies were available in 255 (60.1%)

patients. The mean age of the study group was 49.3 years, 180 (70.6%) were male and 221 (86.7%) were Caucasian. The mean duration of post transplant follow-up of the patients was 5.3 years. Pre-transplant IFN therapy was administered to 98 (38.4%) patients and 132 (51.8%) patients received post-transplant IFN therapy for HCV recurrence.

Preservation Injury

The incidence of PI as seen on the POD 7 liver biopsy was (n = 176) 69.0%. Among patients with PI, 48.3% had mild injury, 44.9% had moderate injury, and 6.8% had severe injury. Table 1 compares donor and recipient demographic characteristics and transplant related data between patients with and without PI. Recipient and donor age, race, gender, or ABO group did not influence the occurrence of PI. Table 1 also compares liver function tests among patients with and without PI. The first postoperative week peak AST and ALT levels were found to be significantly greater in those with PI compared to patients without PI. When comparing all patients, patients that had 7-day liver biopsy with those who did not, they were very similar in most of the parameter except for CIT and donor gender. These characteristics were also compared between patients with different grades of PI severity as shown in table 2.

Correlation between peak AST levels one-week post LT and presence and severity of PI as diagnosed by one week biopsy was assessed. The Shackleton et al. classification was used to categorize AST values.[23] Overall, 75.4% of patients with AST<600IU; 81.9% of patients with AST 600-2000IU and 97.1% of patients with AST>2000IU showed presence of PI on biopsy (p=0.008). Severity of PI was also found to correlate with peak AST levels (p<0.001). Thirty six percent of patients with AST<600IU; 47.7% of patients with AST 600-2000IU and 79.4% of patients with AST>2000IU demonstrated moderate-severe PI on biopsy.

Fibrosis

The association between occurrence of PI and prevalence of fibrosis progression was analyzed. The number of patients with available protocol biopsy data at 4 months, 1 year and 2 years was 76.9% (n=196), 82.3% (n=210), and 72.5% (n=185), respectively. Figure 1 shows the comparison of prevalence of RF amongst patients with PI at 4 months, 1 year and 2 years. The prevalence of RF was also compared between patients with different severities of PI and at 4 months, it was 55.1% with mild PI and 48.4% with moderate to severe PI (P=0.277); at 1 year, it was 74.6% among patients with mild PI and 78.2 % among patients with moderate to severe PI (p=0.377); and at 2 years, it was 54.0% among patients with mild PI and 60.9 % among patients with moderate to severe PI (p=0.269).

Hepatitis Activity Index

The overall prevalence of advanced Hepatitis Activity Index (HAI) >4 at one year was 25.4%. Among patients with PI the prevalence of advanced HAI at one year biopsy was 29.5% and it was 15.6% among patients without PI (p=0.081). The prevalence of advanced HAI at one year was compared between patients with different grades of PI, and it was 32.7% among patients with mild PI and 26.7% among patients with moderate to severe PI (p=0.286).

Survival

The median survival among patients with PI was 10.07 years and it could not be reported in patients without PI as more than 50% of the patients were alive at the end of the study period (Figure 2a). However, on comparison of the survival curves, no difference was found between patients with and without PI (p=0.893). The severity of the PI also did not influence

patient survival at one, three and five years (Figure 2b). Five-year survival rates in patients with mild, moderate and severe PI were 82%, 83% and 92%, respectively ($p=0.909$). Post transplant survival rates were compared between RF and SF (Figure 2c). Overall 7.1% of the cohort underwent re- transplantation for various indications, the major ones being- hepatic artery thrombosis, recurrent hepatitis C and primary non-function of the graft. We analyzed the impact of PI on allograft survival and did not find any difference in graft survival between patients with and without PI (0.897). (Figure 2d)

DISCUSSION

In our study, the incidence of PI on a day seven biopsy post-LT was found to be 69%. Also, the presence of PI and the severity of PI were not associated with the development of rapid fibrosis in the HCV LT population up to two years after LT. Presence of PI did not affect patient or graft survival up to five years when compared to patients without PI. The severity of PI also did not influence patient survival up to five years after LT. Although the five-year survival rates between RF and SF were not statistically significant, there was a trend towards improved survival with the SF. When compared to patients without PI, patients with PI had a statistically significant higher peak AST, ALT, and INR laboratory values during the first week post LT. There was also a statistically significant difference in GGT and CIT between patients with PI and without PI, and interestingly, patients with PI were found to have shorter CIT and lower GGT levels.

Our results also show a higher percentage of PI after LT compared to other reported studies. [12] However, our results are similar to the study by Killackey et al where a correlation could not be found between PI and the frequency and timing of histologic HCV recurrence. Their study also showed that the severity of PI did not impact patient survival.[22] However, protocol liver biopsies were not performed in this study. This is in contrast to the analysis performed by Watt et al.[11] In their analysis, patients with HCV and any degree of PI were at an increased risk of death, and those with moderate to severe PI were at the highest risk. It was also suggested in their analysis that recurrent HCV disease appeared to be more rapidly progressive in patients with early PI on liver biopsy. Similar to the Killackey et al study, protocol liver biopsies were not performed and therefore earlier recurrence of HCV in the setting of early PI could not be confirmed. Other variables such as donor age, moderate to severe macrovesicular steatosis, CIT, prolonged stay in the intensive care unit, peak hepatic transaminases post LT, and high inotropic drug use have also been shown to be associated with PI.[11;22;24] In a previous study from our institution, WIT>60 minutes and older donor age were found to be associated with rapid fibrosis.[20] These two factors were not found to be different between patients with and without PI hence eliminating any possible interference from these variables. However, as similarly shown by other studies, CIT does not always correlate with the severity of PI.[22] CIT has also been shown to not affect the severity of HCV post LT.[25] Though we cannot explain why the CIT was longer in patients without PI, this factor probably did not influence the outcome.

Even though we did have a large sample size, our study was mainly limited by its retrospective nature. Another limitation is the selection bias due to the lack of POD 7 liver protocol biopsies in every patient that was transplanted in our center. Only a small percentage of the patients (0.02%) lost their graft prior to day 7 so we do not think that a statistical significant number of severe PIs were excluded from the study. Another subset of patients (18%) underwent 7-day biopsy for abnormal LFTs and not as per protocol. However, in our study the histopathologic findings correlated very well with the biochemical findings so we think that only a small number of livers with PI were potentially excluded. Finally, another possible limitation is the long term nature of the study. When we

compared the incidence of PI before and after 2002, when pegylated interferon was introduced, we did not find a significant difference.

In conclusion, this large analysis of post LT HCV patients showed that presence and severity of PI, defined by using POD 7 day liver biopsies, were not associated with the development of rapid HCV recurrence. PI also did not impact five-year patient or graft survival. Recurrence of HCV continues to remain a significant dilemma in the LT population particularly given the associated accelerated course and treatment difficulties. Further studies are needed in attempt to identify variables and risk factors in patients who develop rapid HCV recurrence after LT, since this could impact the initiation of antiviral therapy and subsequent patient and graft survival.

REFERENCES

1. Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Ann Intern Med.* 2006; 144:705–714. [PubMed: 16702586]
2. Wasley A, Alter MJ. Epidemiology of hepatitis C: geographic differences and temporal trends. *Semin Liver Dis.* 2000; 20:1–16. [PubMed: 10895428]
3. Verna EC, Brown RS Jr. Hepatitis C and liver transplantation: enhancing outcomes and should patients be retransplanted. *Clin Liver Dis.* 2008; 12 637-63x.
4. Charlton M, Seaberg E, Wiesner R, Everhart J, Zetterman R, Lake J, Detre KM, Hoofnagle J. Predictors of patient and graft survival following liver transplantation for hepatitis C. *Hepatology.* 1991; 28:823–830. [PubMed: 9731579]
5. Gallegos-Orozco JF, Yosephy A, Noble B, Aqel BA, Byrne TJ, Carey EJ, Douglas DD, Mulligan D, Moss A, de PG, Williams JW, Rakela J, Vargas HE. Natural history of post-liver transplantation hepatitis C: A review of factors that may influence its course. *Liver Transpl.* 2009; 15:1872–1881. [PubMed: 19938138]
6. Ghobrial RM, Steadman R, Gornbein J, Lassman C, Holt CD, Chen P, Farmer DG, Yersiz H, Danino N, Collisson E, Baquarizo A, Han SS, Saab S, Goldstein LI, Donovan JA, Esrason K, Busuttil RW. A 10-year experience of liver transplantation for hepatitis C: analysis of factors determining outcome in over 500 patients. *Ann Surg.* 2001; 234:384–393. [PubMed: 11524591]
7. Manez R, Mateo R, Tabasco J, Kusne S, Starzl TE, Duquesnoy RJ. The influence of HLA donor-recipient compatibility on the recurrence of HBV and HCV hepatitis after liver transplantation. *Transplantation.* 1995; 59:640–642. [PubMed: 7878772]
8. Manousou P, Samonakis D, Cholongitas E, Patch D, O'Beirne J, Dhillon AP, Rolles K, McCormick A, Hayes P, Burroughs AK. Outcome of recurrent hepatitis C virus after liver transplantation in a randomized trial of tacrolimus monotherapy versus triple therapy. *Liver Transpl.* 2009; 15:1783–1791. [PubMed: 19938143]
9. Rosen HR, Chou S, Corless CL, Gretch DR, Flora KD, Boudousquie A, Orloff SL, Rabkin JM, Benner KG. Cytomegalovirus viremia: risk factor for allograft cirrhosis after liver transplantation for hepatitis C. *Transplantation.* 1997; 64:721–726. [PubMed: 9311709]
10. Velidedeoglu E, Mange KC, Frank A, Abt P, Desai NM, Markmann JW, Reddy R, Markmann JF. Factors differentially correlated with the outcome of liver transplantation in hcv+ and HCV-recipients. *Transplantation.* 2004; 77:1834–1842. [PubMed: 15223900]
11. Watt KD, Lyden ER, Gulizia JM, McCashland TM. Recurrent hepatitis C posttransplant: early preservation injury may predict poor outcome. *Liver Transpl.* 2006; 12:134–139. [PubMed: 16382465]
12. Lee YM, O'Brien CB, Yamashiki N, Behro M, Wepler D, Tzakis AG, Schiff ER. Preservation injury patterns in liver transplantation associated with poor prognosis. *Transplant Proc.* 2003; 35:2964–2966. [PubMed: 14697950]
13. Tillery W, Demetris J, Watkins D, Goldstein R, Poplawski S, Husberg B, Klintmalm G. Pathologic recognition of preservation injury in hepatic allografts with six months follow-up. *Transplant Proc.* 1989; 21:1330–1331. [PubMed: 2652439]

14. Baron PW, Sindram D, Higdon D, Howell DN, Gottfried MR, Tuttle-Newhall JE, Clavien PA. Prolonged rewarming time during allograft implantation predisposes to recurrent hepatitis C infection after liver transplantation. *Liver Transpl.* 2000; 6:407–412. [PubMed: 10915160]
15. Camargo CA Jr, Madden JF, Gao W, Selvan RS, Clavien PA. Interleukin-6 protects liver against warm ischemia/reperfusion injury and promotes hepatocyte proliferation in the rodent. *Hepatology.* 1997; 26:1513–1520. [PubMed: 9397992]
16. Selzner M, Camargo CA, Clavien PA. Ischemia impairs liver regeneration after major tissue loss in rodents: protective effects of interleukin-6. *Hepatology.* 1999; 30:469–475. [PubMed: 10421656]
17. Brokelman W, Stel AL, Ploeg RJ. Risk factors for primary dysfunction after liver transplantation in the University of Wisconsin solution era. *Transplant Proc.* 1999; 31:2087–2090. [PubMed: 10455977]
18. Busquets J, Figueras J, Serrano T, Torras J, Ramos E, Rafecas A, Fabregat J, Lama C, Xiol X, Baliellas C, Jaurrieta E. Postreperfusion biopsies are useful in predicting complications after liver transplantation. *Liver Transpl.* 2001; 7:432–435. [PubMed: 11349264]
19. Ploeg RJ, D'Alessandro AM, Knechtle SJ, Stegall MD, Pirsch JD, Hoffmann RM, Sasaki T, Sollinger HW, Belzer FO, Kalayoglu M. Risk factors for primary dysfunction after liver transplantation--a multivariate analysis. *Transplantation.* 1993; 55:807–813. [PubMed: 8475556]
20. Firpi RJ, Abdelmalek MF, Soldevila-Pico C, Cabrera R, Shuster JJ, Theriaque D, Reed AI, Hemming AW, Liu C, Crawford JM, Nelson DR. One-year protocol liver biopsy can stratify fibrosis progression in liver transplant recipients with recurrent hepatitis C infection. *Liver Transpl.* 1991; 10:1240–1247. [PubMed: 15376304]
21. Ishak K, Baptista A, Bianchi L, Callea F, De Groote J, Gudat F, Denk H, Desmet V, Korb G, MacSween RN, et al. Histological grading and staging of chronic hepatitis. *J Hepatol.* 1991; 22:696–699. [PubMed: 7560864]
22. Killackey MT, Gondolesi GE, Liu LU, Paramesh AS, Thung SN, Suriawinata A, Nguyen E, Roayaie S, Schwartz ME, Emre S, Schiano TD. Effect of ischemia-reperfusion on the incidence of acute cellular rejection and timing of histologic hepatitis C virus recurrence after liver transplantation. *Transplant Proc.* 2008; 40:1504–1510. [PubMed: 18589139]
23. Shackleton CR, Martin P, Melinek J, Stothers L, Millis JM, Olthoff KM, Imagawa DK, Kinkhabwala M, Rudich S, Seu P. Lack of correlation between the magnitude of preservation injury and the incidence of acute rejection, need for OKT3, and conversion to FK506 in cyclosporine-treated primary liver allograft recipients. *Transplantation.* 1995; 60:554–558. [PubMed: 7570950]
24. Briceno J, Marchal T, Padillo J, Solorzano G, Pera C. Influence of marginal donors on liver preservation injury. *Transplantation.* 2002; 74:522–526. [PubMed: 12352912]
25. Boker KH, Dalley G, Bahr MJ, Maschek H, Tillmann HL, Trautwein C, Oldhaver K, Bode U, Pichlmayr R, Manns MP. Long-term outcome of hepatitis C virus infection after liver transplantation. *Hepatology.* 1997; 25:203–210. [PubMed: 8985291]

Figure 1.

Shows the prevalence of RF amongst patients with PI at 4 months, 1 year and 2 year

Figure 2.

Comparison of survival curves

(a) Comparison of patient survival between patients with and without PI (b) Comparison of survival between patients with difference grades of PI (c) Comparison of survival between patients with Rapid and slow fibrosis (d) Comparison of graft survival between patients with and without PI

Table 1

Comparison of characteristics between patients with and without preservation injury

Variable	Factor	Preservation injury (n=176)	No Preservation Injury (n=37)	P value
Recipient Age	Mean (range)	49.3 (14–72)	50.9 (40–68)	0.973
Recipient Gender	Male	120 (68.2%)	28 (75.7%)	0.436
	Female	56 (31.8%)	9 (24.3%)	
Recipient Race	Caucasian	155 (88.1%)	30 (81.1%)	0.502
	African American	7 (3.9%)	2 (5.4%)	
	Other	14 (7.9%)	5 (13.5%)	
Recipient Blood group	A	80 (45.4%)	16 (43.2%)	0.405
	AB	8 (4.5%)	2 (5.4%)	
	B	28 (15.9%)	2 (5.4%)	
	O	60 (34.1%)	17 (45.9%)	
Donor Age	Mean (SD)	42.8 (18.3)	35.8 (16.6)	0.616
Donor gender	Male	106 (60.2%)	26 (70.3%)	0.682
	Female	70 (39.7%)	11 (29.7%)	
Donor Race	Caucasian	142 (80.7%)	31 (83.8%)	0.429
	African American	21 (11.9%)	2 (5.4%)	
	Other	13 (7.4%)	4 (10.8%)	
HCC	Present	28 (15.8%)	6 (16.2%)	0.471
	Absent	148 (84.1%)	31 (83.8%)	
Pretransplant Interferon	Yes	66 (41.8%)	14 (45.2%)	0.843
	No	92 (58.2%)	17 (54.8%)	
Immunosuppression	Cyclosporine	47 (26.7%)	6 (15.4%)	0.214
	Tacrolimus	129 (73.3%)	31 (84.6%)	
CIT (hours)	Mean (SD)	7.57 (2.0)	8.47 (3.1)	0.015
1-week AST	Mean (SD)	1617.07 (2105.30)	833.9 (518.54)	0.003
1-week ALT	Mean (SD)	1034.70 (1132.14)	603.9 (440.00)	0.007
1-week Bilirubin	Mean (SD)	4.05 (3.42)	3.15 (2.65)	0.115
Pre-LT Bilirubin	Mean (SD)	4.72 (6.85)	4.03 (4.70)	0.335
1-week INR	Mean (SD)	1.68 (0.34)	1.52 (0.20)	0.023
1-week AP	Mean (SD)	81.89 (83.95)	84.36 (71.86)	0.993
1-week GGT	Mean (SD)	97.82 (110.19)	136.33 (309.10)	0.007

SD, standard deviation; HCC, hepatocellular carcinoma; CIT, cold ischemia time; WIT, warm ischemia time; AST, aspartate aminotransferase; ALT, alanine aminotransferase; INR, international normalized ratio; AP, alkaline phosphatase; GGT, gamma-glutamyltransferase

Table 2

Comparison of characteristics between patients with different grades of preservation injury

	Grade of PI	Mean	Range	P value
CIT (hours)	Mild	7.34	1–12	0.091
	Moderate-severe	7.79	3–17	
	Moderate-severe	45.61	13–94	
1-week AST	Mild	1045.13	126–10700	<0.001
	Moderate-severe	2169.05	172–15748	
1-week ALT	Mild	704.45	72–3780	<0.001
	Moderate-severe	1353.44	142–8130	
1-week Bilirubin	Mild	3.3843	0.20–13.50	<0.001
	Moderate-severe	5.9966	0.40–30.20	
1-week AP	Mild	85.19	36–1030	0.460
	Moderate-severe	78.70	33–379	
1-week GGT	Mild	87.69	18–468	0.346
	Moderate-severe	107.71	17–1148	
1-week INR	Mild	1.6048	1.20–2.60	0.048
	Moderate-severe	1.7477	1.30–3.30	

CIT, cold ischemia time; WIT, warm ischemia time; AST, aspartate aminotransferase; ALT, alanine aminotransferase; AP, alkaline phosphatase; GGT, gamma-glutamyltransferase; INR, international normalized ratio