Digestive Disease Conference: Day One

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Abstract 8
The Incidence of Hepatocellular Carcinoma in the United States; Is It Still Rising?

Hashem B. El-Serag, Jessica Davila, Nancy Petersen

Background:

Increasing incidence rates for hepatocellular carcinoma (HCC) were previously reported in the United States, possibly due to chronic HCV infection. However, alternate explanations were diagnostic and/or reclassification bias, and changes in the demographics of the general population. The purpose of this study is to update recent trends in HCC incidence through 1998 and to examine temporal changes in incidence while adjusting for changes in age, gender, ethnicity within geographic regions.

Methods:

Using information from the Surveillance, Epidemiology, and End Results (SEER) program, we identified all histologically confirmed cases of primary HCC during 1975-98. Age-adjusted incidence rates (AIR) were calculated for consecutive 3-year periods during 1975-98. We used Hierarchical Poisson multivariate regression to examine temporal trends in HCC controlling for changes in age, gender, and race among HCC cases and in the underlying population at risk, while accounting for potential clustering of persons with similar characteristics within geographic regions.

Results:

The overall AIR increased from 1.4/100,000 in 1975-77 to 3.0/100,000 in 1996-98; 114% overall increase. There was a 25% increase over the last 3 years of the study. The proportions of patients with liver cancer undergoing microscopic confirmation remained relatively stable over time. The increase in HCC affected most age groups above 40, with the greatest increase between ages 45 and 49. For instance, there was a striking 110% increase during the 1990s in white men (including Hispanic) between 45-49. The AIRs were 2-folds greater in blacks than whites and 2-folds greater in Asians than blacks. However, white men and black women had the greatest percentage increase (31%) in the last time period (1996-98) as compared to 1993-95. The Poisson hierchichal regression model confirmed an almost two fold increase in HCC incidence between 1975 and 1998. A significant interaction between time of diagnosis and race such as that a greater increase in HCC incidence occurred in whites compared to blacks and Asians during more recent time periods.

Conclusions:

The incidence of HCC continues to rapidly increase in the United States. Although this increase has affected most age, gender, ethnic groups, the fastest rising rates have been observed in white men between the ages of 45 and 55. These findings are consistent with a true increase in HCC and could be explained by consequences of HCV acquired earlier in life during the 1960s and 1970s.

Editor's Note:

Dr. Hashem commented that the causative agent (HCV, HVV or alcohol) for the increase in liver cancer was unclear but it is believed that while the incidence of HCC caused by HBV and alcohol has remained stable, HCV related HCC has increased by 50%.

There was a small increase in the adjusted incidence rate of HCC in 1999-2000 to 3.1/100,000

Possible reason why males are more likely to develop liver cancer may be the role that testosterone plays as a carcinogenic in the liver.

Abstract 9

Is Obesity a Risk Factor for Cirrhosis-Related Death or Hospitalization? A Population-Based Cohort Study.

George N. Ioannou, Noel S. Weiss, Kris V. Kowdley, Jason A. Dominitz

Context:

Obesity has been associated with the presence of advanced fibrosis in patients with chronic liver disease.

Objective:

To determine whether increased body mass index (BMI) in the general population is associated with cirrhosis-related death or hospitalization.

Design:

Prospective cohort study.

Setting:

The first National Health and Nutrition Examination Survey and Epidemiologic Follow-up Study, a nationally representative survey.

Participants:

11,465 persons aged 25-74 years without evidence of cirrhosis at entry into the study, or during the first 5 years of follow-up, were subsequently followed for a mean of 12.9 years.

Measurements:

The BMI measured at baseline was used to categorize participants into normal-weight (BMI < 25 kg/m^2, N=5,752), overweight (BMI 25 to < 30 kg/m^2, N=3,774) and obese (BMI >= 30 kg/m^2, N=1,939). Deaths and hospitalizations due to cirrhosis were identified from death certificates and hospitalization records.

Results:

Cirrhosis resulted in death or hospitalization of 89 participants during a total of 150,233 person-years of follow-up (0.59/1000 person-years). Cirrhosis-related deaths or hospitalizations were more common in obese persons (0.81/1000 person-years, adjusted hazard ratio 1.69, 95% CI 1.0-3.0) and in overweight persons (0.71/1000 person-years, adjusted hazard ratio 1.16, 95% CI 0.7-1.9) compared to normal-weight persons (0.45/1000 person-years). Among persons who did not consume alcohol, there was a particularly strong association between obesity (adjusted hazard ratio 4.1, 95% CI 1.4-11.4) or overweight (adjusted hazard ratio 1.93, 95% CI 0.7-5.3) and cirrhosis-related death or hospitalization. In contrast, this association was weaker among persons who consumed up to 0.3 alcoholic drinks per day (adjusted hazard ratio 2.48, 95% CI 0.7-8.4 for obesity, and adjusted hazard ratio 1.31, 95% CI 0.4-4.2 for overweight) and no association was identified among those who consumed more than 0.3 alcoholic drinks/day (adjusted hazard ratio 0.80, 95% CI 0.3-2.1 for obesity, and adjusted hazard ratio 0.97, 95% CI 0.5-1.8 for over weight).

Conclusions:

Obesity appears to be a risk factor for cirrhosis-related death or hospitalization among persons who consume little or no alcohol.

Abstract 12
Hepatic Steatosis on Ultrasound: Associated Factors and Relationship with Steatosis on Liver Biopsy

Matthew J. Hepburn, Sigurd J. Torgerson, Eric J. Lawitz

Introduction:

Ultrasonography is commonly employed in screening patients infected with hepatitis C virus (HCV). The significance of steatosis observed during these screening tests is unclear. The factors associated with steatosis on ultrasonography and the relationship between steatosis on ultrasound vs. biopsy in HCV-infected patients merit further investigation.

Methods:

A retrospective review was conducted of all reports of liver ultrasound performed on HCV-infected patients seen at our hepatitis clinic. The presence or absence of steatosis was recorded as a binomial variable. Liver biopsies on these patients were reviewed by a single pathologist, and graded for the degree of steatosis, with the following scale: 0: none, 1: 1-30%, 2: 30-70%, 3: >70%. Other clinical parameters were obtained, including: gender, age, ethnicity, metavir stage, histologic grade, genotype, history of diabetes mellitus, body mass index (BMI), baseline alanine aminotransferase (ALT) and alpha fetoprotein (AFP). Patients with ultrasound imaging before and after combination therapy for HCV were also analyzed.

Results:

Pretreatment ultrasounds were available on 144 patients. Patients with steatosis on ultrasound had a higher incidence of the following parameters compared to patients without steatosis: diabetes (12/45 or 27% vs. 5/99 or 5%, p<0.0001), metavir stage >2 (15/43 or 35% vs. 13/94 or 14%, p=0.005), histologic grade >2 (18/41 or 44% vs. 8/77 or 10%, p<0.0001), BMI (28.5 kg/m2 vs. 26.7 kg/m2, p=0.014), ALT (130.9 IU/L vs. 95.1 IU/L, p=0.013) and AFP (8.1 ng/ml vs. 13.8 ng/ml, p=0.015). Patients with steatosis on ultrasound were more likely to have more steatosis on liver biopsy (p=0.02). However, 12% (7/57) of patients with a normal ultrasound had > 30% steatosis on biopsy, while only 1/11 (9%) patients had steatosis detected on ultrasound with no steatosis on liver biopsy. In 22 patients with ultrasound performed before and after combination therapy, steatosis resolved in 6/12 patients with initial steatosis, while steatosis developed in 1/10 patients with normal baseline ultrasounds (p=0.06).

Conclusions:

Steatosis on ultrasound is closely related to markers of inflammation and fibrosis in HCV-infected patients, as well as BMI and diabetes, suggesting a multifactorial etiology for steatosis in this population. Ultrasonography is an approximate but imperfect predictor of steatosis on biopsy. Ultrasound may provide an indirect mechanism to document the improvement of steatosis after HCV therapy.

Editor's Note:

Speaker's comments:

- Steatosis common in people with HCV genotype 3
- Ultrasound test failed to find steatosis in mild to moderate cases of steatosis
- Ultrasound test succeeded in finding steatosis in moderate to severe cases of steatosis
- Fibrosis may affect ultrasound finding of steatosis – therefore should be studied as a predictor of fibrosis
- Higher percentage of steatosis in patients with diabetes

- At this point, ultrasound should be used with caution in diagnosing steatosis.

Abstract S902
The 13C-Caffeine Breath Test: A Non-invasive, Quantitative Test of Liver Function

Gordon J.-H. Park, Peter H. Katelaris, Brian Jones, Francis Seow, David G. Le Couteur, Meng C. Ngu

Background & Aim:

There is an ongoing clinical need for a quantitative liver function test that is safe, convenient, and yields reliable data on disease severity and prognosis. The properties of caffeine render it an ideal substrate for a CO_2 breath test of liver function. To date, the major role of the caffeine breath test (CBT) has been to study the effect of various drugs on the activity of CYP1A2. A previous study involving the intravenous administration of radioactively labeled 14C-caffeine demonstrated that the breath test correlated with plasma clearance and reflected varying degrees of liver dysfunction. These data have not been validated and no prospective studies comparing the CBT to traditional markers of disease severity and prognosis have been performed. Further, the intravenous route is invasive and repeated exposure to a radioactive substance, if the test was applied serially to monitor disease evolution or therapeutic response, is undesirable. The aim of the present study was to determine if the CBT using orally administered 13C-caffeine correlates reliably with plasma caffeine clearance and reflects varying degrees of liver dysfunction.

Methods:

The CBT and plasma caffeine clearance were simultaneously assayed in 9 healthy controls, 7 outpatients with chronic hepatitis B or C and 14 cirrhotics. The 13C-enrichment of expired CO_2 was determined by isotope ratio mass spectrometry. Plasma levels of 13C-caffeine were measured using gas chromatography mass spectrometry. Results: Cirrhotics were characterized by significantly reduced 1h-CBT (CBT_1) values (mean 1.30 ± 0.79 %/mg) compared to normals (2.37 ± 1.20) and hepatitics (2.26 ± 1.37)($P = 0.02$, normals vs cirrhotics). Over a broad range of clearance (CL) values, the CBT exhibited a highly significant correlation with CL ($r=0.84$, $P < 0.0001$). The same results were obtained using CBT parameters at 2h ($r=0.85$) and at 3h ($r=0.85$). Smokers had a mean CBT_1 value of 2.59 ± 1.26 compared to nonsmokers (1.30 ± 0.60, $P < 0.01$). The intraclass correlation coefficient between 13 repeated CBTs was 0.92 ($P < 0.001$). Multivariate analysis revealed that only smoking ($P = 0.001$) and disease status ($P = 0.02$) were significant predictors of the CBT.

Conclusion:

Our data confirm that the oral 13C-CBT represents a valid indicator of systemic caffeine clearance and correlates reproducibly with hepatic dysfunction. CBT values at 1, 2, and 3h are equivalent in terms of correlating with CL and suggest that a 1h measure is adequate, simplifying the test. Smoking induces the activity of CYP1A2 and is a cofounder although its influence appears to be consistent over the spectrum of liver dysfunction studied. The potential clinical applications of the CBT are myriad. These include study of other acute and chronic liver diseases, assessment of hepatic therapies (e.g. antiviral, surgery) prediction of drug hepatotoxicity, examining the effects of ageing in the liver, and exploring the possible connection between CYP1A2 activity and carcinogenesis. The test demonstrates excellent reproducibility over a broad spectrum of liver function.

Abstract S1163

The Influence of Donor Age on Fibrosis Progression Rate in Recurrent Hepatitis C Post-Liver Transplantation.

M. Isabel Fiel, Daniel D. Gan, Arief Suriawinata, Monika Hartono, Swan N. Thung, Thomas D. Schiano

Background:

Recurrence of HCV infection is universal in post-liver transplant (LT) patients. This often is due to an accelerated fibrosis that occurs in the transplanted liver as rapid progression to cirrhosis occurs in certain patients resulting in graft failure. Certain factors such as donor age gender mismatch, may influence the development of this accelerated fibrosis.

Aims:

We sought to determine the rate of progression of fibrosis in post-LT HCV recurrence using the METAVIR system and to determine if donor age has any influence on the development of this fibrosis. Methods: All post-OLT HCV adult patients having two or more liver biopsies were identified from the liver transplantation and pathology data base. A trichrome-stained slide of the most recent biopsy with recurrent hepatitis was assessed by blinded pathologist to grade the amount of fibrosis using the METAVIR system (F0- no fibrosis, F1- portal fibrosis, F2- fibrous septa, F3- many fibrous septa, F4- cirrhosis). The time of LT was considered time 0. To determine the rate of fibrosis progression rate (FPR), METAVIR score was divided by the time (in years) after LT. Patients were first divided into 2 groups, those whose donors were 30 and below and those >30 years. Patients were then divided into those with donors 50 and below and those>50 years. The FPR scores of these patients were distributed as follows: <0.1 units/yr (slow fibroser), 0.1-0.5 unit/yr, 0.5-1.0 unit/yr >1.0 unit/yr (rapid fibrosers). Chisquare was used to assess statistical significance.

Results:

There was a total of 134 patients, 39 female, 95 male, average age 52.5 years. Table 1 shows the results which show significant difference in younger vs. older donors with p value = 0.0002 in the 1st group and p value of 0.05 in the second group.

Conclusions:

Liver fibrosis occurring with post-LT HCV infection progresses slower in livers from donors <age 50 especially when < age 30. This is in agreement with the more rapid fibrosis seen in patients with chronic active hepatitis initially infected at an older age.

Abstract S1164
Predictive factors of HCV recurrence after liver transplantation (OLTx)

Sara Pevere, Sara Boninsegna, Dino Martines, Umberto Cillo, Patrizia Burra, Patrizia Boccagni, Giacomo Zanus, Davide F. D'Amico, Remo Naccarato, Stefano Fagiuoli

Introduction:

Post-OLTx HCV recurrence is virtually universal but rate and severity of graft disease and the identification of the factors influencing recurrence are still controversial.

Aim:

The aim of this study was to evaluate features and factors predictive of recurrent HCV in patients transplanted for HCV-related cirrhosis.

Patients and Methods:

108 consecutive patients transplanted for HCV related ESLD were evaluated (85 M/23 F, mean age 51±9.2. Mean follow-up was 63.8±32 months. 1, 5, 7-year survival rate were 78%, 72%, 68% respectively. Patients with peri-operative mortality (16, 15%) were excluded from the analysis. HCV recurrence, defined as HCV-RNA positivity and biopsy-proven hepatitis, was found in 84/92 (91%) overall. Median time of HCV recurrence was 15±2 months. Biochemical hepatitis (HEP, presence of ALT≥2 nv) during first six months after OLTx occurred in 45/92 (48.7%). Recurrent HCV cirrhosis developed in 17/92 (18.4%) in a median time of 54±3 months. 1, 3, 5, 7-year recurrent cirrhosis rate were 2%, 9.7%, 14% and 18.4% respectively. Factors influencing time of recurrence, HEP and development of recurrent cirrhosis (Cirrh) were evaluated see table below.

Conclusions:

1. Time of recurrence appears to be influenced by the presence of concomitant alcoholic etiology (longer) and pre-existent HCC (shorter).
2. Early recurrence seems to be influenced by total ischemia time.
3. Late recurrence is influenced by number of rejection episodes. The development of cirrhosis appears to be mostly related to younger age at OLTx (≤50 years).

Factors predictive of HCV recurrence

Factors	*Chi-square test*				*Logistic regression*			
	Recurrence≤12 months	Recurrence≤6 months	HEP	Cirrh	Recurrence≤12 months	Recurrence≤6 months	HEP	Cirrh
	p	p	p	p	p	p	p	p
Age at OLT£ 50	ns	ns	0.05	0.02	ns	ns	ns	0.02
C vs C and ETOH	0.01	0.07	ns	ns	0.004	0.01	ns	ns
HCC	0.04	0.02	0.03	ns	ns	ns	0.02	ns
N rejection	0.02	ns	ns	ns	0.01	ns	ns	ns
Response to IFN	-	-	-	0.05	-	-	-	0.07
Ischemia time	ns	0.08	ns	ns	ns	0.02	ns	ns

Abstract S1165
Comparison of MELD Scores in Hepatitis C Patients Prior to and After Adoption of the MELD Scoring System.

Douglas Meyer, Guy Neff, Marzia Montalbano, Kamran Safdar, Halim Muslu, Nuri Ozden, Jose Nery, Andres Tzakis, Eugene Schiff

Introduction:

Hepatitis C (HCV) is the leading indication for liver transplantation in the United.States prior to 3/2002, allocation of livers for transplantation was based on the Child-Pugh scoring system. This system was partly subjective due to the inclusion criteria of ascites and hepatic encephalopathy. The MELD scoring system was adopted to avoid subjectivity by using creatinine, INR and total bilirubin as inclusion criteria.

Aim:

The aim of this study was to compare the MELD scores of HCV liver transplant patients prior to and after adoption of MELD scoring system to evaluate for any differences in current allocation of liver transplants.

Methods:

A retrospective evaluation of the MELD scores peri-transplantation and prior three months in HCV patients transplanted after adoption of the MELD scoring system. In addition, retrospective determination of MELD scores peri-transplant and prior three months in HCV patients transplanted within one year prior to the adoption of the MELD scoring system. Furthermore, the two groups were analyzed for any differences in term of gender, age at transplant, percentage with hepatocellular carcinoma (HCC) and co-existence of alcohol cirrhosis. Results were analyzed using chi-square and student t-tests.

Results:

- *Group 1*, there were 26 males and 1 female with mean age of 49.8 yrs (range 37-68.9) transplanted after the adoption of the MELD scoring system. Group 1, there were 8 HCC found at transplant (30%), one was an incidental finding.
- *Group 2*, there were 27 males and 7 females with mean age 53.1 yrs (range 29.5-72.3) transplanted prior to the adoption of the MELD scoring system. Group 2, there were 8 HCC found at transplant (24%), three were incidental findings.

There was no statistical difference between the two groups in terms of gender, age, alcohol cirrhosis, percentage with HCC and if the HCC was an incidental finding. The mean MELD score at transplant for group 1 was 19 (range 11-35) compared to 17.2 (range 7-31) in group 2 (p=NS). Furthermore, there were no statistical difference in the MELD scores at transplant in terms of gender or patients without HCV between the two groups. Furthermore, there were no differences between the two groups when comparing the change in MELD scores over a 1, 2 or 3 month period prior to transplant.

Conclusions:

The adoption of the MELD scoring system does not appear to change the manner in which livers are being allocated for transplantation. However, there appears to be a current trend in transplanting more HCV patients with HCC, which is not an incidental finding.

Abstract S1167
Hepatitis-C-Recurrence after Liver Transplantation: Is it really that bad?

Lukas Hinterhuber, Ivo W. Graziadei, Alfred Koenigsrainer, Karin Nachbaur, Raimund Margreiter, Wolfgang Vogel

Introduction:

Liver Transplantation (LT) is the only effective therapy of end-stage liver disease due to Hepatitis C (HCV). HCV related cirrhosis is the most common indication for liver transplantation worldwide. HCV-reinfection of the graft occurs almost universally. The clinical manifestations vary significantly from asymptomatic to severe cholestatic courses. The pathophysiology, risk factors and the natural history of recurrent HCV are not clearly understood and remain controversial. A recent study showed a rapid progression of HCV infection after liver transplantation leading to cirrhosis in about 30% of patients.

Aim:

In this study we analysed the different clinical types of HCV recurrence, potential contributing factors and the

long term outcome of HCV patients after liver transplantation.

Patients and Methods:

Between 03/1986 and 03/2002 118 HCV patients (84male/34female; mean age 56ys) underwent liver transplantation in our center. The mean follow-up was 51 months (range: 1-194 ms). The diagnosis of HCV recurrence was based on biochemical (elevated transaminases) and histologic parameters. Genotype 1 was predominant (75%) followed by 2 (15%) 3 (8%) and 4 (3%). Immunosupression (IS) consisted of CyA/ FK 506, prednisolone (taper within 3 months) and/or azathioprine / MMF. Acute rejections were treated with a steroid bolus.

Results:

The actuarial 1-,2-,5-,10-year survival rates were 83%, 79%, 68% and 59%, respectively, which were comparable to those of other indications. A positive HCV-RNA was seen in 114/118 patients (97%) after LT. A histologic HCV recurrence was diagnosed in 64/118 patients (54%) with a mean period of 33 months. Only a mild portal, lobular or mixed hepatitis was seen histologically in the majority of cases. Twelve patients (10%), however, developed the severe cholestatic form, of whom 9 died. Six patients (5%) developed a cirrhosis within a mean time period of 54 months (range 30-82) following liver transplantation. Except for the cholestatic type HCV recurrence did not adversely influence patient and graft survival. Only two retransplantations were necessary secondary to HCV-cirrhosis. Concerning possible risk factors neither virologic (genotype, virus load) nor recipient-parameters (IS, CMV, rejection) were found to be significant. Only the age of the donor showed a negative impact on HCV recurrence and on long term outcome.

Conclusion:

Our study showed, that HCV recurrence after LT is in most cases mild, except the cholestatic type, and had no negative impact on the long term outcome. Regarding possible risk factors only donor age turned out to play an important role.

Abstract 1169
Histological Criteria for the Distinction of Hepatitis C Recurrence Post-Liver Transplantation in Patients With Other Hepatic Complications

Talat Bessissow, Victoria Marcus, Marc Deschenes

Introduction:

Hepatitis C virus (HCV) related liver disease is the most common indication for liver transplantation (LT). Post-LT HCV viremia is universal and recurrent hepatitis is seen in 50-80%.

Aim:

To define the constellation of histological features associated with HCV hepatitis recurrence post-LT that differentiates it from other common post-operative complications.

Methods:

Liver transplant recipients with HCV, anastomotic biliary stenosis, acute cellular rejection (ACR) and early allograft dysfunction (EAD) were identified from the MUHC computerized LT database. EAD was defined according to the NIDDK LTD criteria and was used as a marker of severe ischemia/reperfusion injury. (If one

of the following was present: bilirubin> 10mg/dl; PT>17 seconds; and hepatic encephalopathy days 2-7 post-LT). Then, liver biopsy materials performed within the first six months following LT were evaluated in a blinded fashion by a single observer. For each biopsy, forty-five criteria were scored from 0 to 3 along a semiquantitative scale. Finally we compared the different scores between the categories of four diagnoses: HCV alone; HCV & biliary stenosis; HCV & ACR; HCV& EAD.

Results:

72 liver biopsies in 42 recipients of LT performed in 2000 and 2001 were reviewed—liver biopsy 0 today 180 post liver transplant were identified through PLATYUS computerized system. In comparing recipients with HCV alone and HCV & ACR, no variable was identified as an independent differentiating feature. More severe steatosis and lesser amounts of acidophilic bodies differentiated severe ischemic-reperfusion injury in recipients with EAD & HCV from those with HCV alone. A trend (p=0.07) for greater sinusoidal dilatation in patients with biliary obstruction compared to those with HCV alone was observed.

Conclusion:

In general, in liver transplant recipients for HCV associated liver disease, it is difficult to differentiate between the histological findings pertaining to recurrent HCV from those of otherwise common complications seen after liver transplantation. We found that more severe steatosis and the presence of lesser amounts of acidophilic bodies are features differentiating ischemic-reperfusion injury from HCV. Given the difficulty in differentiating ACR from HCV and the long-term negative impact of corticosteroids, perhaps we should be less aggressive in the treatment of ACR in patients with equivocal findings.

Abstract S1169
Histological Criteria for the Distinction of Hepatitis C Recurrence Post-Liver Transplantation in Patients With Other Hepatic Complications

Talat Bessissow, Victoria Marcus, Marc Deschenes

Introduction:

Hepatitis C virus (HCV) related liver disease is the most common indication for liver transplantation (LT). Post-LT HCV viremia is universal and recurrent hepatitis is seen in 50-80%.

Aim:

To define the constellation of histological features associated with HCV hepatitis recurrence post-LT that differentiates it from other common post-operative complications.

Definitions:

- HCV: (+) anti HCV and HCV-RNA pre-LT
- BD: stenosis (+)ve ERCP post – LT
- ACR: treated with corticosteroid boluses for compatible clinical picture (increase enzyme, biopsy findings)
- Severe I/R injury, fulfills criteria for NIDDK LTD definition of EAD
- EAD: Between day 2 and 7 post LT. Bilirubin > 170 µmol/h and/or PT> 17 sec

Methods:

LT recipients with HCV, anastomotic biliary stenosis, acute cellular rejection (ACR) and early allograft dysfunction (EAD) were identified from the MUHC computerized LT database. EAD was defined according to the NIDDK LTD criteria and was used as a marker of severe ischemia/reperfusion injury. (If one of the following was present: bilirubin> 10mg/dl; PT>17 seconds; and hepatic encephalopathy days 2-7 post-LT). Then, liver biopsy materials performed within the first six months following LT were evaluated in a blinded fashion by a single observer. For each biopsy, forty-five criteria were scored from 0 to 3 along a semiquantitative scale. Finally we compared the different scores between the categories of four diagnoses: HCV alone; HCV & biliary stenosis; HCV & ACR; HCV& EAD.

Results:

72 liver biopsies in 42 recipients of LT performed in 2000 and 2001 were reviewed. Liver biopsy from 0 to day 180 post LT were identified through Platypus Computerized System

.

- 69% (n = 29 male), 31% (n = 13 female)
- Main etiologies of liver disease for LT were:
  - HCV reoccurrence alone 21% (n = 29)
  - HCV and EAD 10% (n = 4)
  - HCV and Obstruction 12% (n = 5)
  - HCV and ACR 7% (n = 3)
  - Obstruction alone 12% (n = 5)
  - EAD alone 5% (n = 2)
  - Others 26% (n = 11)
  - Indication for LT
  - Cirrhosis 81% (n = 34)
  - Hepatoma 21% (n = 9)
  - Fulminant hepatic failure 2% (n = 1)

In comparing recipients with HCV alone and HCV & ACR, no variable was identified as an independent differentiating feature. More severe steatosis and lesser amounts of acidophilic bodies differentiated severe ischemic-reperfusion injury in recipients with EAD & HCV from those with HCV alone. A trend (p=0.07) for greater sinusoidal dilatation in patients with biliary obstruction compared to those with HCV alone was observed.

LOGISTIC REGRESSION

- HCV alone versus HCV and ACR: No variable was identified as an independent differentiating feature
- EAD and HCV versus HCV alone: More severe steatosis (odds ratio 20.37; 95%CI 2.09 - 198.65) and less acidophilic bodies (odds ratio 0.16; CI 0.03 – 0.9) in EAD and HCV
- Biliary obstruction versus HCV alone: A tied (p = 0.07) for more sinusoidal dilatation in patients with biliary obstruction

Conclusion:

In general, in LT recipients for HCV associated liver disease, it is difficult to differentiate between the histological findings pertaining to recurrent HCV from those of otherwise common complications seen after LT. We found that more severe steatosis and the presence of lesser amounts of acidophilic bodies are features differentiating ischemic-reperfusion injury from HCV. Given the difficulty in differentiating ACR from HCV and the long-term negative impact of corticosteroids, perhaps we should be less aggressive in the treatment of ACR in patients with equivocal findings.

Abstract 1170
Liver Transplantation for Hepatitis B - a Single Center Study

Aaron Benner, Sandeep Mukherjee

Introduction:

College of Medicine, Sections of Gastroenterology and Organ Transplantation, University of Nebraska Medical Center, Omaha, Nebraska. Background: Since the introduction of hepatitis B immunoglobulin (HBIG) and antivirals in the past decade, results of liver transplantation (LT) for hepatitis B virus (HBV) have been excellent. Recently resistance to antivirals has emerged as a concern whose clinical significance is unclear, as graft loss is uncommon.

Aim:

The aim of this study was to evaluate outcomes of liver transplantation for HBV and to describe the prevalence of drug resistance from a single liver transplant center.

Methods:

A retrospective chart analysis and review of the University of Nebraska Medical Center organ transplant database was performed to identify all patients transplanted for HBV between 12/87 and 5/03 who survived greater than 3 months.

Results:

31 patients were transplanted for HBV during the study period; 4 for fulminant hepatic failure and 27 for decompensated cirrhosis. Mean follow-up was 5.2 y (range 0.3-14.8). There were 23 males and 8 females, with an average age of 48.8 y at LT (range 17.9-73.3). 25 patients were hepatitis B surface antigen (HBsAg) positive and 2 were negative; data were unavailable for 4 patients. Of HBsAg positive patients, 7 were also hepatitis B e antigen positive. 25 patients had HBV DNA studies; 18 were HBV DNA positive. Hepatitis C and hepatitis D each coinfected 2 patients. HBIG was administered to all patients (27) transplanted since its availability, but was withdrawn in 3 patients due to severe side effects. Lamivudine was used in 18 patients pre-LT and in 24 patients post-LT. Drug-resistant HBV developed in 2 patients receiving lamivudine, and adefovir was substituted with subsequent improvement in liver tests, HBV DNA, and histology in both patients. 17 patients were on cyclosporine, 8 were on FK506, and 1 patient each was on rapamycin with either cyclosporine or FK506. Rejection was rare in this group, occurring at an average of 1.3 episodes per patient. 4 patients have survived at least 5 y and 21 are currently living, with a mean survival of 3.2 y (range 0.3-15.4). Causes of death in 10 patients were respiratory failure (3), metastatic cancer of unknown primary (2), renal failure (2), sepsis (1), cerebrovascular accident (1), and cerebral edema (1).

Conclusion:

Liver Transplantation is indicated for patients with HBV with survival rates comparable to other liver transplant recipients. Lamivudine resistance is rare in this series of patients, but in the presence of progressive liver injury, responds to adefovir substitution.

Abstract S1554
New Artificial Liver Support System Is Valuable Alternative to Liver Transplantation

Kazuaki Inoue, Makoto Yoshiba

Introduction:

Fulminant hepatic failure is a fatal syndrome accompanied by various metabolic disorders. Among these metabolic disorders, bleeding tendency due to impairment in synthesis of coagulation factors synthesis and hepatic coma due to impairment in detoxication of neurotoxic substances are two major life threatening symptoms. Artificial liver support systems are expected to be effective for these two major symptoms. Plasma exchange has been most prevailing artificial liver support method in Japan. Although plasma exchange is an effective method of replacement of depleted coagulation factors, its capacity in removal of toxic substances with a large pool is limited.

Method:

To solve this limitation, we developed a new artificial liver support system consist of plasma exchange and hemodiafiltration using high performance membranes. Fifty-four patients with fulminant hepatic failure were admitted Showa University Fujigaoka Hospital from 1997 to 2002 underwent this artificial liver support system. Eighteen cases were acute type and 36 cases were suacute type. Diagnosis criteria of fulminant hepatic failure is a combination of prothrombin time less than or equal to 40% of control and hepatic coma greater than or equal to grade II. Acute type is defined as coma occurring within 10 days of the onset of first symptom and subacute type is defined as coma occurring later than 11 days. This artificial liver support system consist of plasma exchange and hemodiafiltration. Plasma exchange is performed by the membrane separation method using Plasmaflo (Asahi Medical co, Tokyo) with 40-60 units of fresh frozen plasma. Hemodiafiltration is performed with protein permeable synthesize high polymer membrane (BS-1.8 Torey Medical, Tokyo). Total amount of replacement fluid is 20-40l infused through postdilution route within 5-10 hours. Dialysis fluid flows concomitantly through hemodiafiltration apparatus at a speed of 500ml/min. Replacement fluid and dialysis fluid contains bicarbonate buffer because a change from acetate to bicarbonate is impaired in fulminant hepatic failure.

Results:

Of 54 patients 51 (94.4%) fully regained their consciousness fully from their initial coma, and 38/54(70.4%) patients survived. Brain edema was observed only in two patients who fell into grade IV coma before admission. Hepatorenal syndrome was observed in two patients. This artificial liver support system is highly effective and safe. The annual surveillance of Ministry of health labor and welfare 2001 reported that more than 80% of major hospitals in Japan adopted this artificial liver support system and improved survival rate of acute type of fulminant hepatic failure(62.7%).

Conclusion:

This artificial liver system is highly effective and safe. The annual surveillance of Ministry of Health Labor and Welfare 2001 reported that more than 80% of major hospitals in Japan adopted this artificial liver support system and improved survival rate acute type of fulminant liver failure (62.7%). This artificial liver support system combined with intensive medical treatment is a valuable alternative to liver transplantation.