
Improving Access to Liver Transplantation: the University of Puerto Rico Experience

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Liver transplantation is the only treatment for end-stage liver disease. It is costly, difficult, and not performed in Puerto Rico. For these reasons, it has been a limited option for Puerto Ricans with advanced cirrhosis, especially for those with no medical insurance to cover for the procedure. In an effort to improve access to the procedure and offer this chance of life to more Puerto Ricans facing death from complications of advanced liver disease, the Gastroenterology and Liver Diseases Division of the University of Puerto Rico, in collaboration with LifeLink Transplant Institute in Tampa, Florida and the Office of Catastrophic Funds of the Commonwealth of Puerto Rico, opened a clinic for liver transplant evaluation at the Medical Sciences Campus. The purpose of this clinic is to coordinate the pre-transplant evaluation of candidates for this therapy, provide the evaluation by the transplant surgeon in Puerto Rico, expedite the process in seriously ill

patients, and offer post-transplant follow-up upon the patient's return to Puerto Rico. The purpose of this article is to describe the experience in this clinic from 1999 to 2003.

One hundred ninety-three patients were seen from September 1999 to January 2003. The most common causes for liver disease were hepatitis C and alcohol, alone or in combination. One hundred thirty four were accepted as candidates for evaluation. Of these, 63 had completed the process, 33 were listed for transplantation and 21 had been transplanted by January 2003. Neither education level, marital status, health insurance nor Child score were associated with successful outcome.

This clinic offers Puerto Ricans, especially those with limited resources, with a viable access to liver transplantation.

Key words: Liver transplant, Puerto Rico, Access

Liver transplantation is the only definitive treatment for end-stage liver disease (1). Although patients undergoing the procedure have a one-year survival of 85 to 90%, the operation is costly, not performed in Puerto Rico and requires moving to a transplant center in the United States. Lifelong follow-up and medications are necessary to ensure the success of the transplant.

In the past, patients in Puerto Rico suffering from advanced chronic liver disease with limited socioeconomic resources were expected to die without any chance of being considered for a liver transplant. As the number of Puerto Ricans seeking this treatment increased, an awareness of this therapeutic option began to grow in the

community. The complete evaluation required the patients to travel to the chosen transplant center in mainland United States. Frequently, patients and their immediate family moved to the area of the center for months or even years before they received the liver transplant. The high costs of therapy and the socioeconomic and psychological burden created by the transfer to the United States of the patients and their family was a deterrent for many. Orthotopic liver transplant was barely recognized by the general community as a treatment opportunity and was not commonly presented to patients as a therapeutic option by their physicians. Socioeconomically limited or medically indigent patients were allowed to follow the natural course of their disease. To address the increasing number of Puerto Ricans with end-stage liver disease in need of a liver transplant, the Division of Gastroenterology and Liver Diseases of the University of Puerto Rico School of Medicine (UPR) in affiliation with LifeLink Transplant Institute (now LifeLink Healthcare Institute) in Tampa, Florida and in collaboration with the Catastrophic Funds of the Government of the Commonwealth of Puerto Rico,

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for Organ Sharing (UNOS), if transplantation was achieved, and if death occurred. Reasons for not completing any stage of the process were recorded specifically when known. If a patient died, cause and date of death were recorded when available.

Transplant. Orthotopic liver transplants were performed at the Tampa General Hospital by LifeLink Transplant Institute staff. Information regarding complications, medications and outcome were recorded in specific cases, when available.

Data Analysis. The database was created using Epi Info Version 6.04D (CDC, Atlanta, GA). Descriptive statistics were determined using Epi Info; statistical associations between categorical variables were determined by Pearson chi-square or Fisher's exact test, using SAS software.

Results

One hundred ninety-three patients were evaluated from September 1999 to January 2003. One patient was withdrawn from analysis, because he continued evaluation at another liver transplant center in the United States. The study group (n=192) consisted of 116 (60.4%) men and 76 (39.6%) females. The mean age of the males was 50.3±10.17 and of the females was 53.5± 8.28. The majority of the patients were referred from the metropolitan area (Carolina, Bayamón and San Juan). Most were married (67.7%) and the most frequent school level achieved was high school (25%). At the time of evaluation, 22.4% had employment, 14% were unemployed, 18.75% were housewives, 23.4% were retired, 3.6% were disabled, and in 17.7% employment status was not recorded. Health insurance was as follows: 96/192 patients (50%) had private health insurance, 73 (38%) were covered by the government managed care health plan, and 16 (8.3%) had only Medicare. No medical insurance information was available in the chart in 7 patients.

The etiologies of chronic liver disease are shown in Table 2. The most common etiologies of CLD in these patients were hepatitis C (HCV) and alcohol (ETOH), either alone or combined. The most frequent manifestations of decompensated CLD reported were ascites in 119/192, encephalopathy in 67/192 and variceal bleeding in 62/192. Less frequent were spontaneous bacterial peritonitis in 20/192, and 9/192 reported a history of hydrothorax.

Of the 192 patients seen initially, 134 (69.8%) were accepted as candidates for evaluation. The main reasons for not being evaluated were: no evidence of synthetic dysfunction (Child A, 26/58) or lack of substance abuse rehabilitation (10/58). Three patients declined to continue evaluation. Three patients that were previously turned

Table 2. Etiology of CLD

CLD etiology	% (n)
Hepatitis C	34.9 (67)
Hepatitis C/Alcohol	18.8 (36)
Alcohol	17.2 (33)
Cryptogenic	7.8 (15)
Primary biliary cirrhosis	6.3 (12)
Autoimmune hepatitis	4.16 (8)
Hepatocellular carcinoma	4.16 (8)
Budd chiari	2 (4)
Hepatitis B	1.5 (3)
Hemochromatosis	1.5 (3)
Wilson's disease	1 (2)

down because they had no proof of alcohol rehabilitation were re-evaluated later and one was accepted for evaluation, increasing the number of candidates to 135.

Sixty-three of the 135 (46.7%) candidates for liver transplant completed evaluation. Forty-eight of the patients (35.5%) did not complete their evaluation. Most of them were lost to follow-up (30) and 13 died during the process. Two patients were referred to other transplant centers in USA, one was undergoing cardiac evaluation, one was found with rectal cancer and one was awaiting approval of funding. The remaining twenty-four patients were still in the process of completing the evaluation when the analysis was performed. Thirty-three patients were finally listed. Of the thirty patients not listed, eighteen were awaiting the final liver transplant board evaluation, eight had died, one was found with a large hepatocellular carcinoma, one had regressed to Child A, and two had no proof of substance abuse rehabilitation.

As of January 2003, 21 patients had received liver transplants. There were 11 males with a mean age of 49.6 ± 13.1 and 10 females with a mean age of 47.1 ± 8.9. The twenty-one transplanted patients were in the majority married (16/21) and had a high school diploma as highest level of education (11/21). Only seven had studies beyond high school, while three had less than a high school diploma. Twelve patients had private health insurance, seven had the government health plan, one patient had only Medicare and in one patient the health insurance was not identified. Most of the liver transplant recipients had disease related to HCV. Seven patients had HCV, 5 patients had HCV/ETOH and 3 had PBC. The other diagnoses were Wilson's Disease (1), alcoholic liver disease (1), Budd-Chiari (1), non-alcoholic steatohepatitis (1) and cryptogenic cirrhosis (2). One of the recipients died one year after transplant due to recurrent HCV.

Of all the patients seen in the clinic, 39/192 (20.3%) patients were lost to follow-up and 27 (14.1%) died. An advanced liver disease complication was the reason of death in fourteen of these patients. In the remaining

initiated a Liver Transplant Evaluation Clinic in September 1999. The development of the UPR Transplant Clinic has provided an additional treatment option to these underserved patients, offering them a window of opportunity and improving their survival.

The purpose of the clinic is to provide the initial evaluation for patients in Puerto Rico with advanced chronic liver disease that are considered possible candidates for a liver transplant. The clinic performs the initial screening process for possible transplant candidates. Patients are evaluated by the Gastroenterology and Liver Diseases staff to determine indication for transplant (severity of disease or other indications), contraindications for the procedure, social support, psychological status, and rehabilitation of previous substance abuse (1, 2). Health insurance coverage for transplant is established. Patients deemed to be candidates for a complete evaluation but having no health insurance coverage or economic resources for the procedure are referred to the Catastrophic Funds Office. The Fund corroborates the medical need and evaluates the socioeconomic situation of the patient and offers coverage for the transplant according to the patient's needs. After documenting that financial coverage exists for the liver transplant, an extensive work-up is performed (Table 1).

Table 1. Pre-Transplant Evaluation

<ul style="list-style-type: none"> • Liver disease <ul style="list-style-type: none"> -Complete etiologic work up -Ultrasound with Doppler -CT with liver volumes • EKG • 2-D echocardiogram • Dental evaluation • General surgery evaluation • Social history • Psychological evaluation • Basic laboratory exams • Renal function • Arterial blood gases <ul style="list-style-type: none"> -Pulmonary function tests 	<ul style="list-style-type: none"> • Infectious <ul style="list-style-type: none"> Hepatitis A, B, C HIV CMV, EBV, VZ PPD • Cancer <ul style="list-style-type: none"> PSA Alpha-fetoprotein Mammogram Pap smear Colonoscopy (age≥50) • Chest X Ray • EGD
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Those patients wishing to be referred to another transplant center in the United States undergo an initial assessment for indications and suitability and are referred to the center of their choice. Upon completion of the evaluation work-up and confirmation that there are no contraindications for the procedure, all other patients are referred to LifeLink Transplant Institute for further consideration. Patients with severe end stage liver disease that qualify for a priority listing, as determined by (MELD) Model for End-Stage Liver Disease score (3) are given an appointment for the final evaluation and decision at the LifeLink Transplant Institute in Tampa. Patients with less severe disease are seen by a Puerto Rican transplant surgeon from LifeLink

Transplant Institute in the clinic at the University of Puerto Rico. The final decision of listing is made by the transplant team in Tampa with all the available information. The patients that are accepted for listing but who are still in a low priority stay in Puerto Rico and are monitored regularly in the Clinic. After transplantation, patients return to Puerto Rico once they are stable, to be followed by their referring gastroenterologist or at the UPR Clinic in close communication with the transplant center staff.

The aims of this paper are to describe the population seen in the Liver Transplant Evaluation Clinic including social, demographic, economic and medical characteristics; to determine the proportion of patients qualifying for orthotopic liver transplantation; to describe the outcome of those patients undergoing evaluation (i.e. proportion of patients completing evaluation, referred to the transplant center, listed, transplanted; and survival) and to identify any patient characteristic that correlates with successful outcome.

Methods

Patients. Data was collected on 193 consecutive patients referred for liver transplant evaluation at the UPR Liver Transplant Evaluation Clinic between September 1999 and January 2003. All patients signed a consent providing access by the clinic staff to their medical record information. The University of Puerto Rico Medical Sciences Campus Institutional Review Board approved the study.

Clinical Data. Medical records of the patients referred to the clinic were systematically retrieved to obtain information. Data regarding demographics and socioeconomic status such as age, gender, town of residence, nationality, relatives living in mainland USA, education, occupation, marital status, religion and health insurance was gathered. Medical data included date of initial evaluation, referring physician and specialty, etiology of chronic liver disease (CLD), age at diagnosis, manifestations of decompensated CLD, medications, comorbid illnesses, surgical history, family history of liver diseases and Child-Pugh score and MELD score. Additional information regarding toxic habits was gathered.

Outcome. After obtaining the above information, the clinic physician determined if the patient was a candidate for evaluation for liver transplant. Candidates without health insurance coverage for liver transplantation were referred to the Catastrophic Funds Office for approval of funds for the procedures and tests that are core to the evaluation. Date of the letter of approval of funds was recorded. Outcome recorded included whether the patient completed the evaluation, was listed in United Network

thirteen patients, cause of death was unknown. The time of death was prior to completing evaluation in 15/27 (55.6%), prior to listing in 10/27 (37.7%), prior to transplant in 1/27 (3.7%) and after transplant in 1/27 (3.7%).

As completing evaluation is the requisite for achieving liver transplantation, several variables were analyzed for correlation with successful completion of evaluation in the 135 patients that were accepted for evaluation. Marital status (married or living with a partner in a stable relationship) did not correlate with completing evaluation (49/61 versus 45/63 with available information, $p=0.3$). Neither did level of education. Information of schooling was available in 79 of the 135 candidates. Of these, 36/53 completing evaluation had high school level or less of schooling, compared to 18/26 of those not completing the process ($p=0.9$). Child score at the initial visit also failed to correlate with completing the evaluation, with 29/70 Child B and 26/52 Child C patients completing the process ($p=0.14$).

As of January 2004, close to 400 patients have been received in the clinic and 41 have undergone liver transplantation, with 95% survival.

Discussion

In the United States, there were 16.7 per 100,000 deaths due to chronic liver disease or cirrhosis in 1998. This represents 25,192 or 1.1% of all deaths reported and is the 10th leading cause of death. The inclusion of other liver-related diagnoses raises this number to 44,677 and makes liver disease the 8th cause of death in the United States (4). Statistics for Puerto Rico reveal 19.6 per 100,000 deaths due to chronic liver disease or cirrhosis in 1998, with liver disease being the 10th leading cause of death over all and the 5th for ages 35-39 and 4th for ages 40 to 64 (5). There were 17,302 patients in the waiting list for liver transplantation in the United States on April 2, 2004. In 2003, 5,671 liver transplants were performed in the United States (6, 7). Approximately 10% die while in the waiting list, but a much larger number of patients die of liver disease without a chance at this therapy. Issues limiting liver transplantation as a therapeutic option include lack of knowledge about transplantation, access to transplant programs, lack of economic resources to undergo the procedure and the life-long post-transplant medical care and immunosuppressive regimen, poor social support, absence of rehabilitation from substance abuse, waiting time, poor physical condition that precludes transplant, intervening complications, and development or progression of liver cancer not amenable to transplantation. (1)

Puerto Rico has no liver transplant program, so there is

no immediate geographic access to this therapy. Patients must travel to the United States with their family or supporting person, to await their turn for transplantation at the transplant center where they are listed. This results in loss of income, abandonment of gainful employment by the patient and/or the relative, fragmentation of the family nucleus and support system, and for some, severe socioeconomic hardship. These difficulties effectively discard transplant as a therapeutic option for some patients. The scarcity of organs also renders this process with uncertainty. The waiting time ranges from a few weeks to years. Severity of disease, as reflected by the MELD score, determines the priority for receiving an organ (3). The recent introduction of the MELD score as the method to allocate organs has made possible for Puerto Ricans awaiting a liver transplant to delay relocating to the United States and has decreased their waiting time away from home. This in itself represents a cost saving measure in this very expensive process. Waiting time varies by region, as the number of transplants depends on the number of available organs and the number of patients in the waiting list. Tampa is in UNOS region 3, which has a median waiting time much lower than the national median (6, 7). This has helped our patients, who often are referred for evaluation late in the course of their disease, and face a higher mortality while waiting for an organ.

It is well established that minorities have less access to health care, and that ethnic, cultural and language barriers are also factors in addition to the socioeconomic disparities (8). Decreased access to transplantation has been studied mostly in African Americans with end stage kidney disease (9, 10). The number of African Americans referred for transplantation, the number actually completing evaluation, and the number eventually receiving a kidney transplant is significantly less than for Caucasians. The relative rate of transplant for African Americans was found to be 0.55 (10), and the transplant rate was 16.9% vs. 52.0% for whites (9). Decreased graft and patient survival has been reported in African Americans after liver transplant (11), but the issue of decreased access to liver transplantation is less clear. An analysis of the UNOS database from 1990 to 1992 showed that women, Hispanic-Americans and Asian-Americans waited longer for transplant and had a higher risk of dying on the waiting list (12). Ozminkowski also noted that minorities were less likely to receive a liver transplant in the late 1980's (13). According to the Organ Procurement and Transplantation network data, as of April 2, 2004, 14.9 % of the candidates waiting for a liver transplant were identified as Hispanics, 6.9 % as black and 72% as white. In 2003, 13% of patients undergoing liver transplant were Hispanic, 9.2% were black and 71.7% were white. (7) A

comparison of these percentages with the ethnic distribution of the population of the United States for the census of 2000 shows a similar proportion for Hispanics (12.5% of the population) but a lower one for African Americans, which comprise 12.3% of the population (14). These numbers show that the proportion of Hispanics in the liver transplant list is similar to that of the general US population, whereas this is not so for African Americans and could suggest that access to transplantation may no longer be an issue for Hispanics.

The location of a transplant evaluation clinic in Puerto Rico, with a Puerto Rican transplant surgeon as well as local staff, removes the language and cultural barriers that impact the access of minorities to healthcare. A support group of Puerto Ricans has been established in Tampa to help our patients during relocation. With these interventions, one of the limitations in achieving transplant for our population has now been considerably modified.

Our findings that education, marital status and health insurance were not predictors of successful evaluation and transplantation are important. Long-term outcome in our patients is still unknown, but short-term survival was excellent. A recent study evaluating socioeconomic status based on neighborhood income, education and health insurance (15) reported a lower survival in patients with Medicare and Medicaid, but no influence on survival of neighborhood income and minimal influence of education. The authors suggest that these findings point out the importance of identifying support for lifelong immunosuppressants and medical care. A similar issue can be raised in those of our patients whose health coverage does not include this benefit.

An important issue impacting the success of our clinic, as measured by transplants achieved, is the advanced stage of disease of many of the patients when first seen. Patients with a Child score of 5 or 6 (Child A) are deemed too early for referral, as these patients have an estimated 90% survival rate at 5 years. On the other hand, one third of patients with a Child score of more than 10 (Child C) will die within a year. Therefore, evaluation for liver transplant is generally started when a patient shows evidence of synthetic dysfunction (Child B), exhibit their first complication (ascites, variceal bleed, encephalopathy), or develop hepatocellular carcinoma (1). Education of health professionals as well as the general public can help improve identification and timely referral of appropriate candidates for liver transplant evaluation.

A long-range goal of our program is the institution of a liver transplant program in Puerto Rico. This requires identification of resources for developing the necessary infrastructure, economic and social support for the patients, educational campaigns and training of health

providers in the therapy of transplantation. Until this is achieved, the UPR Liver Transplant Evaluation Clinic will offer an opportunity of life to a number of patients with end-stage liver disease that would otherwise die.

Resumen

El trasplante de hígado es el único tratamiento para enfermedad terminal hepática. Es un procedimiento costoso, difícil, y no está disponible en Puerto Rico. Por estas razones, ha sido una opción terapéutica limitada para puertorriqueños con cirrosis avanzada, especialmente para aquellos cuyos seguros médicos no incluyen este procedimiento. En un esfuerzo por mejorar el acceso y ofrecer esta oportunidad de vida a más puertorriqueños, la División de Gastroenterología y Enfermedades de Hígado de la Universidad de Puerto Rico, en colaboración con el LifeLink Transplant Institute de Tampa, Florida y la Oficina de Fondos Catastróficos del Gobierno de Puerto Rico, estableció una clínica para la evaluación pre-trasplante hepático en el Recinto de Ciencias Médicas. El propósito de esta clínica es coordinar la evaluación pre-trasplante de los candidatos para esta terapia, proveer la evaluación por el cirujano de trasplante en Puerto Rico, aligerar el proceso en pacientes seriamente enfermos, y ofrecer cuidado post-trasplante cuando el paciente regresa a Puerto Rico. Este artículo describe la experiencia de la clínica desde el 1999 hasta el 2003.

Ciento noventa y tres pacientes fueron vistos desde septiembre de 1999 hasta enero de 2003. La causa más común de enfermedad hepática fueron hepatitis C y alcohol, solas o combinadas. Ciento treinta y cuatro pacientes fueron aceptados como candidatos para evaluación. De éstos, 63 habían completado evaluación, 33 estaban en lista de espera para trasplante, y 21 se habían trasplantado para enero del 2003. Ni el nivel de educación, estado marital, seguro médico o puntuación de Child se asociaron estadísticamente con un resultado exitoso.

Esta clínica ofrece a puertorriqueños, en especial aquellos con recursos limitados, un acceso viable a trasplante de hígado.

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