LIVER TRANSPLANTATION: A 10-YEAR SINGLE CENTER EXPERIENCE IN PERNAMBUCO- NORTHEASTERN BRAZIL

Transplante Hepático: Experiência de 10 anos de um centro transplantador em Pernambuco – Nordeste do Brasil

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ABSTRACT

Purpose: The aim of this study is to analyze a ten-year single center experience in liver transplantation in Pernambuco - Northeastern region of Brazil. **Methods:** Data were retrospectively collected from medical records of 302 patients who underwent Orthotopic Liver Transplantation (OLT) between 1998 and 2008 at Oswaldo Cruz University Hospital, Pernambuco – Brazil. We analyzed just the outcomes and survival curve of 195 adult liver transplantation recipients from deceased donor. **Results:** Data concern liver donor, surgery technical aspects and liver transplantation recipients' postoperative evolution are presented and discussed. This center has a significant experience in liver transplantation using conventional technique with no venovenous bypass. Efficient management of liver transplantation practice has made it feasible to keep the cold ischemia time within 6-7 hours. Because of the organ shortage, we have used a large amount of extended criteria liver donor. The survival 1-year rata was 76.4%. **Conclusion:** It is possible to provide a high-quality public medical assistance in an efficient and continuous manner in less developed areas of Brazil.

Keywords: Transplantation; Survivorship; Liver

INTRODUCTION

The first orthotopic liver transplantation (OLT) in Brazil was carried out in 1968.[1] In 1993, Lecerda *et al*. performed the first OLT in the Northeastern region of Brazil. Since 1998,[2] in this large region of the nation, an effective and uninterrupted OLT center has been functioning in a university hospital (Oswaldo Cruz University Hospital – OCUH).[1] Although in recent years the amount of centers providing liver transplant (LT) has significantly increased in this country, OCUH LT-Center is still the most productive and experienced across the Northern and Northeastern regions. Even today, this is the only center in that region performing OLT in children, and extensively employing conventional OLT technique with no portal systemic shunt. In this study, we presented outcomes of 302 cases which have undergone deceased and living donor LT since the program started in our center in April 1998.

MATERIALS AND METHODS

The records of 302 patients who underwent OLT in the OCUH from August 1998 to December 2008 were reviewed. All operations were carried out by the same surgical team. Patients with acute liver failure below 16 years olf, living donor transplantation, split liver transplantation, domino liver transplantation, intraoperative deaths, and incomplete records were excluded from survival and results analysis. The procedure for liver graft recovery from deceased donors followed the protocol for our standard surgical technique. The grafts were perfused using Belzer or Celsior

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Recebido em: 11.05.2010 **Aceito em:** 25.06.2010

solutions and packed up to the moment of the liver implant.

Liver transplant recipients underwent hepatectomy with inferior vena cava preservation (piggyback fashion) or conventional technique, both with no venovenous bypass. Conventional hepatectomy technique requires clamping of both the portal flow from the viscera and vena cava flow from the lower body, whereas the piggyback technique requires clamping of portal flow only, reducing the duration of the ischemia, since it requires one less anastomosis before reperfusion compared to the conventional technique. The use of conventional or piggyback technique was the surgeon's choice. The pedicle elements were anastomosed using standard techniques. Immunosuppression was achieved using tacrolimus, mycophenolate mofetil, and corticosteroids. We weaned patients off corticosteroids as soon as possible based on clinical and laboratory evaluations, except in cases of autoimmune hepatitis, primary biliary cirrhosis, and primary sclerosis cholangitis.

Morbidity was assessed by analyzing the incidence of biliary, vascular, septic, and renal complications within 6 months after LT. Acute renal failure was considered if recipients required hemodialysis. Biliary complications were defined by stenosis if a decrease in biliary duct diameter could be confirmed by cholangiography or magnetic resonance image (MRI) of the biliary duct in the presence of clinical or laboratorial cholestasis, biliary leakage if peritoneal bile collection was diagnosed at reoperation, abdominal computerized tomography (CT) or ultrasound. Portal and hepatic artery thrombosis was diagnosed using abdominal ultrasound and hepatic arteriography, respectively, during routine tests or under clinical suspicion. Sepsis was identified whenever a life-threatening clinical state was caused by an established and attested infection disease. Primary liver failure was diagnosed if there was a liver retransplant indication, and primary dysfunction was identified whenever there was transaminase level of > 2000 IU, both until 7 days following the first LT.

An extended criteria liver scoring system, as suggested by Briceño was used to assess the graft conditions: age of the donor >60 years, ICU stay >4 days, cold ischemia times >13 h, hypotensive episodes <60 mmHg and >1 h, bilirubin >2.0 mg/dl, ALT > 170 U/l, and AST >140 U/l,[3] and were scored with the value of 1. The use of >10 µg/kg/min dopamine doses and >155 mEq/l peak serum sodium were labeled with a value of 2. We considered the graft to be an extended criteria graft when the score reached 3 (i.e., ≥ 3).

The cumulative patient's survival rate was calculated according to the Kaplan–Meyer method. Data of surgical periods were shown as mean and standard deviation or median and range, when appropriate. Calculation was performed using the Prism 4.0 software (GraphPad, San Diego, California, USA).

RESULTS

A total of 302 patients underwent OLT during such period. Among the 302 cases, 195 (64.5%) cases underwent OLT with graft obtained from deceased donors and were considered to the analysis of survival and results. The causes of exclusion and the LT category are listed in Table 1. Brain traumatic injury and brain hemorrhage were the most common causes of brain death (Table 2). We used 63.5% of extended criteria grafts, i.e., grafts with Briceño scoring system of ≥3 131 (67.2%) of LT male recipients. The patients' diagnostics are listed in Table 3. It can be observed that viral hepatitis is the most significant diagnostic among liver graft recipients. In 64.1% of all cases, OLT using conventional techniques with no venovenous shunt was the surgeon's choice for most severe cases (Table 4), which may be due to the fact that the surgical team felt comfortable using this technique. Furthermore, a short cold ischemia time (Table 4) is result of a high degree of surgical planning and strong cooperation among members of the surgical team. Reoperation was carried out under postoperative bleeding, hepatic abscess, and ischemic necrosis of the liver cases (Table 5). Postoperative complications are shown in Table 5, and the overall 1-year patient survival rate was 76.4% (Figure 1).

Table 1 - *Liver transplantation category and causes of exclusion*

Parameters	n
Decesead donor - Adult	195
OLT recipient under 16 year-old	59
Acute liver failure	8
Intraoperative deaths	3
Living donor Liver transplantation	2
Portocaval hemi transposition	2
Split liver transplantation	2
Sequential liver transplantation	5
Double transplant (Liver/Kidney)	1
Retransplantation	10
Incomplete data	15

Table 2 - *Liver donor demographic data*

Parameters	n
Donor causes of death	195
Brain hemorrhage	100 (53.2%)
Traumatic Brain Injury	67 (35.6%)
Others	21 (11.2%)
Age (yr)	36.7±14.4
Weight (kg)	68.4±14.2
Graft macrosteatosis	68 (34.8%)
Graft weight	1.477±370g
Graft weigth/ recipient weight	2.15±0.78

Continuous data are present as mean±SD

Table 3 - *Hepatic liver transplantation recipients demographic data*

Liver transplantation recipient diagnostic	N (%)
Viral hepatitis	52 (26,7%)
Hepatocarcinoma	47 (24,1%)
Alcohol cirrhosis	32 (16,4%)
Cholestatic disease	19 (9,7%)
Cryptogenic cirrhosis	22 (11,3%)
Others	23 (11,8%)
Gender	
Male	131 (67.2%)
Age (Yr)	50.31±13.6
Weight (kg)	71.2±15.8
IMC	25.9±4.6
ABO blood	
O	88 (45.1%)
A	77 (39.5%)
B	21 (10.8%)
AB	09 (4.6%)
Child-Pugh Class	
A	40 (20.5%)
B	94 (48,7%)
C	60 (30,8%)
MELD	15.8±5.2

Table 4 - *Operative characteristics*

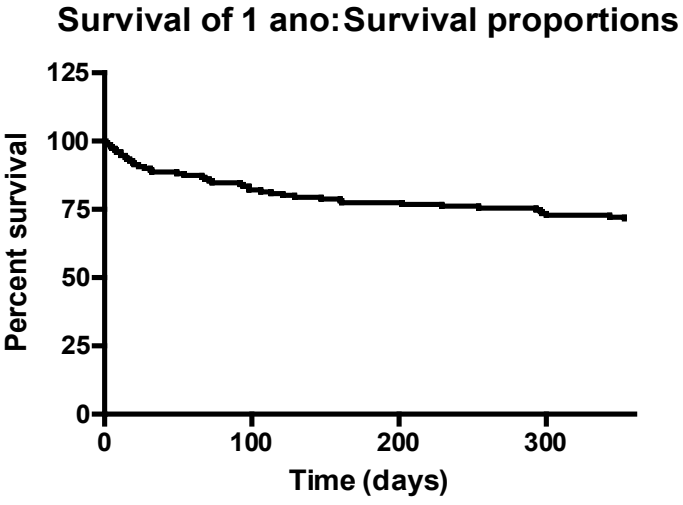
Parameters	N
Type of surgery	
Conventional technique without venovenous bypass	125 (64,1%)
Piggyback technique	70 (35,9%)
Biliary anastomosis	
Choledochocholedochostomy without T tube	157 (80.5%)
hepaticojejunostomy	38 (19.5%)
Surgical time	
Operative time	6h 51min ±2h 6min
Cold ischemia time	6h 17 min±2h23min
Warm ischemia time	51min±15min
Blood Transfusion Requirement	(units)
Packed Red Blood Cell	3,9 (0-27)
Fresh Frozen Plasma	5,1 (0-32)
Platelet (units)	4,4 (0-30)

Surgical times are presented as mean ± SD; Blood transfusion requirement are presented as median (range).
Surgical time, total operation time – from incision until closure of the abdomen; cold ischemia time – from the in situ infusion of the donor organ until the liver is removed for ice for implantation; Warm ischemia time – time between the liver is removed from ice untiluntil reperfusion via portal vein.

Table 5 - *Postoperative evolution*

Parameter	1º/5º postoperative day (mean±SD)
AST (U/L)	1352.7± 2208.6/134.4±197
ALT (U/L)	890.5±1.039.6/440.7± 497
Prothrombine time (INR)	2.30±1.0/1.3±0.4
Creatinine (mg/dL)	1.18±0.8/1.37±1.0
Orotracheal tube withdrawn time	**N**
Immediately	51 (26%)
Less than 6 hour	63 (32.8)
Between 6 and 12 hours	42 (21.9%)
More than 12 hours	36 (18.4 %)
Complications	
Sepsis	19 (8.25%)
intra-cavitary postoperative Bleeding	14 (7.1%)
Biliary leakage	5 (2.5%)
Biliary stenosis	18 (9.2)
Hepatic artery thrombosis	14 (7.22%)
Vena Porta thrombosis	3 (1.55%)
Reoperation (not bleeding)	20 (10.2 %)
Primary liver failure	3 (2.58%)
Primary dysfunction	8 (4.1%)
Acute renal failure	18 (9.7%)

Figure 1 - *One-year-patient survival curves for liver transplantation recipients.*



DISCUSSION

This retrospective study included a series of patients who underwent OLT up to December 2008 in the first LT center located in the poorest region of Brazil. We worked in a public hospital, thoroughly

paid by public resources and providing medical assistance to the poorest layer of the society. There are many markers characterizing the profile of this single center. We analyzed only the outcomes of adult LT recipients from deceased donors to reduce bias. Currently, this is the only LT center all over the Northern/Northeastern Brazil, performing LT in children.[4] Children from the poorest region of the country who had moved to more developed states in Brazil in order to achieve medical care have now a medical center where they can attain means to their disease. Although this fact represents an important improvement in medical and social assistance for these children often from unassisted families, only 56 of them were transplanted by us in the last 10 years. This fact can be explained by the severe shortage of organ donors compatible with the children's weight. This issue has been partially managed by the implementation of the Meld criteria for organ allocation since July 2006, which has favored children on the waiting list for organ donation.

This LT center has a significant experience, using conventional technique without venovenous bypass, because in the early days of its conception, many logistic restrictions had to be overcome. Believing that liver transplantation could be safely done with no venovenous by pass,[5,6] this surgical team was encouraged to initialize the liver transplantation program even though a venovenous bypass could not be carried out due to technical constraints. Thus, with the increasing experience in using such technique, it became the most frequent and safe option to be employed by the surgical team, even when dealing with the most severe cases. In our records, we have not observed severe complications resulting from OLT using conventional technique without venovenous bypass, when compared with OLT using piggyback technique.[5]

Furthermore, we attained a rather short cold ischemia time. Although the scientific publication on LT sets that cold ischemia time can be extended up to 14 h using Belzer or Celsior solutions without posing a harm to the graft or to the OLT outcome,[7-10] we effectively believe that shortening of the cold ischemia time can improve outcomes of the OLT. Hence, we strived to reduce the cold ischemia time through a well-organized synchronization between the liver donors' surgery and the recipient LT. This efficient management of LT practice made it feasible to keep the cold ischemia time within 6–7 h.

The 1-year survival rate was 76.4%, which is lower than the ones demonstrated by top LT centers around the world.[11] Nevertheless, we presume that if data survival after OLT is right, it is indispensable considering the mortality on the waiting list for organ donation. Thus, in order to decrease mortality on the waiting list, we employed extended criteria liver donors. This medical option is strongly based on published data certifying that patients who suffer from terminal liver disease can benefit from LT even using grafts from extended criteria donors.[12,13] Although this OLT policy may have a beneficial effect over the waiting list mortality by offering a chance of OLT to more patients, it may have some impact over 1-year survival after OLT, because more severe patients may receive a graft that may not be the optimum choice.

Complications, primary liver failure, need of blood products, and in-hospital time observed in our study were not different from those published in earlier studies.[14-18] This transplantation center has witnessed few cases of live donor and split OLT. Ethical reasons concerning live donor safety have limited the indication of this kind of OLT in a few cases, and split LT may probably be a good choice to increase the pool of grafts to OLT in the near future. Besides, our center has the same difficulties as others in Asia and in the rest of Latin America, such as shortage of deceased donor liver grafts, lack of financial coverage, education and organization.[19,20] Furthermore cultural and religious barriers restrict the amount of transplants in Asian centers.[21]

CONCLUSIONS

Although this study has a few limitations, including the fact that it was a retrospective study, it has an interesting historical significance. Here, we reported the 10-year outcomes of the first LT center functioning in the less developed region of Brazil. It is amazing to note that just 11 years ago, patients needing LT all over the Northern/Northeastern parts of Brazil had no other treatment option than going to centers located in more developed Brazilian states or even abroad. Thus, the results discussed here support the conclusion that it is feasible to provide a high-quality public medical assistance in an efficient and continuous manner in less developed areas of Brazil.

RESUMO

Objetivo: O objetivo deste estudo é analisar a experiência de 10 anos de um centro transplantador em Pernambuco, nordeste do Brasil. **Métodos:** Dados foram retrospectivamente coletados de arquivos médicos de 302 pacientes que foram submetidos a um transplante ortotópico de fígado entre 1998 e 2008 no Hospital Universitário Oswaldo Cruz, Pernambuco, Brasil. Analisamos apenas os resultados e curva de sobrevida de 195 transplantes hepáticos com receptores adultos de doadores falecidos. **Resultados:** Dados relacionados ao doador de fígado, aspectos técnicos da cirurgia e evolução pós-operatória dos pacientes transplantados são apresentados e discutidos. Esse centro tem uma experiência significante em transplante hepático usando a técnica convencional sem bypass venovenoso. O manejo eficiente da prática do transplante hepático tornou factível permitir a isquemia fria dentro de seis a sete horas. Devido à escassez de órgãos, usamos uma grande quantidade de critérios estendidos de doador de fígado. **Conclusão:** É possível proporcionar assistência médica pública de alta qualidade de forma eficiente e contínua em áreas menos desenvolvidas do Brasil.

Descritores: Transplante; Sobrevida; Fígado.

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