

Experience of Virgen De Las Nieves University Hospital in Liver Transplantation Using Uncontrolled and Controlled Donors after Cardiac Death

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Abstract

The imbalance between the number of candidates to liver transplantation (LT) and the number of liver grafts (LG), leads to increase waiting list mortality. Due to this, it is necessary to explore new donation sources in order to expand the donor pool.

The use of LG from donors after cardiac death (DCD) is an alternative source of donation with a promising and interesting potential.

The aim of this study is to describe initial outcomes of our experience with uncontrolled and controlled DCD. An observational, prospective study was conducted to analyze the variables of ten cases in this donation types in our center, from 2011 to November 2014.

After the analysis of results, we have only obtained two deaths (one in each group). Actually, the other patients are alive without any complications.

Owing to low specific complications rate and high survival rate, we conclude that, in spite of the limited size in our serie, results coincide with which has found in larger series. Hence, we propound to use this alternative donors source. It is capable to satisfy an ever-growing demand, with promising outcomes. However, DCD shall not replace conventional donors.

Keywords: Donors after cardiac death; Liver transplantation; Normothermic Extracorporeal Membrane Oxygenation (NECMO); Ischemic cholangiopathy

Abbreviations: BMI: Body Mass Index; DBD: Donors after Brain Death; DCD: Donors after Cardiac Death; ERCP: Endoscopic Retrograde Cholangiopancreatography; LG: Liver Graft; LT: Liver Transplantation; MELD: Model for End-Stage Liver Disease; NECMO: Normothermic Extracorporeal Membrane Oxygenation; NRP: Normothermic Regional Perfusion; PNF: Primary Non-Function; SETH: Sociedad Espanola de Trasplante Hepatico

Introduction

The imbalance between the number of candidates to liver transplantation (LT) and the number of liver grafts (LG) leads to increase waiting list mortality all over the world [1]. Due to increasing indications of LT, decreasing the number of donors after brain death (DBD) as well, it is necessary to explore new donation sources in order to expand donor pool, considering non-conventional donors such as: split liver, domino donation, living donor, and donors after cardiac death (DCD).

The use of LG from DCD is an alternative source of donation with a promising and interesting potential [2]. Initially, this activity has developed in Spain by means of the uncontrolled DCD, or Maastricht

type II donation. Controlled DCD or Maastricht type III donation was dropped because of ethical reasons in our country at first [3,4]. Recent changes in legal framework, in line with draft bill about the end-of-life rights, could favour the development of this type of donation [1].

In 2013, 159 asystolic donations took place in 21 specialized centers in Spain. They represented 10% of all donations that occurred [1,4]. Spain brings the most experience in uncontrolled DCD (Maastricht II) all over the world [5]. Virgen de las Nieves University Hospital is the only center in all of Andalusia that has developed a strict protocol for Maastricht II and III donation. This protocol provides the use of preservation technique with normothermic regional perfusion (NRP), also called normothermic recirculation or normothermic extracorporeal membrane oxygenation (NECMO) with promising short and medium-terms outcomes [6].

Methods

A prospective observational study has been performed, including all patients who underwent LT with LG from uncontrolled and controlled DCD in our center from 2011 to November 2014. Clinical variables were recorded for both donors and recipients. The following variables were included: characteristics of donors (demographics, clinicals and analyticals); characteristics of donation and preservation process for both uncontrolled and controlled DCD and surgery of LT features. Incidence of biliary complications and the presence of early allograft

dysfunction were analyzed in recipients. Data was analyzed with IBM SPSS Statistics 19 software.

The protocol of our center has been performed based on strictly recommendations of the Consensus of Spanish Liver Transplantation Society (SETH) in 2012 [1].

Results

Ten patients underwent LT with LG from uncontrolled (Maastricht II) and controlled (Maastricht III) DCD. All transplant recipients had a minimum 3 months follow-up.

Maastricht type II donation

Donors: Six LG were harvested (5 males, 1 female). Mean age and Body Mass Index (BMI) were 45 years, and 28 kg/m² respectively. Mean pump time was 175 minutes. Mean warm ischemia time was 125 minutes and mean cold ischemia time was 287 minutes.

Recipients: Two of the patients were on the waiting list because of primary biliary cirrhosis; two by alcoholic cirrhosis; one hepatocellular carcinoma caused by hemochromatosis and the last one from cryptogenic cirrhosis. Four of the patients were male. Mean Model for End-Stage Liver Disease Index (MELD) was 16. Only one patient suffered post-reperfusion syndrome. During the early post-operative period there was one case of mild acute rejection with good response to immunosuppressive adjustment. One of the patients died during the first 24 hours following coagulopathy and refractory hemorrhagic shock. During the late post-operative period, one of the patients developed stenosis in the bile duct anastomoses. It was treated by endoscopic retrograde cholangiopancreatography (ERCP) and stent with good results. Currently, five of them are alive without any complications.

Maastricht type III donation

Donors: Four LG were harvested. Mean age and BMI were 51 years and 28.6 kg/m², respectively. Mean pump time was 44 minutes. The mean of functional warm ischemia and cold ischemia time were 19 and 254 minutes, respectively.

Recipients: Two of the patients were on the waiting list for alcoholic cirrhosis, one caused by hepatitis C cirrhosis and one patient due to chronic Budd-Chiari syndrome. Mean MELD was 16. One patient died at the Intensive Care Unit in the first week after LT. The main cause of death was a septic shock. Three of four patients are still alive without complications.

Discussion

Patients with an irreversible, catastrophic illness have served as non-heart-beating donors after withdrawal of care in a controlled hospital setting and after achieving set criteria for cardiac death [7].

The DCD is an alternative source of donors with comparable results to which have been reported with DBD. Studies comparing recipients of organs from DCD donors with standard brain-dead deceased donors have been variable, with some showing similar outcomes, while other suggest decreased graft and patient survival following receipt of a DCD donor organ [8-11]. However, many of the studies are limited by the fact that they were not randomized, potentially leading to disparate outcomes that were not the result of the type of donor organ.

Spain is the country with the highest activity level in LT from uncontrolled DCD [2]. Our country has begun to use LG from controlled DCD recently, with intriguing prospects [4]. The protocol for controlled DCD is based on that life support is usually withdrawn in the operating room. The patient is observed until the time of death, which is declared by a clinician who is not part of the transplant team. An additional one to five-minute waiting period is mandated before organ retrieval is initiated with femoral artery cannulation and infusion of cold University of Wisconsin storage solution.

The main concern is occurrence of primary non-function (PNF) of the LG and ischemic cholangiopathy, which are dependents on hypoxic-stress [12].

Initial graft function is a major factor influencing the clinical outcome after LT, but a reliable method for assessing and predicting graft dysfunction directly after LT is not available [13].

PNF of the LG is associated with many factors, such as status of donor, quality of hepatic graft, long-term warm ischemia, cold ischemia, primary liver disease, status of liver function of recipients and operative techniques [14]. PNF is manifested by hepatic cytolysis and rapidly rising transaminases, absence of bile production, severe liver-related coagulation deficit, hypoglycemia, high lactate levels, and hepatic hemodynamic instability [15].

Related to our deceased patient due to coagulopathy and refractory hemorrhagic shock (Maastricht II), we cannot totally exclude the diagnosis of PNF of the LG, because PNF can be presented as this manifestation. Nevertheless, we have not confirmed its diagnosis with liver biopsy, which is the most accurate diagnosis.

Furthermore, despite of having daily monitoring of liver function, renal function, blood coagulation function, hemodynamic and respiratory parameters, he had not any rising transaminases or other parameters of liver dysfunction.

One potential way to minimize the ischemia and reduce the complications rate is to restore circulation with oxygenated blood to the abdominal organs in situ, using NECMO at body temperature, as we have performed in our series.

It was adopted in a prospective case-control study on adult patients undergoing LT, and the results are encouraging [16].

Re-transplantation is also higher among these patients, whose main cause is the ischemic cholangiopathy. Despite this fact, in last series, the prevalence of these complications has been reduced substantially, as well as its impact on the LG and recipients survival. In the most recent series, survival is higher than 80% in the first year after LT, and ischemic cholangiopathy rate is lower than 3% [12,17].

Although there may be an increased risk of graft loss and biliary complications, judicious use of DCD donors could provide a substantial number of needed organs. According to some estimates, this practice could expand the organ supply by up to 1000 livers per year [7].

In our experience we had no cases of severe and diffuse ischemic cholangiopathy or re-transplantation in recipients of LG from uncontrolled and controlled DCD, although we cannot exclude one case of PNF of the LG. In spite of a short time of follow-up in our serie, the graft and recipient survival were acceptable. The application of our strict protocol for asystolic donation contributes to obtain a low rate of complications.

Conclusions

In our experience, the number of complications after LT from DCD has been low and survival rates has been acceptable (80% survival in 3 months).

These results are similar which obtained with LG from conventional donors. However, DCD shall not replace conventional donors.

The main limitation of our study was a short sample size from a unique center. Therefore we need to obtain studies with high level of evidence.

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