



Emergency Organ Transplantation in Spain: Liver Emergency and Outcomes

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ABSTRACT

The 2 main indications for emergency liver transplantation are severe acute hepatic insufficiency and emergency retransplantation. In Spain, since the creation of the National Transplant Organisation (NTO), known as “the Spanish model,” there have been high rates of donation, with a mean of 33.9 donors per million inhabitants in 2003 and 34.6 donors per million inhabitants in 2004. According to data provided by the NTO, there were 169 liver emergencies in the 2-year period 2003–2004. The time on the waiting list in an emergency situation was limited; 82.8% of cases were resolved in less than 48 hours. During this 2-year period, there were 2077 liver transplantations, including 128 emergency patients, which accounted for 6.1% of transplantations.

THE 2 MAIN indications for emergency orthotopic liver transplantation (OLT) are severe acute hepatic insufficiency (SAHI) and emergency retransplantation. SAHI was defined by Trey and Davidson¹ in 1970 as an acute liver disease that develops encephalopathy in the first 8 weeks after the onset of symptoms, without previous liver disease; it is potentially reversible. In recent years,^{2,3} the terms hyperacute, acute, and subacute hepatic failure have been introduced with clinical and prognostic implications. The most common causes of SAHI are acetaminophen ingestion after a suicide attempt in English-speaking countries, and viral infection, especially due to hepatitis B and C virus, in the rest of the world.^{4,5} Other causes are Wilson’s disease, fatty liver of pregnancy, surgery-related acute ischemia, *Amanita Phalloides*, or *Lepirotas* poisoning.⁶

Patients with SAHI present with hemodynamic alterations, hypoglycemia, and alterations in coagulation due to a deficit in the synthesis of hepatic factors associated with increased peripheral consumption and even disseminated intravascular coagulation.⁷ Prothrombin time and factor V are common indicators to assess liver damage.⁸ Encephalopathy may appear at any time in the evolution of the disease progressing to grades III–IV, when the patient risks developing cerebral edema, which represents the main cause of death. The mortality rate of patients with grade III–IV encephalopathy ranges from 75% to 5%. Only emergency OLT may reverse this high mortality, achieving survival rates of 50–80% of cases. However, the difficulty in such critical situations is obtaining OLT, at the right time, not too early when there are possibilities of spontaneous recovery, or too late when the patient has irreversible

cerebral lesions. Some authors^{9–12} have published SAHI prognosis models based on multivariate analyses applied to clinical and analytical variables, including the Clichy criteria, by Bernuau et al¹⁰ and the London criteria, by O’Grady et al.¹¹

Another issue of great importance is the availability of an organ at the time OLT is indicated. Various authors¹³ consider that the final assessment should be made when the graft becomes available. OLT would be performed if there are no contraindications of irreversibility of cerebral lesion, sepsis, multiorgan failure, or clinical factors suggesting spontaneous recovery.

Emergency liver retransplantation (ReTx) is indicated when there is irreversible graft failure.^{14–17} The main causes are primary nonfunction (PNF), complications related to the surgical technique,¹⁸ and hyperacute or acute rejection. The main cause of mortality in emergency ReTx is infectious complications leading to the development of sepsis and multi-organ failure. ReTx should always be done before multi-organ failure, because it is a poor prognostic factor in all series.^{12,13,15,19}

In Spain, since the creation of the National Transplant Organization (NTO), there have been high rates of donation, namely a mean of 33.9 donors in 2003 and 34.6 donors

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per million in 2004.²⁰ In collaboration with various OLT groups in Spain, the NTO has designed a Code Zero, which since 1988 has enabled more than 70% of patients requiring an emergency liver to undergo transplantation within 48 hours. Code Zero of the NTO includes the following: (1) severe acute hepatic insufficiency in the absence of previous hepatopathy, and (2) retransplantation required within 7 days. It implies the following (1) national priority, (2) acceptance of any weight except in children, with the possibility of a partial transplant depending on the criteria of the team, and (3) length of stay on this code, 3 days, which can be extended by explanation from the team. In the event of several Code Zero emergencies coinciding, the organs are adjudicated with the following priority: (1) child recipients, and (2) order of inclusion. Performing a transplantation via this code implies that the team's shift is passed on, as with an elective transplantation.

RESULTS

According to the data provided by NTO, there were 169 liver emergencies in the 2-year period 2003–2004 (86 in 2004), of which 140 were adult patients (69 in 2004) and 29 children (17 in 2004). The most common diagnoses were acute hepatic insufficiency in 107 cases and retransplantation in 60 cases. The 2 remaining cases were patients in an anhepatic situation during surgery. The time on the waiting list in an emergency situation was limited; 82.8% of the cases were solved in less than 48 hours.

During this 2-year period, we performed 2077 OLT, of which 1037 were done in 2003 and 1040 in 2004. Of the 2077 OLT, 128 were patients in emergency situations, which accounted for 6.1%. Furthermore, the 128 transplantations were performed in the 169 liver emergencies, meaning that 75.7% of the emergencies were resolved with a transplantation. The distribution of blood groups between donors and recipients in emergency situations revealed a predominant use of isogroup grafts (62.5% of the cases) and compatible grafts (35.9% of the cases). Only 1.6% of cases were incompatible grafts.

According to the 6th Report of the Spanish Liver Transplant Register,²¹ the survival rates of 479 patients undergoing emergency OLT between 1991 and 2002 were 77.3%, 71.7%, 66.5%, 63.3%, and 54.9% at 1, 3, 12, 36, and 120 months, respectively. The survival rates of the grafts (n = 827) in the same period were 70.5%, 62.1%, 56%, 52%, and 40.4% at 1, 3, 12, 36, and 120 months, respectively. If we analyse graft survival according to ABO compatibility in emergency OLT, the survival rate of incompatible grafts was less than 30% at 3 years, ($P < .01$; Table 1).

Last, it should be noted that there are various factors in emergency OLT that increase patient mortality and reduce graft survival. These factors suggest a late clinical stage prior to transplantation, such as grade of encephalopathy, renal insufficiency, or suboptimal conditions of the donor liver (steatosis, split liver, ABO incompatibility, and so on).

Table 1. Graft Survival According to ABO Compatibility in Emergency OLT (1991–2002)²¹

Survival	1 mo	3 mo	12 mo	3 mo	10 mo
Isogroup (n = 558)	74.2%	65.3%	59.7%	55.1%	39.5%
Compatible (n = 192)	66.7%	59.8%	54.9%	53.7%	50.5%
Incompatible (n = 77)	53.3%	46.8%	35.1%	28%	21.6%

NOTE: Global Wilcoxon test ($P < .01$). Incompatible vs rest ($P < .01$). Compatible vs Isogroup ($P = .3$).

DISCUSSION

Emergency OLT is the only therapeutic alternative for patients with SAHI or requiring a ReTx in the immediate postoperative period. Within the Spanish National Health System, the NTO, with its organizational model known as “the Spanish model,” has enabled more than 70% of patients requiring an emergency OLT to access an organ, generally of appropriate isogroup, within 48 hours of being included on the national waiting list.

REFERENCES

1. Trey C, Davidson CS: The management of fulminant hepatic failure. *Prog Liver Dis* 3:282, 1970
2. O'Grady JG, Schalm S, Williams R: Acute liver failure: redefining the syndromes. *Lancet* 342:373, 1993
3. Williams R: In Lee WM, Williams R (eds): *Acute Liver Failure*. Cambridge, Cambridge University Press, 1997, p 1
4. Hoofnagle JH, Carithers RL, Shapiro C, et al: Fulminant hepatic failure: summary of a workshop. *Hepatology* 21:240, 1995
5. Schiodt FV, Atillasoy W, Shakil AO, et al: Etiology and outcome for 295 patients with acute liver failure in the United States. *Liver Transplant Surg* 5:29, 1999
6. Ramirez P, Parrilla P, Sánchez-Bueno F, et al: Fulminant hepatic failure after Lepiota mushroom poisoning. *J Hepatol* 19:51, 1993
7. Shakil AO, Kramer D, Mazariegos GW, et al: Acute liver failure: clinical features, outcome analysis, and applicability of prognostic criteria. *Liver Transplant* 6:163, 2000
8. Izumi S, Langley PG, Wendon J, et al: Coagulation factor V levels as a prognostic indicator in fulminant hepatic failure. *Hepatology* 23:1507, 1996
9. O'Grady JG, Alexander GJM, Hayllar KM, et al: Early indicators of prognosis in fulminant hepatic failure. *Gastroenterology* 97:439, 1989
10. Pauwels A, Mostefa-Kara N, Florent C, et al: Emergency liver transplant for acute liver failure: evaluation of London and Clichy criteria. *J Hepatol* 17:124, 1993
11. Anand AC, Nightingale P, Neuberger JM: Early indicators of prognosis in fulminant hepatic failure: an assessment of the King's criteria. *J Hepatol* 26:62, 1997
12. Brandsater B, Hockerstedt K, Friman S, et al: Fulminant hepatic failure: outcome after listing for highly urgent liver transplantation—12 years experience in the Nordic Countries. *Liver Transplant* 8:1055, 2002.
13. Wiesner RH: MELD/PELD and the allocation of deceased donor livers for status I recipients with acute fulminant hepatic failure, primary nonfunction, hepatic artery thrombosis, and acute Wilson's Disease. *Liver Transplant* 10(suppl 2):S17, 2004
14. Rosen HR, Madden JP, Martin P: A model to predict survival following liver retransplantation. *Hepatology* 29:365, 1999
15. Azoulay D, Linhares MM, Huguet E, et al: Decision for retransplantation of the liver. *Ann Surg* 236:713, 2002

16. Biggins SW, Beldecos A, Rabbin JM, et al: Retransplantation for hepatic allograft failure: prognostic modelling and ethical considerations. *Liver Transplant* 8:313, 2002
17. Yoo HY, Maheshwari A, Thuluvath PJ: Retransplantation of liver: primary graft nonfunction and hepatitis C virus are associated with worse outcome. *Liver Transplant* 9:897, 2003
18. Sánchez-Bueno F, Robles R, Ramirez P, et al: Hepatic artery complications after liver transplantation. *Clin Transplant* 8:399, 1994
19. Adam R, McMaster P, O'Grady JG, et al: Evolution of liver transplantation in Europe: report of the European Liver Transplant Registry. *Liver Transplant* 9:1231, 2003
20. Organizacion Nacional de Transplantes (ONT): Memoria de Actividades ONT 2003 (1ª parte). Trasplante hepático. *Rev Esp Transplantes* 13:71, 2004
21. Registro Español de Trasplante Hepático (RETH). 6ª Memoria de Resultados. 1984–2002. Equipos españoles de trasplante Hepático. Available at: <http://www.ont.es>