



SCIENTIFIC LETTER

Third liver transplant: How far should we go?☆

Tercer injerto hepático: ¿hasta dónde deberíamos llegar?

J. Gutiérrez Gutiérrez*, J. Czapka Mital, T. Grau Carmona

Servicio de Medicina Intensiva, Hospital 12 de Octubre, Madrid, Spain

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Dear Editor,

Retransplantation is a therapeutic option when a first liver graft fails. The second operation is technically more complex, and survival is shorter than that of the first graft, but in some cases it is the only treatment option for the patient.^{1,2} A series in our center showed retransplanted patients to have a 5-year survival rate of 64%, versus over 80% in the case of patients with a single transplant.³ We report two patients subjected to three consecutive liver transplants, and describe the evolution in each case.

The first case corresponded to a 67-year-old male with a history of stage A5 cirrhosis (Child-T-Pugh classification) and a Model End-Stage Liver Disease (MELD) score of 15, secondary to hepatitis C and hepatocarcinoma. The patient received a graft from a brain dead donor (BD), with a good immediate postoperative course. After 48 h hepatic artery thrombosis developed, with multiple infarctions, and the patient was entered on the retransplantation list (emergency 0). After two days he received a graft from a non-heart beating donor, with a poor intraoperative course (hypovolemic shock with multiple transfusions and prolonged

ischemia and clamping times, with secondary intestinal necrosis). In the immediate postoperative period the patient presented refractory shock and multiorgan failure secondary to primary graft failure. In view of the poor clinical situation, he was again entered on the retransplantation list, with the start of Molecular Adsorbent Recirculating System (MARS) therapy. The patient received a graft from a BD donor, with prolonged surgical times due to technical difficulties in the surgical bed. The postoperative course was poor, with multiorgan failure and a need for respiratory support, prolonged weaning and tracheostomy, and extrarenal replacement support. Hemodynamically, high dose amines were required, and the patient suffered intestinal perforation and ischemia, with associated rhabdomyolysis. The chronic multiorgan failure persisted, with invasive *aspergillosis* overinfection. The patient died after two months in the Intensive Care Unit (ICU).

The second case corresponded to a 37-year-old male with a first liver transplant at 17 years of age due to Budd-Chiari syndrome secondary to polycythemia vera, in the context of chronic rejection and with a MELD score of 24. The patient received a second graft from a BD donor. Biliary tract complications developed, with intraabdominal abscesses and the isolation of multiresistant bacteria, early renal failure requiring extrarenal replacement therapy, and hepatic artery thrombosis despite attempted surgical recanalization and anticoagulation. The patient developed ischemic hepatitis and was placed on the waiting list for retransplantation. During the waiting period he suffered hemorrhagic shock secondary to gastrointestinal bleeding

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* Corresponding author.

E-mail address: gutierrezgju@gmail.com
(J. Gutiérrez Gutiérrez).

and partial thrombosis of the portal vein. In view of the impossibility of administering systemic anticoagulation therapy, with secondary graft failure, we decided to enter the patient on the waiting list for retransplantation with regional priority status. The patient entered the operating room with chronic multiorgan failure and a MELD score of 36. He received the third transplant 1.5 months later, with a poor posterior course, and presenting hemorrhagic shock secondary to upper digestive bleeding that required three reoperations and prolonged mechanical ventilation. Absence of flow in the hepatic artery was evidenced, with areas of liver necrosis, intraabdominal infection due to multiresistant organisms, and with the abdomen open and under hypothermia. The patient finally suffered hemorrhagic shock due to gastrointestinal bleeding, not amenable to surgical management, and limitation of therapeutic effort was decided. The patient died after 2.5 months of hospital stay.

Although retransplantation may be the only option for patients of this kind, the published series confirm a decrease in survival with multiple grafting procedures.⁴ Retransplantation is associated to an increased number of complications and prolonged hospital stays, with long or insufficient recovery periods. In order to avoid futile organ use, attempts have been made to evaluate the factors underlying graft loss and/or mortality risk. Graft quality can be assessed by calculating the Donor Risk Index (DRI),⁵ though in some cases low indices are not correlated to the poor prognosis predicted by other described variables. These particularly include renal failure and/or a need for renal replacement therapy before retransplantation, prolonged mechanical ventilation times, or a high or rising MELD score,⁶ as well as the use of vasopressor drugs, preoperative sepsis or urgent retransplantation priority.⁷ Furthermore, other groups underscore the importance of qualitative variables such as quality of life or mental status before retransplantation.⁸

Both of our patients received a third graft of good quality, with low DRI scores, though they also presented many of the unfavorable clinical variables (need for renal replacement therapy and vasoactive drug support, preoperative sepsis, multiorgan failure and prolonged mechanical ventilation). The transplant team did not consider the contraindication of retransplantation for a number of reasons, and there was no formal request to the hospital Ethics Committee. In using severity scores such as the APACHE II or SOFA, we probably would not have contemplated surgery other than transplantation, even if representing the only alternative to the limitation of therapeutic effort. Our dilemma as intensivists was whether or not to support the criterion of the surgical team, and the cause of our frustration was the poor outcome of the third organ transplant, leading us to present this letter to the editor.

How far should we go with patients of this kind? There is probably no evident answer. The data of the Spanish National

Transplant Organization (ONT) in Madrid, with survival rates following third transplantation of 55%, 46% and 37% after one, 5 and 10 years, respectively,⁹ and our own experience, question whether the prognostic indices are enough to avoid futility. We therefore should take into account scales such as the APACHE II and SOFA, and these patients moreover should be considered by the hospital Ethics Committee, either upon request from any of the implicated Departments, or through regional coordination supervision. We have reasonable doubts that the principles of no ill intention and distributive fairness have been adequately observed in these cases. The presentation of these patients aims to draw attention to the need to consider this issue in order to have all the information available in decision making, and thus offer the best possible outcomes for our patients and their families.

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