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IMPACT OF LIVER TRANSPLANTATION ON SURVIVAL IN PUGH B ALCOHOLIC CIRRHOTIC PATIENTS: A MULTICENTER RANDOMIZED TRIAL. *Jean-Philippe Miguet, Claire Vanlemmens, Unit of Liver Transplantation, Besançon, France; C Milan, Centre d'épidemiologie de Population PI 106, Dijon, France; Michel Messner, Hôpital Pontchaillou, Rennes, France; Anne Minello, Le Bocage, Dijon, France; Christophe Duvoux, Henri Mondor, Créteil, France; Vincent Di Martino, GH Pitié-Salpêtrière, Paris, France; J-M Perarnau, Bon Secours, Metz, France; Marie A Piquet, CHU, Caen, France; Georges-Philippe Pageaux, Saint-Eloi, Montpellier, France; Sébastien Dharancy, Claude Huriez, Lille, France; Christine Sylvain, Jean Bernard, Poitiers, France; Sophie Hillaire, Beaujon Hospital, Clichy, France; Gérard Thieffin, Robert Debré, Reims, France; Jean-Pierre Vinel, Purpan, Toulouse, France; Patrick Hillon, Le Bocage, Dijon, France; Estelle Naudet-Collin, Georges Mantion, Solange Bresson-Hadni, Unit of Liver Transplantation, Besançon, France*

Background: Liver transplantation(LT) has been universally recognized to improve survival of patients suffering from alcoholic cirrhosis at the Pugh C stage. However, for Pugh B patients no evidence of survival advantage has ever been demonstrated up to now. The aim of the present study was to compare survival in alcoholic Pugh B cirrhotic patients treated by LT (arm I) versus standard treatments (arm II). Methods : Between March 1994 and November 2001, 120 patients (23% women) with a mean age of 49.9 (±1.3) years from 13 centers were randomly assigned to arm I (60 patients) or arm II (60 patients). B and C viral infections, hepatocellular carcinomas or other malignancies as well as contraindications to LT were exclusion criteria. A stratification on investigator center, age, sex and complications of cirrhosis was performed. At inclusion, patients of both arms were quite similar. The reasons for inclusion were refractory ascites (78%), spontaneous bacterial peritonitis (10%), recovery from Pugh C stage (22%), recurrent variceal bleeding (16 %) and spontaneous hepatic encephalopathy (7%). For ethical reasons after randomization, if a patient of arm I improved while awaiting LT, or if he developed a contraindication to surgery, he was dropped from the waiting list; conversely, in arm II, if a patient worsened, LT was proposed. In each arm, patients were followed up every 3 months for 5 years, and all patients completed the study. Immunosuppresion was done according to the protocol of each center. Results: At the end point (April first 2003), 41 patients of arm I were transplanted (28 in the first 6 months) as compared with 15 patients of arm II (3 in the first 6 months). 19 patients of arm I were not transplanted due to disease improvement (n = 6), death in waiting list (n = 6) and occurrence of a contraindication to surgery (n=7). The actuarial survival at 2 years was 73% in arm I and 80% in arm II (p=0.21). An unexpected and worrying result was the high prevalence of extrahepatic malignant tumors in transplanted patients (12 out of 56; 21%) as compared with non-transplanted patients (5 out of 64; 8%) (p=0.03). In transplanted patients, malignancies were throat carcinomas (n=3), bronchus carcinomas (n=3), pancreas carcinoma (n=1), lymphoma (n=1), basal-cell carcinomas (n=3) and squamous-cell carcinoma (n=1), whereas in the non-transplanted patients, malignancies were throat carcinoma (n=1), hepatocellular carcinoma (n=1), prostate carcinoma (n=1), breast carcinoma (n=1), colon carcinoma (n=1). The incidence of malignant tumors was higher in transplanted patients than in non transplanted patients (6.99% versus 2.66%; p=0.002).In transplanted patients the risk of tumor was 2.3 times higher than in non-transplanted patients (p=0.004). Malignancies were the causes of death in 6 out of 56 transplanted patients and 2 out of 64 of non-transplanted patients. Conclusion: This first randomized study comparing LT to standard treatment in Pugh B cirrhotic patients did not show better 2-year survival in patients randomized for LT. Moreover, LT was associated with a higher occurrence of extrahepatic malignant tumors.

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A COMPARISON OF IMMUNOSUPPRESSIVE REGIMENS IN LIVER TRANSPLANTATION: PRIMARY SIROLIMUS VS. COMBINATION CALCINEURIN INHBITORS- SIROLIMUS VS. PRIMARY CALCINEURIN INHIBITORS. *Hassan Zaghla, Robert R Selby, Jeffrey A Kahn, Emily Ramicone, John A Donovan, Nicholas Jabbour, Yuri Genyk, Rodrigo Mateo, Singh Gagandeep, Linda S Sher, Linda Chan, Tse-Ling Fong, University of Southern California, Los Angeles, CA*

Background: Sirolimus is a potent immunosuppressive agent that blocks interleukin-2-dependant T cell proliferation. The role of sirolimus in liver transplantation (OLT) is still not well defined.
Aim: To report our experience with sirolimus in OLT recipients who received sirolimus without CNI or in combination with CNI as part of the initial immunosuppressant regimen and to compare the outcomes with patient who received CNI only.
Methods: The medical records of 194 adult patients who underwent OLT between May 1996 and September 2002 were reviewed. They were divided into three groups based on their initial immunosuppressant regimen: Group SA: Sirolimus alone-without CNI (n=31), Group SC: Sirolimus combined with CNI (n=58) and Group CNI without Sirolimus (n=105). The following endpoints were assessed: graft and patient survival, incidence of acute cellular rejection (ACR), renal function including the need for dialysis after transplantation, hematological parameters and the frequency of vascular, biliary, and wound healing complications
Results: One year patient actuarial survival rates were similar; 92.6% Group SA, 98.2% Group SC and 87% Group CNI (p=ns). The incidence of ACR was similar among the three groups; 19% Group SA, 33% Group SC and 26% Group CNI (p=ns). Although baseline mean serum creatinine (Cr) level, was significantly worse in Group SA (Group SA, 2.32 ± 1.54 vs. Group SC, 1.52 ± 1.26 vs. Group CNI, 1.26 ± 0.81 mg/dL, p<0.0001), mean serum Cr among the three groups at one month post OLT was similar (Group SA, 1.29 ± 0.77 vs. Group SC, 1.02 ± 0.55 vs. Group CNI, 1.02 ± 0.51 mg/dL, p=ns). More patients in Group SA required dialysis before OLT (Group SA, 26% vs. Group SC, 9% vs. Group CNI, 5% p=0.003), but at one year post-OLT dialysis rate was similar among the groups (6% Group SA vs. 5% Group SC vs. 3% Group CNI, p=ns). Mean hemoglobin values were lower in Group SA (p=0.0075) while white blood cell and platelet counts were similar in the groups. The incidence of hepatic artery thrombosis (HAT) was similar in the three groups (Group SA, 3.2% vs. Group SC, 1.7% vs. Group CNI, 2.9%). Although biliary leaks occurred at a similar rate (Group SA, 6.4% vs. Group SC, 6.9% vs. Group CNI, 5.7%, p=ns) the frequency of biliary strictures was significantly higher in patients in Group SC (13.9%) vs. Group SA (6.4%) and Group CNI (2.9%)(p=0.028). There was no significant difference in wound healing among the three groups.
Conclusions: Sirolimus is an effective primary immunosuppressant for OLT patients. There was no significant renal protective effect with sirolimus over CNI. Sirolimus was not associated with a higher incidence of HAT and delayed wound healing.

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