TRANSPLANT INTERNATIONAL

ELITA ORAL PRESENTATIONS

EO - 01 SHOULD DONOR AGE BE MATCHED TO MELD OR RECIPIENT AGE IN LIVER TRANSPLANTATION?

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Introduction: The organ shortage lead to an increase use of extended criteria donors. Donor ratio Index (DRI; AJT, 2006)) including the donor age, cold ischemia times and parameters associated with death and resuscitation of the donor has been shown to predict the graft survival. Among the seven variables composing the DRI, the donor age is a key issue in liver transplantation (LT).
Patients and methods: Two centers (Créteil and Milan) provided 508 cases of a first elective non combined liver transplantation in cirrhotic adults between 2005 and 2011. The graft survival was analyzed by Kaplan-Meier and Cox model according to donor and recipient age, MELD score, DRI among many other relevant variables.
Results: The 5-year overall graft survival was 78%. The DRI was higher after 2009 than before (2.2 $\pm$ 0.4 vs. 1.8 $\pm$ 0.3, $P < 0.01$). One hundred and thirty-two patient (26%) received a graft from a donor older than 70. The donor age or the DRI were not correlated to the MELD score, to the age of recipient but it was higher in recipient with hepatocellular. A DRI > 2 was a pejorative factor while the donor age alone was not predictive. Donor >70 lead to similar results whatever the MELD and the age of recipient. PNF and surgical complication were not significantly more frequent. In multivariate analysis, HCC as indication, non-A blood group and recipient age > 60 were independent predictors.
Conclusion: Liver grafts from donors older than 70 gave excellent results independently of the MELD score. There is no reason for matching the liver graft from older donors to the MELD or to the recipient age.

EO - 02 THE AGING LIVER IN THE SETTING OF LIVER TRANSPLANTATION

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Physiological aging: In the absence of liver disease, aging causes reduction in liver size which is approximately 25–35%, resulting in what has been termed "brown atrophy" (1–3). Reduction of hepatic blood flow of approximately 35–40%, as well as reduction of splanchnic blood flow (4,5), as well as nearly 50% reduction in bile flow and bile salt formation (3) are all changes that are observed with aging. Notwithstanding these anatomical alterations brought about by age, the functional capacity of the aging liver is quite conserved, with maintenance of routine liver function tests within normal ranges. Aged livers owe their macroscopic appearance is due to the accumulation of highly oxidized insoluble, cross-linked proteins (lipofucsin) within hepatocytes, which are associated to chronic oxidative stress and a failure to degrade damaged and denatured proteins (6). At a molecular level, progressive telomere shortening with aging was elegantly demonstrated in the study by Takubo and collaborators, analysing liver tissue of 94 subjects aged between 0 and 101 years old, which was similar to the rate observed in the digestive tract mucosa, albeit the latter has a very rapid renewal. Interestingly, however, reduction rate appears to decline upon attainment of middle age (7). Telomere shortening represents a causal factor impairing liver regeneration and accelerating cirrhosis formation in response to chronic liver disease (8).
Increasing age, increasing frequency of comorbidities and polypharmacy: Although the liver might not be directly affected by a primary condition, the prevalence of diseases including cardiopathy, malignancy, hypertension, and diabetes certainly increases with age, and is accompanied by an often substantial number of prescribed medications that can induce liver damage. Pharmacokinetics in the elderly can differ considerably from the conditions under which the drug was originally tested. Oral absorption may be altered due to decreased gastric acid, delayed gastric emptying, and decreased intestinal blood flow, thus altering the onset of action and peak effect of medications. Moreover, advancing age generally entails a decline in muscle mass and an increase in the proportion of body fat, increasing the volume of distribution of lipophilic drugs (9,10). Reduction of hepatic blood flow, reduction in liver mass and intrinsic metabolic activity (including the CYP450 enzymatic system), with phase 1 reactions being much more affected that phase 2 reactions, characterize the hampered drug metabolism observed in the elderly (11). Finally, drug elimination may be altered in ageing due to both hepatic and renal function reduction, potentially increasing circulating levels of the agent, and potentially causing hepatotoxicity.
Natural history of liver diseases in the elderly: The incidence of liver disease increases with age while the ability to withstand a hepatic insult falls with each decade (6). Cirrhosis is a cause of increased mortality from both hepatic and nonhepatic causes in elderly patients (12), and comorbid conditions frequently complicate management. The immunological system undergoes progressive decline in function with increasing age (13), which is clinically translated into an increased susceptibility to infections, neoplasia, and autoimmunity (14–16). On the other hand, this particularity allows for some degree of tolerogenicity, which is beneficial in the liver transplant setting, with lower rates of rejection and lower immunosuppressive drug demands in the elderly.

Hepatitis A has been associated with higher mortality and higher frequency of acute liver failure in the elderly (17). In hepatitis C, it has been shown that age at infection plays a crucial role in fibrosis development; while fibrosis rate is low when individuals become infected before 20 years of age, intermediate in those infected between 21 and 40 years of age, and increased in those infected between 40 and 50 years of age, patient age over 50 years at infection determines an accelerated fibrosing course (18,19). In the United States, due to the prevalence of HCV-related liver disease distribution according to birth year cohorts, especially those born in or before 1955, it is expected that by 2015 an increasing proportion of patients newly registered on the liver transplant waiting list with HCV, will have HCC and will be ≥60 years old (20). In the United States, seroprevalence of past/present Hepatitis B infection markedly increase with age; reportedly individuals 50 years of age or older have a 1.7 and 12.8 times higher seroprevalence with respect to subjects aged 20–49 and 6–19 years, respectively (21,22). Considering that these studies excluded incarcerated, homeless, institutionalized, and recent immigrants, it is likely that the prevalence of chronic HBV infection in the elderly is largely underestimated. (23) Although the risk of progression to chronic hepatitis B is inversely related to age at the time of infection, the rate of progression to chronic hepatitis B upon infection is higher in elderly individuals than in younger adults (24). Several studies and a meta-analysis have demonstrated that normal transaminases are often present in patients with chronic hepatitis B in spite of significant underlying fibrosis, especially in patients above 30–40 years of age (25,26). In primary biliary cirrhosis, age is an independent risk factor for poor outcome, in addition to the presence of portal hypertension and impaired liver function (27–29). Reportedly 17–56% of all patients with autoimmune hepatitis are over 65 years old at presentation (30–33), and the most common presentation is jaundice and/or fatigue with 10-fold elevation of serum alanine transferase levels (33). In spite of the often important necroinflammatory and fibrotic changes observed histologically in the elder when compared to younger patients, the former have an excellent prognosis (34,35). Alcoholic disease frequently debuts in the elderly, with one study reporting that 28% of patients first presented after age 60 (36), and in this study, the 1-year mortality rate for cirrhotic patients over age 60 was 50%, vs. 7% for patients under 60.
Liver transplantation for older recipients: Physiological, not chronological, age determines whether an older patient can be accepted for liver transplantation, with careful attention to comorbidities and functional status (37). In fact, according to the AASLD guidelines, in the absence of significant comorbidities, older recipient age (>70 years) is not a contraindication to liver transplantation, issued as a recommendation 2-B (38). Overall outcomes are acceptable in recipients >70 years of age, although they are inferior to those in younger age groups (39). Clearly, a thorough pretransplant evaluation of elderly candidates is warranted to exclude especially coronary artery disease, bone disease, and the presence of neoplasms. It has been demonstrated that moderate to severe coronary artery disease is highly prevalent (27%) in patients with liver disease and age >50 (or age >45 in patients with cholestatic liver disease) (40). Moreover, the mortality of patients with coronary artery disease who undergo liver transplantation is reportedly as high as 50% (41).
The elderly donor: The increase of donor pool including elderly donors was initially controversial, but is increasingly used, due to the overall aging population and to the recognition that in certain scenarios, outcomes of receiving a transplant from an older donor may well outweigh the risk of remaining on the waiting list for liver transplantation. In fact, no definite consensus exists on the limit of age for acceptance of organs. A recently published study based on the UK national transplant registry reported that the donor population has become older (from 14% to 35% ≥60 years old) during the last decade (42). In a study analyzing offered livers and reasons for refusal in the United States, Lai *et al.* reported that donors of livers that were offered to patients who then died or were delisted vs. transplanted candidates were significantly older and more likely HCV-antibody positive (43). However, non-standard donors, including donors of ages as advanced as 80 years old and even 97 years old (44), are increasingly being employed to counteract donor shortage, and these grafts are preferentially allocated to recipients with

hepatocellular carcinoma (donor age 55.57 years ± 18.23 vs. 50.78 years ± 19.09, for patients with and without hepatocellular carcinoma, respectively, $P < 0.0001$) (44).

In particular settings, however, as in the case of Hepatitis C in the recipient, the use of older donors has been associated with worse outcomes. In recipients transplanted for Hepatitis C, advanced donor liver age seems to have a negative impact in general (45,46), as well as related to the increased fibrosis progression after transplant (47) and therefore, careful donor/recipient matching is warranted to avoid increased risk combinations (48). Although short-term survival rates are similar between recipients of older donors vs. younger donors, long term survival is lower in recipients of octogenarian donors ($P = 0.04$), and mortality related to HCV recurrence is greater in this subgroup (49). In a recently published study proposing a new donor risk model for African Americans in the United States, the negative effect of increasing donor age on graft and patient survival, was attenuated by receipt of an organ from an African American donor (50).

Expanding the donor pool with elderly donors also results in an increased frequency of Hepatitis C virus infection in the donor, owing to the increased prevalence of this infection in the general population (51). In general, the use of organs from HCV-positive donors does not seem to affect patient and graft survival (52,53), and seemingly it is only HCV-positivity in the recipient to have a negative impact on outcomes (53,54).

Due to the higher prevalence of anti-HBc-positivity in the elderly population (55), it is likely that organs available from this subgroup will be frequently anti-HBc-positive, entailing the risk of HBV-related disease recurrence with the introduction of immunosuppressive therapy after liver transplant. In a small, single-center study, where 37% of grafts are obtained from donors who are at least 60 years old, donor anti-HBc-positivity was significantly associated with worse post-OLT patient and graft survival rates (56). In the Liver Match study, analyzing 1530 donor/recipient matches, of 245 HBcAb positive donors, 62.5% were allocated to HBcAb positive recipients, but notwithstanding the high prevalence of HBcAb positivity in the recipient population (a total of 761, for a 49.7%), 37.5% were allocated to HBcAb negative recipients (44). However, a systematic review analyzing the use of liver grafts from anti-hepatitis B core positive donors in 903 recipients showed that these grafts can be safely used, preferentially in HBsAg-positive or anti-HBc/anti-HBs positive recipients. Due to the risk of HBV recurrence, HBsAg-negative recipients should receive prophylaxis with lamivudine, while both anti-HBc and anti-HBs positive recipients may need no prophylaxis at all (57). Moreover, a recent study from the Liver Match cohort (58) showed that HBcAb positive donor grafts have better outcomes when transplanted into HBsAg positive than HBsAg negative recipients.

In conclusion, the aging of worldwide population poses new challenges, both as an increasing number of elderly patients require evaluation for liver transplantation and then undergo such procedure, and also in terms of the organ pool available, which is increasingly represented by elder donors.

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EO - 03 FULL LEFT/FULL RIGHT SPLIT LIVER TRANSPLANTATION FOR FULMINANT LIVER FAILURE?

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Introduction: Although split liver is standard part of the liver transplant programmes nowadays, the full left/full right split liver remains to be rarely used for two small adults.
Materials and methods: Two patients, husband and wife, age of 39 and 35 years, blood group A and 0, both poisoned by mistake with mushroom amanita phalloides. Both patients were admitted at the same time to the intensive care unit, having advanced acute liver failure. Patients were listed for urgent liver transplantation with highest possible urgency according to the Kings College criteria.

Shortly after listing graft became available, deceased donor, donor after brain death, blood group A, no severe comorbidities, shortly on ventilation, with normal liver tests. Decision was made to proceed with full left/full right split liver. Procedure has been performed using "in situ" technique, vascular anomalies were identified intraoperatively, left graft at the end of surgery was left with the common bile duct and left sided hepatic artery branch, left and middle hepatic vein with large patch of inferior vena cava. Right sided graft was prepared with common hepatis artery, right sided bile duct, right sided hepatic vein and also large posterior hepatis vein, both within the large patch of inferior vena cava.

Because one of the recipients was AB0i, one session of non-selective imunoadsorption has been performed prior to the transplantation. Transplantation of both patients was uneventful, both liver grafts started to work immediately. Another five sessions of the non-selective imunoadsorption were performed within the first two weeks after transplantation.
Results: The left sided graft recipient developer 2 weeks after surgery biliary leak, the original duct-to-duct anastomosis has been successfully converted to hepaticojejunostomy. There were no other complications during the postoperative course otherwise. The right sided graft recipient had no complications at all.

Both patients are alive and well, having normal liver tests and excellent graft function.
Conclusion: In conclusion the full left/full right split liver transplantation can be safely and effectively used for two adults with fulminant liver failure, even if one is AB0i.

EO - 04 PREVALENCE AND RISK FACTORS OF METABOLIC SYNDROME AFTER LIVER TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE

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Keywords: liver transplantation, metabolic syndrome, risk factors.

Metabolic syndrome (MS) is a frequent condition after liver transplantation (LT). However, most of the studies are focused on the early years after LT, and only few data are available on the long-term prevalence of this condition.

Patients who underwent LT at Padua Liver Transplant Centre between January 2000 and March 2013. Patients <18 years old, who underwent re-LT or multi-organ transplant were excluded from the study. MS has been diagnosed according to the modified NCEP-ATP III criteria, and only post-LT "de novo" MS has been evaluated.

Overall, 165 patients were included in the analysis (74% male, mean ± SD age at LT 52 ± 8 years). Underlying liver disease was: HCV in 48.5% of patients, HBV in 11.5%, HBV and HCV in 3%, alcohol in 16.4%, alcohol and virus in 9.1%, and due to other causes in 10.3%. HCC was diagnosed in 59/165 (35.7%). After a median follow-up time of 6.4 years, prevalence of post-LT MS was 87/165 patients (52.7%): 80.5% male and with a mean ± SD age at LT of 53.4 ± 8.8 years.

Patients with post-LT MS presented hypertriglyceridemia (185.2 ± 92 vs. 110.9 ± 42.3; $P < 0.001$) and significantly lower levels of HDL (38.8 ± 14 vs. 53.3 ± 16.9; $P < 0.001$) compared with patients without MS. No differences in terms of liver disease etiology was found between patients with and without post-transplant MS, as well as in terms of immunosuppressive regimen (steroid use vs. no steroid use and cyclosporine-based vs. tacrolimus-based immunosuppression).

At the multivariate analysis pre-LT diabetes (RR 9.16, 95% CI 1.09–76.9; $P = 0.04$) and pre-LT BMI (RR per 5 unit increase 2.05, 95% CI 1.04–4.03; $P = 0.003$) were identified as risk factors for post-LT MS.

MS is a condition affecting more than the half of recipients in the long-term after LT. Pre-LT diabetes and pre-LT increased BMI are risk factors for the development of post-LT MS. The identification of patients at risk for post-LT MS is crucial in order to develop specific medical strategies acting on modifiable risk factors.

EO - 05 TRENDS IN DONOR AGE OVER THE PAST DECADE– A EUROPE-WIDE STUDY

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Keywords: donor age, liver transplantation, survival

Background: As the demographics of the general population change, the age of potential organ donors increases. This study aims to characterise the donor age distribution for liver transplantation over time and the influence of donor age on patient survival.
Methods: Retrospective analysis of the European Liver Transplant Registry (ELTR; 1st January 2001 and 31st December 2012) and UK Transplant registry (UKTR; 1st January 2001 and 31st December 2011) was performed. Donor characteristics including age were analysed by transplant year. Kaplan-Meier methods were used to determine the impact of donor age on patient survival. A Cox proportional hazards model was used to examine the influence of donor age while controlling for other important variables. Monte Carlo simulations were used to interpret the model.
Results: Mean donor age in ELTR increased per calendar year (0.86 years ± 0.43 SD), with a statistically significant increase in the proportion of older donors (>60 years) over time in both ELTR (χ^2 for trend, $P < 0.001$) and UKTR ($P < 0.001$). Kaplan-Meier analysis showed that probability of patient survival was lower with increasing donor age in both ELTR (logrank test, $P < 0.001$) and UKTR ($P = 0.002$). In a well-fitting multivariable analysis, donor age persisted as a significant predictor of patient death in both datasets, ELTR: Hazard ratio per 10 years 1.10, 95% CI 1.06–1.11, $P < 0.001$; UKTR: HR 1.07, 95% CI 1.03–1.11, $P = 0.002$. Holding all other variables constant and comparing donor age of 40–70 years translates to an increased risk of recipient death at any given time of 28.1% (95% CI 20.4–36.3%; ELTR) and 22.3% (95% CI 8–38%, UKTR).
Conclusion: The proportion of recipients receiving grafts from older donors is increasing over time. This is highly likely to be associated with an increased risk of transplant recipient death, although this analysis does not account for the larger number of transplants being performed and any subsequent reduction in waiting list death.

EO - 06 LIVER TRANSPLANTATION DUE TO ALCOHOLIC LIVER CIRRHOSIS – LONG TERM FOLLOW-UP AND CLINICAL OUTCOME INCLUDING ALCOHOL RELAPSE

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Keyword: liver transplantation, alcoholic cirrhosis, alcohol relapse

Liver transplantation (LT) due to alcoholic liver cirrhosis (ALC) is the only therapy for chronic liver failure.[1] However, it induces more debate than any other indication, mainly due to apprehensions about post-LT alcohol abstinence.[2] The need of a certain abstinence period before listing to LT is still controversially discussed in literature. Livelong observance of patients with LT for ALC is a big challenge and therefore data about long-term follow-up is of great importance.

A retrospective analysis of prospectively collected data from patients listed for LT with ALC as main or secondary indication between 1996 and 2012 was performed. Primary endpoints were long-term patient and transplant survival as well as the incidence of alcohol relapse. The latter was strictly defined as any post-LT alcohol consumption, evaluated by a specialist psychologist involved in pre- and post-LT long-term evaluation. A defined period of sobriety before LT was not required at our institution.

From 1996 to 2012, 458 patients were listed for LT due to ALC as main or secondary indication. Out of these 382 (83%) were transplanted, 36 (8%) died on the waiting list and 40 (9%) were removed from the waiting list („too-sick" $n = 6$, non-compliance $n = 6$, tumor progression $n = 17$, "too-good" $n = 11$). From patients receiving LT, ALC was the main indication in 290 and the secondary indication in 90 patients. The median follow-up amounted 73 months (0–213). One-, and 5-year patient and graft survival was 82%, 69% and 82%, 75%, respectively. The alcohol relapse rate at 1- and 3-years showed 4.8% and 12.9%, respectively. Alcohol relapse and ALC as main or secondary indication did not significantly affect long-term patient and graft survival.

This large single center analysis presents excellent long-term outcome in patients with LT for ALC. Our alcohol relapse rate was compared to published data very low, although a strict definition was applied. A main factor for this outcome might be the involvement of a specialist psychologist in pre- and post-LT evaluation.

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EO - 07 ALPHA-FOETOPROTEIN SLOPE AND RADIOLOGICAL PROGRESSION AS SELECTIVE TOOLS FOR HCC LIVER RECIPIENTS: AN INTENTION-TO-TREAT ANALYSIS

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Introduction: Milan criteria are recognized as the best selection for hepatocellular cancer (HCC) patients listed for liver transplantation (LT). Several other criteria have been put forward to better stratify patients, their results are however controversial. The aim of this study is to investigate the role of parameters which are available during the waiting period as potential predictors of drop-out and post-LT recurrence.
Methods: Data from 821 HCC patients listed for LT during the period July 1987-November 2011 were obtained from a prospectively collected database of six collaborating European centers. Median follow-up for the entire population was 3.7 years (range 1.3–7.2). One hundred thirteen (13.8%) patients dropped out, 47 (5.7%) due to cancer-related causes.
Results: At multivariate Cox regression analysis, alpha-foetoprotein (AFP) slope > 15 ng/mL/mo and mRECIST progression were the unique independent risk factors for both cancer-related drop out and post-LT recurrence ($P < 0.0001$). Patients with AFP slope > 15 ng/mL/mo had a worse 5-year intention-to-treat (ITT) survival (42.9%) and high recurrence (53.1%) rates ($P < 0.0001$). Similar results were observed in patients with radiological tumor progression (42.8 and 41.3%; $P < 0.0001$).

The presence of both risk factors allowed to stratify better the patients both in relation to ITT survival and recurrence rates when compared with MC. They also allowed to increase the number of potentially transplantable pats by 8.4%.
Conclusions: AFP increase and radiological progression allow to improve the selection of HCC patients waiting for LT. Tumor progression, according to both parameters, significantly increases the risk of drop out on the waiting list and of post-LT recurrence. Monitoring of these parameters seems to be better than the initial MC status defined by imaging; this monitoring should be used in clinical practice in order to further refine the selection of potential HCC liver recipients.

EO - 08 EUROPEAN ELITA ELTR MULTICENTER SURVEY ON THE MANAGEMENT OF BILE DUCT DURING LIVER PROCUREMENT, PRESERVATION AND TRANSPLANTATION

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Keywords: bile duct, management, procurement, preservation, transplantation

Background: Surgical donor/preservation/recipient factors may play a role in the development of biliary strictures. Only scarce data are described on what is the best practice to manage the bile duct during procurement/preservation/LTx.
Aim: To characterize the different techniques used among European transplant centers in terms of bile duct management in case of donation after brain death (DBD) and circulatory death (DCD).
Method: An anonymous European web-survey has been sent to surgeons procuring and/or transplanting livers.
Results: Forty-four percent responded ($N = 210/475$). Fifty-three percent of respondent worked as procurement and transplant surgeon in large transplant centers (>50 procurements/year). Fifty-four percent of protocols are based on center guidelines. Five percent of surgeons never flush bile duct before cold preservation. If flushed, the bile duct is rinsed-out through both the common bile duct (CBD) and the gallbladder by only 21% and 25% of surgeons in case of DBD and DCD, respectively. The cystic duct is ligated during the procurement of DBD/DCD donors in 33%, whatever the decision concerning cholecystectomy. Forty-six percent of surgeons prefer to do a cholecystectomy before implantation in case of DBD/DCD. An arterial back table pressure perfusion is performed by 48% and 54% of surgeons in DBD and DCD LTx, respectively. Two percent and 7% of surgeons prefer to perform a hepatic artery reperfusion first in case of DBD and DCD LTx, respectively. Sixteen percent do not shorten the CBD (until bleeding) before biliary anastomosis. Protective interventions as donor pre-treatment with steroids, fibrinolytics or heparin, prostacyclin analogue in cold preservation solution and recipient treatment with fibrinolytics are described.
Conclusion: Obvious heterogeneity management of bile duct during procurement/preservation/LTx is observed among respondent surgeons in Europe. Internationally recognized guidelines with validated maneuvers to better preserve bile duct are urgently needed, especially with use of less-than optimal livers.

EO - 09 EXTENDED PRE-TRANSFUSION MOLECULAR BLOOD SAMPLE TESTING IN POLYTRAUMATIZED PATIENTS AS A PATH TO ENHANCE THE LIKELIHOOD OF ORGAN DONATION: REPORT OF A CASE

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Keywords: blood component transfusion, agglutination tests, organ donation, trauma

Introduction: Almost 15% of polytraumatized patients require massive blood transfusion (MBT). Prior to MBT, it is imperative to obtain thorough physical examination and detailed patient's medical history. Among routine serological blood group determination (BGD) tests, different molecular blood typing methods have been introduced. We report a case of a potential organ donor in whom routine serological BGD tests failed to reveal precise blood group. Consequently, MBT with non-compatible blood components (BC) was

carried out. As a result the patient did not meet selection criteria for organ donation.
Case report: A 52-year-old driver was involved in a mass collision. The nearest hospital provided primary care for the polytraumatized patient. During reassessment in level I trauma center, discharge letter revealed the patient was transfused with 3 units of "O" negative blood throughout primary care provision. At the time, patient's blood group was unavailable. Blood sample was taken for BGD, and classified as "O" positive. During necessary vascular repair and postoperative care the patient was repeatedly transfused with "O" positive BC. Intensivists identified the patient as potential organ donor. On post trauma day 5 cell typing showed mixed-field agglutination. Request was made for precise information of transfused BC from previous facility. Received data indicated the patient was transfused with additional 6 units of "O" positive blood. Consequently, extended immunochemical and DNA tests for BGD were conducted. Finally, patient's blood group was identified as "A" negative. MBT of non-compatible BC induced false chimerism, which was the reason the patient wasn't suitable for organ donation.
Conclusion: ABO genotyping methods require the use of expensive kits or reagents. Our case showed all polytraumatized patients, in a need of MBT, demand comprehensive immunochemical, and DNA tests for BGD, to avoid possible omissions, and to enhance ones chance for organ donation.

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EO - 10 PROGNOSTIC CRITERIA AFTER ARTIFICIAL LIVER MARS IN FULMINANT HEPATITIS

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Keywords: liver failure, liver transplant, artificial liver, cytokines, detoxification

Background: The aim of this study was to confirm the improvement of prognostic parameters after treatment with the Molecular Adsorbent Recirculating System (MARS) in patients with fulminant hepatitis (FH) respect to analysis effected on 45 pts in 2009.
Materials: New thirty-four pts with diagnosis of FH were enrolled in this study for a total of 79 pts. Continuous variables were provided as medians and interquartile ranges. Continuous variables were compared with the Kruskal-Wallis test. A P-value < 0.05 was considered statistically significant. A receiver operating characteristic (ROC) curve analysis was performed with the intent to validate the investigated score in predicting survival, need for LT or death: sensitivity and specificity were evaluated.
Results: The entire cohort was stratified in two groups: patients alive without LT ($n = 32$) and patients transplanted or dead before LT ($n = 47$). Thirteen pts (18.3%) died before LT and in 34 cases (42.3%) a LT was performed. ROC analysis was performed with the intent to evaluate the predictive role of the scoring system for LT or patient death. The score showed a high AUC (91.4%). The arbitrary cut-off values of 2 and 4 showed high sensitivity (81.4 and 48.8%) and specificity (92.9 and 96.4), respectively. Patients corresponding to the low risk group (scoring points: 0–2; $n = 36$) did not experience deaths, and only 8 (23.5%) of them underwent a LT. Patients with intermediate risk (3–4 points; $n = 22$) were mainly transplanted (20 pts; 90.9%). In the high risk group (5–6 points; $n = 13$), no patient survived.
Conclusions: We were able to confirm that the following criteria: GCS ≥ 11 with ICP < 15 mm Hg, lactate level <3 mmol/l, TNF-a < 20 pg/mL, IL-6 < 30 pg/mL, and a change in hemodynamic instability from hyperkinetic to normal kinetic conditions, after 40 hours by the first MARS treatment, enabled us to determine their outcomes.

EO - 11 COMBINED HEART-LIVER TRANSPLANTATIONS WITHIN EUROPE – RESULTS OF A ELTR-WIDE SURVEY

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Keywords: combined transplantation, familial amyloid polyneuropathy

Introduction: Combined heart-liver transplantations (CHLT) are rarely performed procedures. European experiences are limited to occasional case reports or case series. Therefore, we conducted, in close collaboration with the European Liver Transplant Registry (ELTR), a survey to acquire the current status of CHLT within Europe.
Methods: The survey included an enquiry for recipient and donor demographics, operation data and follow-up data including the immunosuppressive regime after CHLT. The questionnaires were sent to all centres having performed CHLT, which were registered by the ELTR.
Results: We obtained data from 57 CHLT. The 1-year- and 5-year-survival in our cohort is 68.4 and 57.9%. In most cases (52.6%), indication for CHLT was familial amyloid polyneuropathy (FAP). The operation mode differed widely, but mostly either implantations of the liver were performed after weaning of the cardiopulmonary bypass and without use of a veno-venous bypass ($n = 14$; 31.1%) or liver transplantation with the recipients still on cardiopulmonary bypass ($n = 13$; 28.9%). The time period of cardio-pulmonary bypass time was significantly shorter in patients who were liver transplanted after cardio-pulmonary bypass weaning (121 vs. 240 min, $P < 0.000$). The cardio-pulmonary bypass duration was an outcome determining variable: patients with a fastly weaned bypass had a significant better outcome than patients whose liver transplantation was performed while being on cardio-pulmonary bypass ($P = 0.009$). For immunosuppression, most centres used the usual liver protocol (71.4%) of their centre, followed by the use of the usual heart protocol (24.5%).
Discussion: This series represents by far the largest European cohort of CHLT recipients. Furthermore, it is the largest series describing the operation technique and the immunosuppressive strategies in CHLT patients. Main indication was familial amyloid polyneuropathy. The duration of the cardiopulmonary bypass played an important role in the survival of the recipient and should be taken in account when planning this procedure.

EO - 12 AIR EMBOLISM DUE TO INTRAPULMONARY SHUNT RESPONSIBLE OF MULTIORGAN ISCHEMIA IN A HIV/HCV CO-INFECTED LIVER TRANSPLANT RECIPIENT

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Keywords: liver transplantation, HIV, HCV

Hepatopulmonary syndrome (HPS) is characterized by arterial hypoxemia due to intrapulmonary vascular dilatation in patients with end-stage liver disease. Confirmation of the diagnosis of HPS rests on the findings of contrast-enhanced echocardiography or bubble study. The presence of intrapulmonary shunts due to HPS has been reported as a potential facilitator of cerebrovascular accident (CVA) or TIA. Also left atrial dilatation increased risk of HPS. At our centre a liver transplant in a 43 y/o hemophiliac, HIV-HCV positive male with an end-stage liver disease (Child-Pugh class C, MELD value 30) was complicated by an ischemic intestinal and cerebrovascular insults occur respectively on post transplant day 11 and 35. These events hesitated in a Hartman procedure and in a left side hemiplegia due to a right fronto-parietal ischemic lesion. In both cases no sign of vascular thrombosis was found. Pretrasplant echocardiography was negative for intracardiac shunts but revealed a severe left atrial dilatation; the bubble study was not performed due to the absence of significant hypoxemia. After the CVA a contrast-enhanced echocardiography with bubble study was performed showing the presence of microscopic air bubbles in the left heart chambers 3 or 4 beats after its appearance in the right atrium suggestive of an HPS grade IV. According to the literature we hypothesized that both ischemic insults, at least the cerebral one, might be explained by peripheral air embolism due to intrapulmonary right to left shunt and so we might conclude suggesting that a contrast-enhanced echocardiography with bubble study should be performed in every patient during the pre-liver transplant workup especially in case of advanced end-stage liver disease, moderate hypoxemia also in the absence of significant dyspnea and evidence of severe left atrial dilatation.

EO - 13 SHOULD WE TRANSPLANT LIVERS FROM OLD DCDS?

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Keywords: DCD, marginal grafts, old donors

Background: Donor age significantly impacts the outcome of the liver transplantation in Donation after Circulatory Death (DCD): according with DRI studies, donor age > 60 years strongly predicts graft failure. European Liver Transplant Registry data showed an increase in the past 10 years of the rate of cadaveric liver donors older that 60 years. However the use of older donors remains limited particularly in DCD donation. The aim of this study was to analyse the outcome of liver transplantation using grafts from DCD donors older than 60 years old.
Methods: All consecutive DCD donor liver transplants performed between June 2004 and June 2013 were included in the study. Liver grafts from DCD older than 60 years were also compared with DBD grafts used in the same study period. Donor and recipient characteristics were collected from a prospectively held database. Outcomes analysed include patient/graft survival and vascular/biliary complications.
Results: In the study period a total of 189 Maastricht category III DCD liver transplants were performed at our unit. Fifty-four liver grafts from DCD older than 60 years were compared with 135 grafts from DBD less that 60 years of age and with 125 grafts from DBD older than 60. There were no statistical differences between the three groups in terms of patient survival at 1–3 years: in DCD of ≥60 years it was respectively 85% and 82%, in DCD < 60 y/o, 88% and 82% and DBD group 91% and 85%. Similar results emerged for graft survival at 1–3 years: 81% and 80%, 86% and 81%, 88% and 83% respectively. The rate of vascular/biliary complications was similar in all three groups (15/22%; 11/24% and 12/16%). A stricter selection process was noted in the DCD older than 60 group for lower donor BMI, lower recipient MELD and shorter cold ischemia time.
Conclusion: Older DCD donors, of 60 years of age or older, can be successfully used for liver transplantation with acceptable short and mid-term outcomes provided that there is careful donor and recipient selection.

EO - 14 ARE DCD LIVERS GOOD FOR HCC PATIENTS?

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Keywords: HCC, DCD, marginal grafts

Background: Patients listed for liver transplantation for hepatocellular carcinoma (HCC) is on the rise. However the shortage of organ donors cannot meet the current demand: there is a constant uptrend of patient dropout from the transplant list. In recent years an increasing number of HCC recipients have been transplanted with Donation after Circulatory Death (DCD) livers in the attempt to reduce waiting list mortality. The aim of this study was to analyse the oncological and clinical outcomes of HCC patients transplanted with DCD grafts.
Methods: All DCD donor liver transplants for HCC performed between June 2004 and January 2013 were included in the study and compared with DBD recipients transplanted for HCC in the same study period.

Donor and recipient characteristics were collected from a prospectively held database. Outcomes analysed included patient/graft/disease free survival, vascular/biliary and renal complications. A step-wise multivariate analyses for recurrence was performed.
Results: In the study period a total of 61 DCD liver transplant patients for HCC were compared with 76 DBD HCC recipients. Donor, recipient and tumor characteristics were similar between the two groups (except for an expected higher donor risk index and lower MELD in DCD group).

The DCD group showed a similar patient survival compared with DBD recipients at 1 year (84% vs. 85%), 3 years (69% vs. 71%) and 5 years (50% vs. 62%). Similarly no difference was found for graft survival at 1 year (82% vs. 84%), at 3 years (67% vs. 69%) and at 5 years (49% vs. 63%) and for disease-free patient survival (92% vs. 92%, 87% vs. 87% and 76% vs. 87%). Clinical outcomes were similar between the two groups in terms of primary non-function rates (4% vs. 6.6%), hospital stay (2 days vs. 3) and vascular/biliary complications (7/15% vs. 8/7%). The DCD recipients had a higher rate of renal replacement therapy (38% vs. 21%). AFP levels rather than the type of graft were an independent risk factor for recurrence.
Conclusion: DCD liver grafts in HCC patients provided similar oncological and clinical results compared with DBD recipients. Thus a DCD liver graft is not ad independent risk factor of recurrence. Further studies are needed using matched pair analyses.

EO - 15 LATE LIVER RETRANSPLANTATION WITH DECEASED AND LIVING DONOR LIVER GRAFTS: A COMPARATIVE SINGLE INSTITUTION ANALYSIS

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Keywords: liver retransplantation, deceased donor liver graft, living donor liver graft, living donor liver transplantation

Background: Long-term survival following liver retransplantation (ReLT) is shorter as compared to that of primary liver transplantation. Aim of this study is to perform a comparative analysis of the late retransplantation with deceased (Re-DDLT) and living donor liver grafts (Re-LDLT) in our institution.
Materials and methods: Between January 2000 and March 2014 a consecutive series of 33 late Re-DDLT and 13 Re-LDLT were performed.
Results: Patients undergoing Re-DDLT and Re-LDLT had similar characteristics with comparable MELD score (15.8 ± 5.8 and 14.2 ± 3 P = n.s.). Differences were recorded for waiting time on list (P = 0.004), mean serum creatinine levels (1.6 ± 0.7 mg/dl vs. 1.0 ± 0.2 mg/dl in Re-DDLT and Re-LDLT respectively, P = 0.048); length of hospital stay (35 vs. 58 days respectively, P = 0.03). and warm ischemia (P = 0.003). The incidence of pre-transplant vascular thrombosis was higher in Re-LDLT (30% vs. 25%) (P = ns). Early (≤1 month) graft loss was 3% (1/33) in Re-DDLT and 30.7% (4/13) in Re-LDLT (P = 0.01). Predictors of graft loss were infections 30 days before ReLT (P = 0.037) and Child score >10 (P = 0.01). Five-year graft and patient survival was 58.8% and 62.9% in Re-DDLT and 58.8% and 90% in Re-LDLT respectively (P = ns).
Conclusions: Late ReLT with living donors could be proposed as an alternative to Re-DDLT. However, LDLT should preferably not be offered to patients with pre-existing vascular thrombosis due to the increased surgical risks of graft failure carried by Re-LDLT.

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EO - 16 MULTIVISCERAL TRANSPLANT FOR WIDESPREAD MESENTERIC ARTERIAL INSUFFICIENCY

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Keywords: multivisceral, ischaemia, histopathology

Multivisceral transplant (MVT) is an uncommon transplant procedure whereby the stomach, liver, pancreas and small intestine are simultaneously implanted. Our institution has recently been referred a number of cases in which there has been occlusion of the abdominal mesenteric vessels, causing small bowel infarction and hepatic ischaemia. We report here four such cases which have been successfully managed with MVT.

One patient (33, female) presented with extensive small bowel (SB) and colon infarction with occlusion of her coeliac axis (CA), superior mesenteric artery (SMA) and inferior mesenteric artery (IMA). Following extensive evisceration she was listed for an urgent MVT which was carried out 9 days later. Histology from her explanted arteries was in keeping with an adventitial type of fibromuscular dysplasia (FMD).

Case 2 (48 female), 3 (50 female) and 4 (56 male) all presented with SB infarction due to SMA occlusion and underwent SB resection first. Subsequent investigations (between 2 to 10 months later) revealed CA occlusion and ischaemic hepatitis, including hepatic abscesses in cases 3 and 4. They have all undergone successful MVT. The histology in case 2 revealed segmental arterial mediolysis of the involved arteries. This, like FMD, is a non-atherosclerotic, non-inflammatory vascular disease where patchy lysis of the media layer leads to weakening of the arterial wall. In case 3 JAK2 mutation testing and bone marrow examination were consistent with a JAK2 positive myeloproliferative disorder. A full thrombotic screen and careful examination of the histology has yet to uncover a diagnosis in case 4.

The indications for Multivisceral transplant appear to be changing, with more cases being done acutely in our institution for widespread mesenteric arterial insufficiency, often due to rare diseases. We propose that treatment options for these young patients were previously very limited but multivisceral transplant offers a new strategy.

EO - 17 CYTOKERATIN 18 FRAGMENTS AS A BIOMARKER OF INTESTINAL TRANSPLANT REJECTION

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Keywords: intestinal, rejection, surveillance, biomarker, cytokeratin

Intestine-containing transplants differ from other solid organ transplants in that the graft can be accessed directly for histological examination. However, this is invasive with some risk, albeit minimal, and the inclusion of colon as part of the graft makes this technically more difficult. A reliable biomarker to replace endoscopic surveillance has yet to be found.

One of the earliest changes seen in graft rejection is an increase in mucosal apoptosis. Intestinal involvement in graft versus host disease (GVHD) following bone marrow transplantation is also characterized by mucosal apoptosis. Cytokeratin-18 fragments were shown to be a possible marker of GVHD. Cytokeratin is a filament present in epithelial cells. Induction of apoptosis results in cleavage at two sites, including 396DALD-S, which results in stable fragments (CK18Fs) with a neo-epitope which is recognised by the M30 antibody. A related antibody, M65, recognizes the intact cytokeratin 18 protein. We designed a pilot study to determine if CK18Fs is a marker of intestinal rejection

Serum was obtained from patients on the day of their surveillance endoscopy during the period April to November 2013. ELISA for M30 and M65 was carried out according to the manufacturers instructions. This study was approved by the local ethics committee (Ref 13/LO/0272).

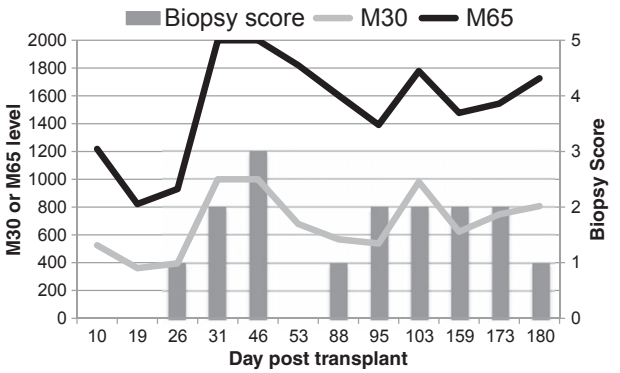

Figure 1. Change in M30 and M65 levels and relation to biopsy score over time in one patient.

Two patients had serial measurements over time and experienced an episode of rejection during the study period. In both cases, the levels of M30 and M65 were higher during the rejection. Another patient, who did not experience any rejection, showed stable levels of both over time.

This pilot study suggests that cytokeratin 18 fragments may be a useful biomarker for intestinal graft rejection and further studies should be carried out in this area.

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EO - 18 INFECTIVE ENDOCARDITIS CAUSED BY *CHLAMYDIA PNEUMONIAE* AFTER LIVER TRANSPLANTATION-REPORT OF A CASE

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Keywords: infective endocarditis, cardiac surgery, liver transplantation, *Chlamydia pneumoniae.*

Background: Endocarditis is an underappreciated form of nosocomial infection in solid organ transplant recipients. The spectrum of organisms causing infective endocarditis in transplant recipients differs from those in the general population. There is also a wider array of clinical features including splenic infarction, septic pulmonary emboli, septic bursitis, cryptococcal meningitis and cerebral embolism.

Case presentation: This is case of a 58-year old female with history of alcoholic cirrhosis of the liver who received a cadaveric liver transplant in February 2000. Despite vaccination before transplantation, she became HbsAg positive in the post-transplant period for which lamivudine was started in 2002. Due to appearance of a lamivudin resistant mutation (YMDD) with plasma HBV-DNA titers reaching 16 840 000/mL, adefovir treatment started. Chronic kidney disease due to calcineurin toxicity was subsequently diagnosed in July 2007. In November 2013 she had a short period of aphasia. Although she remained afebrile, infective endocarditis of the aortic valve was found by transesophageal echocardiography. Systemic septic embolization was also identified. On laboratory tests a mildly elevated CRP (10.9 mg/L), leukopenia (WBC: 2.47 G/L) and a normal procalcitonin level were detected. Initially, a 4-week combination regimen with IV ceftiraxone (2 g daily) and IV gentamycine (60 mg after dialysis treatment) was started. As blood cultures came back negative and serology revealed high titers of antibodies against *Chlamydia pneumoniae*, moxifloxacin was added. Shortly after the initiation of antibiotic therapy a short episode of aphasia recurred. This was thought to have been due to cerebral microembolization. Subsequently, the patient's condition gradually improved with total recovery of neurologic deficits. The post-treatment period was complicated by an acute coronary event with coronary angiography showing a 80–90% diameter stenosis in the LAD and a 70–75%

stenosis in the RCA. Coronary artery bypass and aortic valvuloplasty were performed with resolution of the clinical symptoms.
Conclusion: Immunosuppressive treatment necessary to prevent rejection of the transplanted organs is known to predispose transplant recipients to atypical organisms and invasive fungal infections. In our case, infective endocarditis with an atypical organism also had an atypical clinical presentation. In solid organ transplant recipients, unexplained appearance of a neurological deficit (aphasia in our case) should prompt the physician to rule out endocarditis as it might represent an underlying infectious etiology. Awareness of this possibility may lead to prompt diagnosis and treatment. In addition, a high index of suspicion for atypical organisms such as Chlamydia should be maintained in cases of culture-negative endocarditis to avoid delay in treatment.

EO - 19 ISCHEMIC CHOLANGIOPATHY IN DCD LIVER TRANSPLANTATION IS NOT ASSOCIATED TO THE HISTOLOGICAL SEVERITY OF HEPATOCYTE ISCHEMIA-REPERFUSION INJURY

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Keywords: liver transplantation, donation after circulatory death, biliary complications, ischaemic colangiopathy, ischaemia-reperfusion injury

Ischaemic cholangiopathy (IC) is the most critical biliary complication after liver transplantation with an incidence between 10% and 50% after donation after circulatory death (DCD) liver transplantation (1,2). It is defined as intrahepatic or non-anastomotic, extrahepatic biliary strictures in the presence of a patent hepatic artery (3).

Ischemia-reperfusion injury (IRI) to the transplanted liver is thought to be one of the main triggers for IC development. However the underlying pathogenic mechanism is not yet completely understood (4,5).

Aim of this study is to evaluate the incidence of IC and its relation with IRI of the graft in a high volume, single centre DCD transplant population.
Methods: A retrospective analysis of prospectively collected database of DCD liver recipients from November 2004 to November 2013 was performed. IC was defined on the basis of imaging appearance (MRCP, ERCP) of biliary lesions. IRI was assessed on the basis of histologic appearance (neutrophil infiltration and hepatocellular necrosis) of post-reperfusion biopsies as minimal, mild, moderate and severe.
Results: Two hundred-five DCD transplants were performed over the study period. One year patients' and grafts' survival were 87% and 83% and five years survival 68% and 72%, respectively. The overall incidence of biliary complications was of 24.9%, with IC accounting for 10.2%. Mean time from grafting to development of IC was 5.3 $\pm$ 6.4 months.

Post-reperfusion biopsy was available in 157 patients. Seventy-six patients showed minimal or mild histological IRI features, and in 81 these were moderate to severe. No significant association was found between IC and IRI features, or between IC and donor age, donor warm and cold ischemia time, steatosis of the graft and post-transplant liver function.
Conclusions: No significant association between IC development and the histological severity of hepatocyte IRI was shown. Further not defined mechanisms should be involved in the development of IC other than the solely IRI.

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EO - 20 ITERATIVE LATE LIVER RETRANSPLANTATIONS FOR BILIARY AND VASCULAR COMPLICATIONS FOLLOWING FIRST COMBINED LIVER-KIDNEY ENGRAFMENT (HYPEROXALURIA TYPE 1) AND TEMPORARY IMMUNOSOPPRESSION-OFF WITH IMMUNOMONITORING (IMMUKNOW TEST)

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Keywords: liver, retransplantation, thrombosis, hyperoxaluria

Vascular and biliary complications represent the major causes of graft loss and mortality after liver transplantation (LT). We report a case of a 34 y.o. woman affected by primary hyperoxaluria type 1, which had a combined liver and kidney transplant in 2001.

The first re-transplant was performed three years later due to hepatic artery (HA) thrombosis with recurrent ischemic cholangitis. Biliary stents were successively positioned for biliary stenosis with a patent HA. In 2009 a liver biopsy showed a chronic cholangitis with secondary biliary cirrhosis of the graft and a Piggy-Back thrombosis was found. From 2010 the patient presented recurrent variceal bleeding due to portal-hypertension, treated with TIPSS placement.

Due to further deterioration of her liver function the patient was re-listed for a third liver graft. A thrombosis of the caval anastomosis occurred on the 5th postoperative day (POD). A redo surgery with thrombectomy under temporary TVE of the liver was performed. However, on the 12th POD, a new thrombotic episode was recorded (VCI and the left hepatic vein). A new caval thrombectomy with a left lateral sectionectomy due to partial necrosis of the graft was performed. Three days later, a CT control showed a new thrombus of the retro-hepatic VCI that was treated with a percutaneous procedure (thrombectomy and balloon dilatation of the VCI). The patient was discharged with good flows in all the hepatic vessels, and improvement of hepatic and renal parameters.

One month later she was re- hospitalized due to septic cholangitis. The IS therapy was completely withdrawn since the CD4 activity (Immuknown test) was very low (56 ng ATP/ml). The IS was restored 6 weeks later when the test showed a better immunocompetence (307 ng ATP/ml). During that time no rejection episodes were recorded. After 18 m FU she is in good clinical conditions with well functioning transplanted organs.

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EO - 21 POTENTIAL NET HEALTH BENEFIT OF PRE-TRANSPLANT SOFOSBUVIR TO PREVENT RECURRENCE OF HCV INFECTION AFTER LIVER TRANSPLANTATION: A MULTICENTER, COHORT MODEL STUDY

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Background: New data are now available showing the strong efficacy of pre-transplant Sofosbuvir (SOF) in preventing recurrence of hepatitis C virus (HCV) infection after liver transplantation (LT). The aim of this study was to evaluate the cost-effectiveness of this potential new strategy in the North Italy Transplant program (NITp) area.
Methods: We enrolled 1621 consecutive adult patients with low MELD (<15) entering the waiting list for LT during the period 2004–2009 in the NITp area. We first evaluated the impact of HCV infection on post-LT survival in the study group and prevalence-costs of conventional therapy after LT. Then, using a Markov model applied to the study cohort, we compared two strategies: one using SOF as prophylactic therapy pre-LT (strategy A), and the other using on demand conventional post-LT dual antiviral therapy (strategy B). The endpoints

were: survival benefit measured in quality-adjusted life years (QALYs), costs (C) in €, incremental cost-effectiveness ratio (ICER), willingness to pay (WTP), and net health benefit (NHB), where NHB = survival benefit − C/WTP. The maximum acceptable WTP of SOF in Italy was assumed 50 000$/QALY.
Results: Among the 1242 patients undergoing LT, 798 (49%) were HCV positive and 50% of them had conventional dual antiviral therapy after LT (drugs and adverse effects mean management costs = 16 440 $ for treated patient). HCV etiology had the strongest impact on post-LT survival (Hazard Ratio = 1.89, 95% CI = 1.26–2.88, $P = 0.0020$). Using recent data on SOF efficacy and costs in this setting in the base-case scenario, 3-months pre-LT SOF therapy showed a median survival benefit of 2.2 QALYs, an ICER of 43 159$/QALY, and a NHB of 0.3 QALYs, whereas the ICER and NHB of a 6-months therapy where 78 822$/QALY and −1.3 QALY respectively.
Conclusions: SOF used as prophylactic pre-transplant therapy in low-MELD HCV patients proved to be a cost-effective treatment strategy compared with post-LT dual therapy.
Abbreviations: HCV, Hepatitis C Virus; RFP, Rapid Fibrosis Progression; LT, Liver Transplantation; peg-IFN, pegylated interferon; RBV, Ribavirin; SVR, Sustained Virological Response; DAA, Direct-Acting Antiviral; SOF, Sofosbuvir; FDA, Food and Drug Administration; AASLD, Association for the Study of Liver Diseases; HCC, Hepatocellular Carcinoma; MELD, Model for End-Stage Liver Disease; WL, Waiting List; NITp, North Italy Transplant program; QALYs, Quality-Adjusted Life Years; ICER, Incremental Cost-Effectiveness Ratio; WTP, Willingness To Pay; NHB, Net Health Benefit; DEALE, Declining Exponential Approximation of Life-Expectancy; CEAC, Cost-Effectiveness Acceptability Curve.

Conflict of interest: None.
Funding/Support: None.

EO - 22 THE ITA.LI.CA CRITERIA TO SELECT PATIENTS WITH HEPATOCELLULAR CARCINOMA FOR LIVER TRANSPLANTATION: A MULTICENTRE COHORT STUDY

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Keywords: liver transplantation, HCV recurrence, cost-effective

Background: The Barcelona Clinic Liver Cancer (BCLC) staging system predicts liver transplantation (LT) benefit in patients with hepatocellular carcinoma (HCC). We aimed to identify significant predictors of transplant benefit within BCLC stages to re-formulate selection criteria for LT in HCC patients
Methods: Consecutive non-LT HCC patients ($n = 2419$) from the ITA.LI.CA database ($n = 5183$) were selected based on potential eligibility for LT. Post-LT survival was calculated by using the alpha-fetoprotein (AFP) score, based on preoperative variables (AFP values, nodules' diameter and number). Non-LT survival was predicted including AFP score covariates plus Child-Turcotte-Pugh (CTP) classes in a parametric survival model. "Number of patients needed To Transplant" (NTT) was calculated as measure of 5-year-transplant-benefit (NTT< 5 = effective therapy) based on BCLC stage, AFP score covariates, and CTP classes.
Results: NTT median values at 5-year were respectively: 7.27 for BCLC 0, 6.81 for BCLC A, 4.48 for BCLC B-C, 2.22 for BCLC D. Time horizon (3 vs. 5 vs. 10 years scenario) strongly influenced the impact of liver function and tumor related characteristics on transplant benefit.

We identified the following exclusion criteria for LT: a) Upper limit (NTT< 5 at 10-year) tumor diameter >6 cm and one of the following, multinodular (>3 nodules) or AFP >100 ng/mL; b) Lower limit (NTT< 5 at 3-year), CTP A cirrhosis undergoing loco-regional therapies within above tumor criteria.
Conclusion: Using NNT analysis, we identified new criteria to select, within each BCLC stage, the LT candidates showing the maximal transplant benefit.