Background: In an effort to understand the diminished quality of life (QoL) exhibited by patients with end-stage liver disease (ESLD), we studied the association of frailty and severity of liver disease with quality of life in this patient population.

Methods: In a prospective, single-center cohort study (N = 487), we assessed frailty and QoL in patients with ESLD referred for liver transplant. Frailty was measured on a scale from 0 to 5 by grip strength, gait speed, exhaustion, shrinkage, and physical activity, with scores of 3 or higher characterized as frail. Physical, mental, and combined overall quality of life scores ranging from 0 to 100 were assessed using Short Form 36. Pearson correlation and multiple linear regression were used to identify variables associated with QoL.

Results: Quality of life was notably low in the study cohort (mean: physical, 42.9 ± 24.1; mental, 58.3 ± 23.2). In multivariate analysis adjusted for demographic and clinical characteristics, frailty was significantly negative associated with physical (slope, -22.55, 95% confidence interval, -26.39 to -18.71; P < 0.001) and mental QoL (slope, -17.59, 95% confidence interval, -21.47 to -13.71; P < 0.001). Model for ESLD (MELD) was not associated with QoL.

Conclusion: In ESLD patient referred for liver transplant, diminished QoL appears to be significantly negatively associated with frailty and not with severity of liver disease as measured MELD. With further study, if frailty is shown to be a remediable condition, targeted programs may help decrease frailty and improve quality of life in ESLD patients.
Simulation Modeling of the Impact of Proposed New Simultaneous Liver and Kidney Transplantation Policies


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Background: Increasing use of kidney grafts for simultaneous liver and kidney (SLK) transplants is causing concern about the most effective utilization of scarce kidney graft resources. This study evaluated the impact of implementing the proposed United Network for Organ Sharing SLK transplant policy on outcomes for end-stage liver disease (ESLD) and end-stage renal disease (ESRD) patients awaiting transplant.

Methods: A Markov model was constructed to simulate a hypothetical cohort of ESLD patients over a 30-year time horizon starting from age 50. The model applies the different criteria being considered in the United Network for Organ Sharing policy and tallies outcomes, including numbers of procedures and life years after liver transplant alone (LTA) or SLK transplant.

Results: When 1-week pretransplant dialysis duration is required, the numbers of SLK transplants and LTAs would be 648 and 9,065, respectively. If the pretransplant dialysis duration is extended to 12 weeks, there would be 240 SLK transplants and 9,426 LTAs. This change results in a decrease of 6,483 life years among SLK transplant recipients and an increase of 4,971 life years among LTA recipients. However, by increasing the dialysis duration to 12 weeks from 1 week, 408 kidney grafts would be released to the kidney waitlist because of the decline in SLK transplants; this yields 796 additional life years gained among ESRD patients.

Conclusion: Implementation of the proposed SLK transplant policy could restore access to kidney transplants for patients with ESRD albeit at the detriment of patients with ESLD and renal impairment.
Therapeutic hypothermia in acute liver failure: A multicenter retrospective cohort analysis

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Liver Transplantation Volume 21, Issue 1, pages 4–12, January 2015

The benefit of therapeutic hypothermia (TH) in acute liver failure (ALF) has not been previously demonstrated in a controlled fashion. This study sought to determine the impact of TH on 21-day survival and complications in ALF patients at high risk for cerebral edema. This was a retrospective cohort study of ALF patients in the US Acute Liver Failure Study Group with grade III or IV hepatic encephalopathy. TH (32°C-35°C) was used in 97 patients (8%); 1135 (92%) who were not cooled were controls. Intracranial pressure was monitored in 38 TH ALF patients (39.2% versus 22% of controls, P < 0.001). Rates of bleeding (12% for both) and bloodstream (17% versus 18%) and tracheal infections (21% versus 23%, P > 0.5 for all) were similar. Unadjusted 21-day overall (62% versus 60%) and transplant-free survival rates (45% versus 39%, P > 0.4 for both) were similar. Multivariate models were created for acetaminophen (APAP) patients (n = 582) and non-APAP patients (n = 613). For APAP patients, the Model for End-Stage Liver Disease [MELD; odds ratio (OR) = 0.91 per increment, 95% confidence interval (CI) = 0.89-0.94, P < 0.001] and vasopressors (OR = 0.16, 95% CI = 0.11-0.24, P < 0.001) were associated with decreased 21-day spontaneous survival. Survival was improved with TH in APAP patients who were <25 years old (age of 25 years: OR = 2.735, 95% CI = 1.001-7.467) but worsened for APAP patients who were 64 years old or older (age of 64 years: OR = 0.167, 95% CI = 0.028-0.999). For non-APAP patients, MELD (OR = 0.93 per increment, 95% CI = 0.91-0.95, P < 0.001) and vasopressors (OR = 0.60, 95% CI = 0.40-0.90, P = 0.01) were associated with worse outcomes, whereas TH had no impact (P = 0.93). In conclusion, TH in ALF was not associated with increased bleeding or infections. Although young APAP ALF patients may benefit, TH did not consistently affect 21-day survival. A prospective trial is required to clarify the utility of TH in ALF patients. Liver Transpl 21:4-12, 2015. © 2014 AASLD.
Adverse cardiac events after orthotopic liver transplantation: A cross-sectional study in 389 consecutive patients


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Current American College of Cardiology/American Heart Association guidelines caution that preoperative noninvasive cardiac tests may have poor predictive value for detecting coronary artery disease in liver transplant candidates. The purpose of our study was to evaluate the role of clinical predictor variables for early and late cardiac morbidity and mortality and the predictive values of noninvasive cardiac tests for perioperative cardiac events in a high-risk liver transplant population. In all, 389 adult recipients were retrospectively analyzed for a median follow-up time of 3.4 years (range = 2.3-4.4 years). Overall survival was 83%. During the first year after transplantation, cardiovascular morbidity and mortality rates were 15.2% and 2.8%. In patients who survived the first year, cardiovascular morbidity and mortality rates were 3.9% and 2%, with cardiovascular etiology as the third leading cause of death. Dobutamine stress echocardiography (DSE) and single-photon emission computed tomography had respective sensitivities of 9% and 57%, specificities of 98% and 75%, positive predictive values of 33% and 28%, and negative predictive values of 89% and 91% for predicting early cardiac events. A rate blood pressure product less than 12,000 with DSE was associated with an increased risk for postoperative atrial fibrillation. Correspondence analysis identified a statistical association between nonalcoholic steatohepatitis/cryptogenic cirrhosis and postoperative myocardial ischemia. Logistic regression identified 3 risk factors for postoperative acute coronary syndrome: age, history of coronary artery disease, and pretransplant requirement for vasopressors. Multivariable analysis showed statistical associations of the Model for End-Stage Liver Disease score and the development of acute kidney injury as risk factors for overall cardiac-related mortality. These findings may help in identifying high-risk patients and may lead to the development of better cardiac tests. Liver Transpl 21:13-21, 2015. © 2014 AASLD.
Relationship between sarcopenia, six-minute walk distance and health-related quality of life in liver transplant candidates

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Abstract

Sarcopenia, or loss of skeletal muscle mass, is associated with increased mortality and morbidity in liver transplant (LT) candidates. Six-minute walk distance (6MWD) and health-related quality of life (HRQOL) as assessed by short form 36 scores (SF-36) also impact clinical outcomes in these patients. This study explored the relationship between the sarcopenia, 6MWD, and HRQOL in LT candidates. Sarcopenia was evaluated based on skeletal muscle mass index (SMI) quantified from abdominal computed tomography. Patients were followed until death, removal from the wait list or the end of the study period. Two hundred and thirteen patients listed for LT were included. The mean SMI, 6MWD and mean gait speed were 54.3 ± 9.7, 370.5 m and 1 m/s, respectively. Sarcopenia was noted in 22.2% of LT candidates. There was no correlation between sarcopenia, 6MWD, and SF-36 scores. The 6MWD, but not sarcopenia, was an independent predictor of mortality (hazard ratio = 2.1 [0.9–4.7]). In summary, sarcopenia did not emerge as a significant predictor of waitlist mortality and also failed to correlate with either functional capacity or HRQOL in LT candidates. In patients with ESLD awaiting LT, 6MWD appears to be a more useful prognostic indicator than the presence of sarcopenia.
Exploration of skin perfusion in cirrhotic patients with septic shock

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Background & Aims

Skin perfusion alterations are early and strong predictors of death in patients with septic shock. Cirrhosis is associated with systemic vasodilation and increases mortality from septic shock. We aimed at assessing whether the mottling score and tissue oxygen saturation (StO2) could be used as early predictors of death in cirrhotic patients with septic shock.

Methods

This observational study included cirrhotic patients with septic shock. Each 6 h during the first 24 h, we collected data reflecting macrocirculation (mean arterial pressure, heart rate, central venous pressure, and cardiac output) and organ perfusion (arterial lactate, urinary output, ScvO2, mottling score, thenar, and knee StO2). Data of 75 non-cirrhotic patients with previously reported septic shock were used as control.

Results

42 cirrhotic patients were included. Mortality at day 14 was 71%. At H6, parameters reflecting macrocirculation were not associated with mortality, whereas higher arterial lactate and mottling score were associated with death. Mottling score was the strongest predictor of mortality (sensitivity = 0.63, specificity = 1, OR = 42.4 (2.3–785.9)). At H6, knee StO2 decreased in non-survivors and predicted death (sensitivity = 0.45, specificity = 1). In comparison with control, mottling kinetic was different in cirrhotic patients (delayed mottling appearance in non-survivors, earlier mottling disappearance in survivors). Knee StO2 and skin perfusion, assessed by laser-Doppler, were higher in cirrhotic patients.

Conclusions

Mottling score and knee StO2 at H6 were very specific predictors of death in patients with cirrhosis and septic shock. Their sensitivity was lower in cirrhotic patients due to delayed mottling appearance and higher knee StO2 related to higher skin perfusion.
Management of bleeding and transfusion during liver transplantation before and after the introduction of a rotational thromboelastometry–based algorithm


Roullet, S., Freyburger, G., Cruc, M., Quinart, A., Stecken, L., Audy, M., Chiche, L. and Sztark, F.

Orthotopic liver transplantation (OLT) remains a potentially hemorrhagic procedure. Rotational thromboelastometry (ROTEM) is a point-of-care device used to monitor coagulation during OLT. Whether it allows blood loss and transfusions to be reduced during OLT remains controversial. Excellent correlations and predictive values have been found between ROTEM parameters and fibrinogen. We hypothesized that the use of a ROTEM-based transfusion algorithm during OLT would lead to more fibrinogen transfusion and decreased bleeding and blood transfusion. Sixty adult patients were consecutively included in a prospective, without-versus-with study: 30 in the group without ROTEM results and 30 in the group with the ROTEM-based algorithm. A small and nonsignificant increase in median fibrinogen transfusions was found for the with group (6.0 g versus 4.5 g, P = 0.50). It was not associated with a decrease in blood transfusions or in the number of patients exposed to blood products. Liver Transpl 21:169-179, 2015. © 2014 AASLD.
Central nervous system complications after liver transplantation: Common but mostly transient phenomena.


Although central nervous system complications (CNSCs) are common after orthotopic liver transplantation (OLT), standardized prospective studies are still lacking. This prospective study was aimed at determining the incidence of CNSCs, describing their clinical presentations, and establishing predicting factors. One hundred thirty-six adult patients who underwent OLT at Hannover Medical School between December 2008 and June 2011 were included. Weekly examinations were performed by a neurologist during the hospital stay after OLT. Patient data, donor data, and operative and postoperative variables were collected. Patients with cerebral dysfunction after OLT underwent a diagnostic work-up, which included brain imaging and, if necessary, cerebrospinal fluid analysis. Patients with central nervous system (CNS) symptoms but negative imaging and cerebrospinal fluid results and patients with pontine myelinolysis or posterior reversible encephalopathy syndrome were placed in a metabolic-toxic CNSC group, and patients with strokes, intracranial hemorrhaging, or CNS infections were placed in a nonmetabolic CNSC group. Multiple regression analysis was used to identify independent risk factors for the development of metabolic-toxic CNSCs. After excluding two patients that died after OLT without regaining consciousness, forty-four (32.8%) patients developed CNSCs: 37 of these patients (27.6%) had metabolic-toxic CNSCs, and 7 (5.2%) had nonmetabolic CNSCs. Acute-on-chronic liver failure, the number of subsequent surgeries, and primary sclerosing cholangitis were identified as independent predictors for the development of metabolic-toxic CNSCs. Metabolic-toxic CNSCs were associated with prolonged hospital stays, and nonmetabolic CNSCs were associated with higher mortality. In conclusion, CNSCs are common and relevant complications after OLT. Patients after OLT, especially with risk factors, should undergo a regular standardized neurological examination that would allow early detection of these complications. Liver Transpl 21:224-232, 2015. © 2014 AASLD.
Hemostatic status in liver transplantation: Association between preoperative procoagulants/anticoagulants and postoperative hemorrhaging/thrombosis.


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The delicate rebalanced hemostatic status of liver transplant recipients may lead to both hemorrhagic and thrombotic tendencies in this population. The aim of this study was to investigate the association between pretransplant procoagulants/anticoagulants and posttransplant bleeding and thrombosis among living donor liver transplant recipients. The study subjects were 403 consecutive recipients with chronic liver disease. Perioperative variables, including preoperative values for procoagulants and anticoagulants, were assessed to determine their association with posttransplant hemorrhaging and thrombosis. There were 35 hemorrhagic complications (9%) and 21 thrombotic complications (5%). In logistic regression analyses, a higher Model for End-Stage Liver Disease score (P = 0.01) and a lower fibrinogen value (P < 0.001) were independently associated with hemorrhaging, whereas only a lower protein C value (P < 0.001) was independently associated with thrombosis. In a receiver operating characteristic analysis, a low preoperative protein C value (with the most accurate cutoff value being 25%) was a reliable predictor of thrombotic complications after liver transplantation (area under the curve = 0.921, P < 0.001, sensitivity = 0.9, specificity = 0.8). In conclusion, the decreases in both procoagulants and anticoagulants in liver transplant recipients may additively result in a delicate hemostatic balance and predispose patients to both hemorrhagic and thrombotic complications. A lower preoperative protein C value (<25%) was demonstrated to be a significant and reliable predictor of postoperative thrombotic complications in liver transplant recipients. Liver Transpl 21:258-265, 2015. © 2014 AASLD.