Prospective Study

Hepatic encephalopathy before and neurological complications after liver transplantation have no impact on the employment status 1 year after transplantation

Response letter to reviewer comments

Thank you very much for the review of our manuscript and the constructive comments. In the following we would like to reply to each comment.

Page 10: The authors need to be more specific in their statistical analyses, specifically: (a) how was normality of distribution assessed? (b) how were the regression models built (entry-retention criteria, process, eg. backward or forward conditional, stepwise?). Also, why chi-square and not Fisher's, especially for smaller groups? --After the above clarifications, please provide the full regression models (OR, estimates of fit etc) rather than "multivariate analysis" p-values. --Consider involving someone from the biostatistics department of the affiliated university in analyzing these complex results.

- Thank you for this advice. We have included a more detailed description of the statistical methods applied (page 11). a) Normality of distribution was assessed by the Shapiro-Wilk test. b) The regression model was a binary logistic regression analysis with the method=enter. We changed the chi-square analysis to Fisher's Exact Test where applicable and corrected the p values

accordingly. The full regression model (method, Omnibus Test of Model Coefficients, -2 Log likelihood, Nagelkerke R Square and effects size Cohen's d) was included into the description of the statistical methods applied (page 11). For the variables in the Equation significant at the 0.05 level, Wald statistic, p value, the Odds ratio (Exp(B)) and the confidence interval for the Odds ratio (Exp(B)) were provided. The analysis was performed with the support of Prof. Hartmut Hecker the biostatistics department at Hannover Medical School.

The authors need analyze employed vs. non-employed patients before/after transplant as binary parameters. I am very interested to know (acknowledging the numbers were small) if there were any significant differences, or 'trends' as the authors call them, between 'discordant' and 'concordant' groups, i.e. patients who lost their employment after OLT compared to those employed pre- and after, and also patients who were not employed before but were employed after OLT, compared to those who remained not employed.

- Thank you for this suggestion. We have included a comparison of patients employed before and after OLT to patients that were employed before but did not return to employment after OLT as well as of patients that were not employed before and after OLT to patients not employed before OLT that were reintegrated into employment after OLT (page 13). The results support our already existing analysis. Patients reintegrated into employment after OLT showed better results in the cognitive function testing and a better health related quality of life (Tables 5 and 6) compared to patients that did not return to their pre OLT job. Concerning the comparison of patients not employed before and after OLT to patients not employed before but reintegrated into

employment after OLT no significant differences were found except for age (p=0.03) and CFF (p<0.01). The patients reintegrated into employment after OLT were younger and showed better CFF values than patients that were not employed before and after OLT (Tables 7 and 8). The results of this subgroup analysis, however, are limited due to a small number of patients.

Based on the above and already existent results, perhaps the authors could elaborate a little more on behavioral, medical and social interventions that could be undertaken to optimize engagement in work after OLT and quality of life improvement.

- We have extended the discussion (page 19) about possible behavioral, medical and social interventions which might be undertaken to facilitate the reintegration of patients after OLT into the pre OLT job based on a recent review by Aberg (reference 36).

As a transplant ID doctor, I am curious, was there any information on infection and how did it correlate with studied outcomes?

- This is a very interesting question but unfortunately we do not have sufficient information about infections of our patients after OLT.

What were the causes of death after OLT?

- The cause of death was multi-organ failure in 5 cases, sepsis, heart failure or abdominal bleeding in 3 cases each, subarachnoid haemorrhage in one case, meningitis/encephalitis in one case and unknown in 2 cases. (page 12)

Page 8: Why were patients aged >60 excluded? I suspect it likely has to do with age of employment/retirement, but the authors should explain.

- Patients older than 60 were excluded because of the high probability of age related retirement above the age of 60 and the expected low probability of reintegration into employment after OLT. The explanation was included into the description of the exclusion criteria. (page 8)

Page 12: I would rephrase "the level of significance between the 2 patients groups was missed, however, the trend indicated a higher incidence in not employed patients." as .... was more frequent, but the difference did not reach statistical significance at the 0.05 level.

- Thank you for this advice. The sentence was changed accordingly. (page 12)

Also, the authors keep using the term "academics". What does that mean, does it refer to a university degree or employment in the field of academia? I would use a different term accordingly.

- The term "academic" refers to the acquired university degree. Patients with a university degree were classified as academics and patients with a vocational training for qualification were classified as non-academics. The description of the terms academic and non-academic were changed accordingly. (page 10 and 11)

In the tables, please include one %, not both (eg. 40% instead of 40/60%).

- Thank you for this comment. We have changed our tables accordingly.

In Fig. 4 legend, please indicate *P<0.05 instead of 'significant'

- The sentence was changed accordingly. (page 46)

Kind regards,

Dr. Henning Pflugrad