

Royal Free Perioperative Research Group
Department of Anaesthesia
Royal Free Hospital
Pond Street
London
NW3 2QG

Dear Jin-Xin.

Re: Manuscript NO: 29058-manuscript revision

Thank you for considering our manuscript for publication in your journal. We are very grateful to the reviewers for their comments and suggestions and have amended the manuscript accordingly. Please find below a summary of comments made by the reviewers, my response and a quote of the highlighted / amended section within the text.

I was unable to subject the manuscript to CrossCheck analysis as I do not have membership access for this facility. Upon google scholar checking, my title does not appear.

1. The introduction is long enough – The abstract has been shortened and the introduction has been left as is.
2. Did the authors include pts with HCC? The cohort of patients did include those with HCC but were recorded as having concomitant underlying liver cirrhosis. The text has been changed to reflect this.
The cohort of patients reviewed had transplantation for chronic end stage liver disease, with or without hepatocellular carcinoma.
3. Performance of the assay used for determination of coagulation parameters are necessary. All laboratory assays undergo both external and internal quality control processes and this has been reflected in the text as:
All assays are controlled and monitored using laboratory quality assurance processes.
4. Some comments regarding others related articles is needed in the discussion. There was no further additional literature available at the time of writing that reflects the findings of the study in vivo. The main body of work suggesting the contribution of fibrinogen was in Velik-Salschner et al's work in vitro.
5. Abstract is too long, please summarize and only present the key points in the method and results section. The methods and results sections of the abstract have been reduced in size and key points summarized:

METHODS:

A retrospective analysis of our OLT Database (2006 - 2015) was performed. Baseline haematological indices and intraoperative blood transfusion requirements, as a combination of cell salvage return and estimation of 300mls/unit of allogenic blood, was noted as a surrogate for intraoperative bleeding. 2 groups: Excessive transfusion (>1200ml returned) and No excessive transfusion (<1200ml returned) were analysed. All data analyses were conducted using IBM SPSS Statistics version 23.

RESULTS:

Of 322 OLT patients, 77 were excluded due to fulminant disease; redo transplant or baseline haemoglobin (Hb) of <80g/L.

114 (46.3%) were classified into the excessive transfusion group, 132 (53.7%) in the No excessive transfusion group. Mean age and gender distribution were similar in both groups. Baseline Hb ($p<0.001$), platelet count ($p=0.005$), claus fibrinogen ($p=0.004$) and heparinase MA ($p=0.001$) were all statistically significantly different.

Univariate logistic regression with a cut-off of platelets $<50 \times 10^9/L$ as the predictor and Haemorrhage as the outcome showed an Odds Ratio (OR) of 1.393 (95% CI 0.758-2.563; $P = 0.286$).

Review of ROC curves showed an Area Under the Curve (AUC) for platelet count of 0.604 (95% CI 0.534-0.675; $P=0.005$) as compared with AUC for fibrinogen level, 0.678 (95% CI 0.612-0.744; $P<0.001$). A multivariate logistic regression shows UKELD ($p=0.006$), Hb ($p=0.022$) and Fibrinogen ($p=0.026$) to be statistically significant, whereas Platelet count was not statistically significant.

6. Add footnote to spell out all abbreviations at the bottom of tables. Foot notes have been added to each table to spell out abbreviations. In some cases, whole words have been used instead of abbreviations.

¹ N= number; SD = standard deviation; UKELD: United Kingdom end stage liver disease score; ALD = Alcoholic liver disease; NASH = Non-alcoholic steato-hepatitis;

PSC = Primary sclerosing cholangitis; PBC = Primary biliary cirrhosis; AIH= Autoimmune hepatitis; HB = Haemoglobin; Hep MA = Maximum amplitude on heparinase thromboelastography.

²N= number; SD = standard deviation; UKELD: United Kingdom end stage liver disease score; ALD = Alcoholic liver disease; NASH = Non-alcoholic steato-hepatitis; PSC = Primary sclerosing cholangitis; PBC = Primary biliary cirrhosis; AIH= Autoimmune hepatitis; HB = Haemoglobin; Hep MA = Maximum amplitude on heparinase thromboelastography.

³OR = Odds ratio; 95% CI = 95% Confidence Interval

⁴OR = Odds ratio; 95% CI = 95% Confidence Interval; UKELD = United Kingdom End-stage Liver Disease score; Hb= Haemoglobin; Hep MA = Maximum amplitude on heparinase TEG

7. Please not just put down the raw output figure and tables from SPSS. Please edit the figures and also prepare separation tables for AUROC. Unfortunately, I'm unable to produce editable graphs from SPSS (I have attached outputs to my submission). I have re-produced the separation tables accordingly.

Test	Area under the curve	Standard Error	Asymptotic Significance	95% Confidence Interval
Platelets	0.604	0.036	0.005	0.534-0.675
Fibrinogen	0.678	0.034	<0.001	0.612-0.744

If you require any further information, please do not hesitate to contact me.

Thank you and best wishes,

Sonali Thakrar
MBBS BSC MRCP FRCA