

April 26, 2016

Re: Revised article submission

Dear Editor-in-Chief:

I am enclosing a revised copy of an original research on **“Nationwide Trends and Predictors of Inpatient Mortality in 83,884 Transjugular Intrahepatic Portosystemic Shunt: A 15-year Study in the US”** for your review.

We have answered and edited the manuscript according to the comments of the reviewers and editors (please see below for the point-to-point responses).

I hope you find our manuscript interesting and suitable to publish in the World Journal of Gastroenterology.

Yours sincerely,



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Reviewer 1:

In this study, using the National Inpatient Sample (NIS) database from 1998 to 2012, the authors evaluated several factors contributing to in-patient mortality in 83,884 TIPS performed in the U.S. in 15 years. In general, the main idea is interesting because this is a large-scale, national trends data investigating in-patient death following TIPS. Factors affecting patient survival following TIPS has been extensively studied in the past. However, the majority of these studies are of a limited sample size. No contemporary nationwide analysis of patient demographic, hospital, and diagnostic data to in-patient mortality has been performed.

Comments:

1. There is a lack of MORE DETAIL explanation of statistical methods used in the study.

--- The following detailed statistical methods have been added:

**Proportions or mean  $\pm$  SD were calculated for all studied parameters. General outcomes reported included percentile of in-hospital mortality and mean length of stay  $\pm$  SD. These outcomes were further categorized as ‘before 2005’ or ‘after 2005’ to investigate the effects of the commercial availability of PTFE-covered stents around 2003-2004. Appropriate Z and T tests were utilized for comparison analysis. The primary outcome measure to be evaluated through multivariate analysis was in-hospital mortality. Using multi-nominal logistic regression, we identified the most significant profile factors related to increases in in-patient mortality within the demographic, hospital, and diagnostic categories. Odds ratios with appropriate 95% confidence intervals and p values were calculated alongside a reference point for comparison analysis. For demographic and hospital variables, the reference point was selected among variable outcomes (such as Caucasian for race). For diagnostic variables, the reference of comparison was having no diagnosis of disease or comorbidity. Comorbidity measures are in accordance to the Comorbidity Software designed by the Agency for Healthcare Research and Quality (AHRQ) which identifies a set of comorbidities and separates them from the primary reason for hospitalization for use with large administrative datasets.**

2. “General outcomes were further categorized as ‘before 2005’ or ‘after 2005’ to investigate the effects of the commercial availability of PTFE-covered stents around 2003-2004”. Now that, the article is concerning about the Inpatient Mortality, would it be better if general outcomes were categorized as ‘before 2004’ or ‘after 2004’, as the Inpatient Mortality is remarkable according to the figure2B.

--- Yes, it is correct as it had a significant decrease from 2004 to 2005. However, we analyzed the overall average mortality rate and trend which showed significant change from 1998-2004 vs. 2005-2012. The PTFE-covered stents were not really marketed and used until late 2004/early 2005. Therefore, we were able to make that assumption/correlation.

3. There is a mistake in Figure1, Is the number of unweighted NIS TIPS correct, n=17504? Which is less than that of weighted TIPS.

**--- Yes, the HCUP NIS data is only 20% sampling of the U.S. inpatient database. Therefore, when we correct and weight them, it usually weighs them by 4-5.5x more from the raw data. Therefore, the weighted TIPS data has higher value.**

4. Chi-square P value in table 2, Diagnosis (ICD-9 code) is redundant.

**--- Chi-square value in table 2 has been removed.**

Reviewer 2:

the authors reported the results of a large-scale national trends investigating in-patient death following TIPS. hepatic encephalopathy represents a common diagnosis. to our knowledge, hepatic encephalopathy remains a contraindication. it might be useful to include MELD score in multivariate logistic regression analysis. did the authors try to develop and validate a scoring system for in-patient mortality following TIPS. a validated score can be used in the daily clinical practice in order to select patients to improve post-TIPS mortality and clinical outcome of TIPS.

**--- Unfortunately, NIS database does not give any laboratory values or clinical exam assessment values to determine MELD score or scoring system that can be used in daily patient selection and pre-TIPS assessment. We are currently working on these aspects of TIPS using our own patient data.**