Prognostic Nutritional Index in Short-term Postoperative Outcomes in Hepaticojejunostomy

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ABSTRACT

Objective: To investigate the utility of prognostic nutritional index (PNI) on short-term complications, biliary fistula, mortality, and morbidity in patients undergoing hepaticojejunostomy (HJ) procedure.

Study Design: Observational study.

Place and Duration of Study: Tepecik Training and Research Hospital, Izmir, Turkey, between January 2018 and January 2020.

Methodology: Patients who underwent elective HJ for benign and malignant reasons were scanned retrospectively using the hospital digital record system. Many data such as chronic diseases and PNI values of patients, postoperative 30-day mortality and morbidity, days of hospital stay (HS), postoperative complications, and data of surgery were analyzed.

Results: A total of 81 patients, of whom 42 (52%) were males and 39 (48%) were females, were included in the study. The mean age of the patients was 65.8 ±11.3. In 53 patients (65.4%), surgeries were performed due to malignancy. In 19 (23.4%) patients, grade 3 and 4 complications according to Clavien-Dindo Classification were observed in 12 patients (14.8%), and postoperative 30-day mortality was observed. The rate of grade 3 and 4 complications increased in patients with a PNI below 45, it was not statistically significant (p=0.165). The mortality rate was 4.5% in patients with PNI>45, and 18.6% in patients with PNI<45 but this difference was not significant (p=0.165). The mean HS was significantly shorter in patients with PNI>45 (p=0.02).

Conclusion: At PNI>45, many complications and hospital stay become markedly shorter. Large multi-centre randomised future studies are required to confirm these findings.

Key Words: Prognostic nutritional index, Hepatic duct, Biliary tract, Biliary fistula.


INTRODUCTION

Anastomoses between the biliary system and the gastrointestinal tract are most often applied to the jejunum. It is less frequently applied to the duodenum.¹ Since the first hepaticojejunostomy (HJ) published by Dahl, many different techniques have been applied in many different surgical operations.² These techniques are an important component of hepatopancreaticobiliary (HPB) surgery, including pancreaticoduodenectomy for benign and malignant neoplasms, liver transplantation, bile duct tumors, repair due to bile duct injuries, and cholecodolithiasis.³

When maturing anastomosis, interrupted sutures, continuous sutures, and combined methods are used. The most important complications after a HJ are leakage and stenosis. The frequency of leakage development varies between 2.3% and 5.6%. HJ anastomosis leak prolongs hospital stay and negatively affects mortality and morbidity.⁴ Although there are publications examining the effects of various factors on leaks, data directly related to the effect of nutritional status and prognostic nutritional index on leakage in HJ anastomoses are limited. Nutritional status is an important step in the incidence and prediction of postoperative complications.⁵ Preoperative nutritional assessment is routinely recommended by the International Pancreatic Surgery Working Group (ISGPS) because malnutrition is an important risk factor for surgical complications.⁶ Prognostic nutritional index (PNI) is a scoring system calculated using albumin and lymphocyte counts, reflecting the immunity and nutritional status of the patients.⁷ The aim of this study was to investigate the effect of the prognostic nutritional index on short-term complications,
biliary fistula, postoperative 30-day mortality, and morbidity in patients undergoing HJ procedure.

**METHODOLOGY**

Patients, who underwent elective HJ for benign and malignant reasons in the General Surgery Clinic of Izmir Tepecik Training and Research Hospital between January, 2018 and January, 2020, were included in the study. Patients younger than 18 years of age, patients who were operated on urgent basis, patients with incomplete data, and patients who underwent liver transplantation were excluded from the study. Patients' data was scanned retrospectively using the hospital digital record system. The demographic characteristics of the patients were examined. Types of sutures used in anastomoses (Polydioxanone (PDS), 4/0 or 5/0), postoperative complications according to Clavien-Dindo Classification (CDC), biliary fistula rate, final pathology reports, mean hospital stay (HS), postoperative 30 days mortality, presence of plastic stent or percutaneous transhepatic biliary drainage (PTBD) in the preoperative biliary tract and common bile duct, anesthesia scores according to the American Society of Anesthesiologists (ASA), history of diabetes mellitus (DM), preoperative bilirubin values (>5 mg/dL, <5 mg/dL), preoperative choledochal diameters (>1.5 cm, <1.5 cm) were evaluated. Prognostic nutritional index scores (>45, <45) of the patients were calculated and albumin (>3.5 g/dl, <3.5 g/dl) values were recorded. The effects of related variables on biliary fistula, mean HS, CDC morbidity, and mortality rates were evaluated. When calculating the mean HS, all the patients who developed mortality, were not included.

Onodera’s PNI, calculated as 10×albumin (g/dl) + 0.005×total lymphocyte count (per mm3). Albumin and leukocyte values from the last few days before surgery were used in this assessment. PNI cut-off value was established as 45 in accordance with the literature. Hypoalbuminemia in the adult population is defined as a blood albumin level below 3.5 g/dl.

Surgeries were performed by the same surgeon using a continuous suture technique in all HJ anastomoses surgeries. The common bile duct was resected 0.5 to 1 cm distal to the bifurcation line. For the anastomosis between the common bile duct and jejunum, 4/0 or 5/0 PDS was used and the anterior and posterior walls were matured with continuous tension-free sutures. Use of classical pancreaticoduodenectomy (Whipple procedure) or pyloric-sparing pancreaticoduodenectomy (PPPD) was preferred for periampullary region tumors. The Roux-en-Y procedure was preferred for drainage in surgeries other than PPPD. The Roux-en-Y procedure was also preferred in drainage surgeries performed for cholecodocholithiasis and other benign causes (benign biliary stenosis, sclerosing cholangitis, etc.). In these surgeries, the jejunum efferent ans was applied 40-60 cm distal from the HJ.

The HJ anastomotic leakage criteria developed by the International Study Group of Liver Surgery was used when diagnosing anastomotic leakage after HJP surgery. Accordingly, bile leakage was defined as either the bilirubin concentration in the drain fluid at least 3 times the serum bilirubin concentration on or after the third postoperative day; or the need for radiological or operative intervention due to bile collection/biliary peritonitis.

SPSS version 25.0 was used for statistical analysis. The conformity of the variables to the normal distribution was examined using analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). The categorical variables were shown as frequency (n) and percentage (%) (and the continuous variables who were lying under normal distribution, were expressed as mean ± SD, and the non-parametric variables were expressed median, IQR, and min-max). The t-test was used in the independent groups, and the Mann-Whitney U-test was used in non-normally distributed groups. Pearson’s Chi-square or Fisher’s Exact Chi-Square test was used in the analysis of categorical data. Statistically, the cases where the p-value was below 0.05 were considered significant.

Local ethics committee approval was obtained for the present study. (Decision No.2020/11-5, date: 14.09.2020).

**RESULTS**

A total of 81 patients, of whom 42 (52%) were males and 39 (48%) were females, who met the inclusion criteria, were included in the study. The mean age of the patients was 65.8 ±11.3. The number of patients older than 65 years of age is 46 (56.8%). Fifty-three operations (65.4%) were performed due to malignancy. Thirty-six patients (44.4%) had ASA scores of 3 and 4, and 45 (55.6%) patients had ASA scores of 1 and 2. Twenty-four patients had DM, which was under control with medical treatment. The median hospital stay of the patients was 11 days (Range: 30, IQR: 7).

The most frequently preferred surgeries were PPPD (56 patients, 69.1%). The HJ + Roux-en-Y drainage procedure (21 patients, 25.9%) was performed for benign reasons. Fifty-three patients (65.4%) surgeries were performed due to malignancy. According to CDC, grade 3 and 4 complications were observed in 19 (23.4%) patients, and postoperative 30-day mortality was observed in 12 (14.8%) patients. The biliary fistula was seen in 5 patients (6%).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Subgroups</th>
<th>Number of patients (n) (%)</th>
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</thead>
<tbody>
<tr>
<td>Presence of preoperative stent (plastic stent or PTBD)</td>
<td>Yes</td>
<td>49 (60.5%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>32 (39.5%)</td>
</tr>
<tr>
<td>Cholecodoch diameter</td>
<td>&gt;1.5 cm</td>
<td>41 (50.6%)</td>
</tr>
<tr>
<td></td>
<td>&lt;1.5 cm</td>
<td>40 (49.4%)</td>
</tr>
<tr>
<td>Suture type</td>
<td>4/0</td>
<td>61 (75.3%)</td>
</tr>
<tr>
<td></td>
<td>5/0</td>
<td>20 (24.7%)</td>
</tr>
</tbody>
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PTBD: Percutaneous transhepatic biliary drainage.

When the biochemical parameters were examined, there were 30 (37%) patients with a blood bilirubin level of 5 mg/dl and above. The surgical data of the patients are summarised in Table I.

<table>
<thead>
<tr>
<th>Gender, age groups (≥65, &lt;65), surgical procedures, types of sutures used (4/0, 5/0 PDS), malignant and benign etiologies,</th>
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presence of a preoperative stent, and bilirubin levels \((\geq 5 \text{ mg/dL, } <5 \text{ mg/dL})\), the diameter of the common bile duct \((>1.5 \text{ cm, } <1.5 \text{ cm})\), DM history and blood albumin values \((\leq 3.5 \text{ g/dL, } >3.5 \text{ g/dL})\) were examined. There was not any subgroup that statistically affected the development of biliary fistula \((p>0.05)\).

There was no statistically significant difference in the development of biliary fistula between patients with a PNI score above and below 45 (Table II). Biliary fistula developed in 4 of 32 (13%) patients, who were not stented preoperatively, and in 1 of 49 (2%) patients, who were stented. Stenting in the preoperative period decreased the development of biliary fistula proportionally, but this was not statistically significant \((p=0.077)\).

Nineteen patients (23.4%) had grade 3 and 4 complications in the postoperative period. In the analysis of all the sub-groups examined, there was no group that affected the development of grade 3 and 4 complications statistically \((p>0.05)\). Although, the rate of grade 3 and 4 complications increased in the patients with a PNI below 45, it was not statistically significant \((p=0.294)\) (Table III). Other subgroups such as gender, type of surgery, benign and malignant etiologies, presence of preoperative stent and DM, and common bile duct diameter did not have a significant effect on mortality \((p>0.05)\).

The mean HS was significantly shorter in the patients with a PNI score of 45 and above \((p=0.022)\) (median: 14 days in patients with PNI>45, IQR: 7, median:10 days in patients with PNI<45, IQR: 7). HS of 56 patients, who underwent PPPD, was significantly longer \((p<0.0001)\) than those who underwent the HJ+ Roux-en-Y procedure (median: 13 days, IQR: 6, median: 5 days, IQR: 4). Similarly, the development of grades 3 and 4 (Median: 19 days, IQR: 13) complications according to CDC also significantly prolongs the mean HS compared to grades 1 and 2 (Median: 10 days, IQR: 7) \((p=0.001)\). Age groups, hypoalbuminemia, and preoperative bilirubin level had no significant effect on HS \((p>0.05)\).

**DISCUSSION**

HJ is one of the most commonly used anastomosis types in HPB surgeries. HJ anastomotic leaks prolong hospital stays and increase mortality and morbidity rates.\(^{11,12}\) In the literature, the leakage rate in anastomoses of the biliary tree varies between 2.2% and 10%; this rate is much higher in patients who underwent surgery for cholangiocarcinoma or in the patients with liver transplantation.\(^{13,14}\) 2% for a simple HJ, reaches 50% for some patients after liver transplantation.\(^{3}\) Another controversial issue regarding HJ is the technique used when performing the anastomosis. Contrary to the classical knowledge, in a large study involving 77 hospitals in Germany, it was shown that single, continuous or combined suture methods did not have a statistically significant advantage over each other in the development of complications, but the continuous suture technique was faster than others.\(^{4}\) In the authors’ practice, a continuous suture technique was used for HJ anastomoses. Biliary fistula rate of 6% found in our study is consistent with the literature. There was no subgroup that significantly affected the development of biliary fistula among the groups. Biliary fistula rate was lower in the patients with preoperative biliary stent placement (1%) than in patients without stent (12.5%), but this was not statistically significant.

In the treatment of biliary fistula, a PTBD catheter was inserted in three patients with low-output biliary fistula under the guidance of interventional radiology. In the other two patients with high fistula outflow, revision of the HJ anastomosis was performed in the second operation.

PNI is generally used to evaluate the immunological and nutritional characteristics of the patients undergoing gastrointestinal system surgery.\(^{15}\) The importance of PNI in HPB surgery is clear. Although, the relationship of PNI with pancreatic fistula and its complications, and its association with postoperative mortality, morbidity, and average survival in cancer surgery are frequently examined in the literature results regarding PNI’s effect on HJ complications are limited.\(^{5,6,13-16}\) The International Study Group on Pancreatic Surgery (ISGPS) recommends the evaluation of nutritional status as part of routine preoperative evaluation, as malnutrition significantly increases the risk of surgical complications.\(^{6}\) Kanda et al. found that preoperative low PNI was an independent risk factor for poor survival in patients with pancreatic cancer, it was significantly associated with postoperative complications along with the development of pancreatic fistula.\(^{5}\)

PNI has been shown to be a strong prognostic factor in predicting mean and disease-free survival in patients with hepatocellular cancer (HCC), and it is recommended to be included at every stage in diagnosis and treatment.\(^{11,12}\) The reason why the authors preferred PNI in this study is the advantage of PNI over other evaluation criteria such as neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) in many studies. It has been demonstrated that PNI is an independent risk factor compared to NLR and PLR in predicting postoperative mortality, morbidity, and overall disease-free survival in patients with pancreatic ductal adenocarcinoma.\(^{15}\) In another study, examining patients with PDAC, who underwent surgery after chemoradiotherapy, PNI was found to be the strongest prognostic/predictive factor in showing prognosis.\(^{16}\)

This is the first study to examine the impact of PNI on HJ anastomosis outcomes. In line with the available data, patients with a high PNI score in the series had a significantly shorter postoperative HS. In line with the available data, patients with a high PNI score in the series had a significantly shorter postoperative HS.
Hayashi et al. revealed that the length of stay in the intensive care unit was significantly shorter in the group of the patients with high PNI after cardiovascular surgery.\textsuperscript{17} According to CDC, grade 3 and 4 complications; postoperative 30-day mortality are proportionally higher in the patients with low PNI scores, but this was not statistically significant. Out of the 12 patients, who developed mortality, 11 were in the group with a PNI score below 45. The mortality rate was approximately 4 times higher in the group with a low PNI score than in the group with a high PNI score. Only grade 3 and 4 complications according to CDC, were included in the study. The effect of PNI on total complication rates when grade 1 and 2 complications were included but were not analysed in this article. When the effect on the development of biliary fistula was examined, there was no significant relationship between PNI score and anastomotic leakage. The authors of this study concluded the above outcome to be the limited number of patients.

Another factor associated with poor postoperative outcomes is hypoalbuminemia.\textsuperscript{10} Hypoalbuminemia has been shown to be among the most important predictors of post-HJ morbidity and increased resource use.\textsuperscript{18} In this study, all the patients who developed mortality in parallel with the literature were in the hypoalbuminemia group and this relationship was significant. According to postoperative CDC complication rates (27.1%) and biliary fistula development (6.8%) were higher in the patients with hypoalbuminemia than in the patients without hypoalbuminemia (13.6% and 4.5%, respectively), but this was not significant. Other factors that significantly increased mortality in this study were being over 65 years old and high blood bilirubin. Mortality occurred in 3 out of the 5 patients who developed biliary fistula.

The 14.8% mortality rate found in this study is higher than in the literature. However, the most important reason for this is that the rate of biliary reconstruction performed due to malignancy in the whole population and the number of patients over 65 years of age and ASA 3 and 4 are much higher than in the literature. In a national, retrospective analysis of 67,160 patients who underwent biliary tract reconstruction for 7 years for various reasons in the USA, 37.4% of all surgeries were performed for malignancy, and 45.3% of the patients were over 65 years of age.\textsuperscript{18} In this study, the rate of malignant etiologies was 65.4%, and 56.7% of the patients were over 65 years of age. In addition, 44.4% of all patients have comorbidity of ASA 3 and above. The limitations of the study include its retrospective design, single centre data, a relatively small number of the patients, and failure to examine the long-term effects of PNI on mortality and morbidity. The present study is important because it is the first publication to evaluate the effect of PNI on short-term postoperative outcomes in patients undergoing biliary reconstruction with HJ.
CONCLUSION

Low PNI significantly prolongs the mean hospital stay and increases complication and mortality rates in patients undergoing hepaticojejunostomy. In the current study, no significant effect of PNI on the development of biliary fistula was found.

ETHICAL APPROVAL:

This study was conducted retrospectively and approved by the local ethics committee of the University of Health Sciences Tepeçik Training and Research Hospital, Izmir, Turkey, in September 2020. The approval number of this study is 2020/11-5.

COMPETING INTEREST:

The authors declared no competing interest.

AUTHORS’ CONTRIBUTION:

AD: Contributed to the design, data analysis, writing, and translation of the manuscript.
SCE: Contributed to data analysis and writing of the manuscript.
GKT, CK, IS: Contributed to writing and supervision of the manuscript.

All authors approved the final version of the manuscript to be published.

REFERENCES