A retrospective study of enteral nutrition on immune and inflammatory factors after liver cancer surgery

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Abstract

This retrospective study aimed to explore the effect of enteral nutrition (EN) on immune and inflammatory factors after liver cancer surgery (LCS).

It was retrospectively conducted on enrolled LCS patients between January 2017 and May 2020. The medical records of 528 patient case records were collected and reviewed. After selection, a total of 80 eligible patient case records were finally included. All those patients received routine diet, and they were allocated to a treatment group (n = 40) and a control group (n = 40). In addition, patients in the treatment group also received EN. The primary outcomes were immune factors ($CD4^+$, $CD8^+$, $CD4^+/CD8^+$) and inflammatory factors (interleukin-1, interleukin-6, and tumor necrosis factor-α). The secondary outcomes were postoperative hospital stay (day), time to first bowel sounds (hour), time to first flatus (day), time to first defecation (day), and complications.

There were not significant differences in $CD4^+/CD8^+$ ($P = .34$), postoperative hospital stay ($P = .39$), and time to first bowel sounds ($P = .17$) between 2 groups. However, there were significant differences in $CD4^+$ ($P < .01$), $CD8^+$ ($P < .01$), interleukin-1 ($P < .01$), interleukin-6 ($P < .01$), tumor necrosis factor-α ($P < .01$), time to first flatus ($P < .01$), and time to first defecation ($P < .01$) between 2 groups. As for complications, there were not significant differences between 2 groups ($P > .05$).

The results of this study found that EN may benefit for patients after LCS during the recovery period. Future high quality prospective studies are needed to warrant the present conclusion.

Abbreviations: EN = enteral nutrition, HCC = hepatocellular carcinoma, IL-1 = interleukin-1, IL-6 = interleukin-6, LCS = liver cancer surgery, PLC = primary liver cancer, TNF-α = tumor necrosis factor-α.

Keywords: enteral nutrition, immune factor, inflammatory factor, liver cancer

1. Introduction

Primary liver cancer (PLC) is one of the most common malignancy.[1–4] It is also the most common of cancer-related mortality around the world.[5–7] It was reported that there were 841,080 new PLC cases globally each year.[8] In China, there were

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392,869 new cases, which accounted for about 46.7% of all new cases annually worldwide.[9] It is mostly composed of hepatocellular carcinoma (HCC), and about 75% to 85% of all PLC cases are HCC.[8–11] The 5-year overall survival rate of HCC ranged between 11.2% and 14.0% from 2012 to 2015 in China.[9]

Previous studies have reported that malnutrition is one of the most healthy disorders in cancer patients.[12–14] Studies also suggest that there is firmly association between malnutrition and clinical cancer, such as PLC.[12–14] The other studies have reported that optimization of nutritional status may benefit liver function enhancement, and affect the success of liver cancer surgery (LCS).[15–18] Other studies have reported that enteral nutrition (EN) may impact the immune and inflammatory factors after LCS.[19–21] However, there is still insufficient evidence regarding this topic. Thus, the present study investigated the effect of EN for patients after LCS.

2. Methods

2.1. Ethic approval

This study was approved by the Ethics Committee of Longgang District Maternal and Child Health Hospital. The written informed consent was waived due to the completed patient records.

2.2. Study design

A retrospective cohort study was carried out on patients after LCS in Longgang District Maternal and Child Health Hospital.

We inspected the medical records of 80 patients who were admitted from January 2017 to May 2020. We assigned patients into 2 different groups based on the different managements they received. All 80 patients in both treatment group (n=40) and control group (n=40) received routine diet. In addition, patients in the treatment group also received EN. The clinical retrospective data of characteristics, demographics, clinical endpoints, laboratory tests, treatments, and controls were summarized and analyzed.

2.3. Patients

All patient case records fulfilled the following eligibility criteria. The inclusion criteria were as follows: age between 18 and 80 years old; confirmed diagnoses of PLC by histopathological examination[3,5]; and completed liver resection for PLC without surgical contraindication. Exclusion criteria were: a history of other malignant tumors; mental disorder; neoadjuvant chemotherapy or radiotherapy before surgery; severe diabetes and renal dysfunction; poor glycemic control; surgical contraindications; and incomplete information of patient records.

2.4. Treatment schedule

All patients in both groups received routine diet. Before surgery, all patients received low-fat diet. After surgery, they were given dietary guidance, liquid food, and semi-liquid diet.

In addition to the routine diet, patients in the treatment group also received EN suspension (TP-MCT, 1 kcal/mL, 500 mL each bottle). The amount of oral administration was 500 mL daily for 3 consecutive days before the surgery.

2.5. Outcome measurements

The primary outcomes consisted of immune factors (CD4$^+$, CD8$^+$, CD4$^+$/CD8$^+$), inflammatory factors (interleukin-1 [IL-1], interleukin-6 [IL-6], and tumor necrosis factor-α [TNF-α]). The secondary outcomes included postoperative hospital stay (day), time to first bowel sounds (hour), time to first flatus (day), time to first defecation (day), and complications. We measured all available laboratory findings 7 days after surgery, as well as other outcome indicators postsurgery.

2.6. Statistical analysis

Data were analyzed by SAS package v.9.3 (SAS Institute Inc., Cary, NC). All data were summarized by descriptive statistics of continuous values (mean and standard deviation) and categorical values (number and percentages). We analyzed all continuous data using t test or Wilcoxon test, and categorical data using Pearson chi-square test or Fisher exact test. We defined a 2-side P-value < .05 as having statistical significance.

3. Results

3.1. Patient case records selection process

This retrospective study enrolled 528 patient case records with completed liver resection for PLC between January 2017 and May 2020 (Fig. 1). Of those, 448 patient case records were excluded because of the history of other malignant tumors (n= 61), <18 years old or >80 years old (n=37), mental disorder (n= 23), chemotherapy before surgery (n=88), radiotherapy before
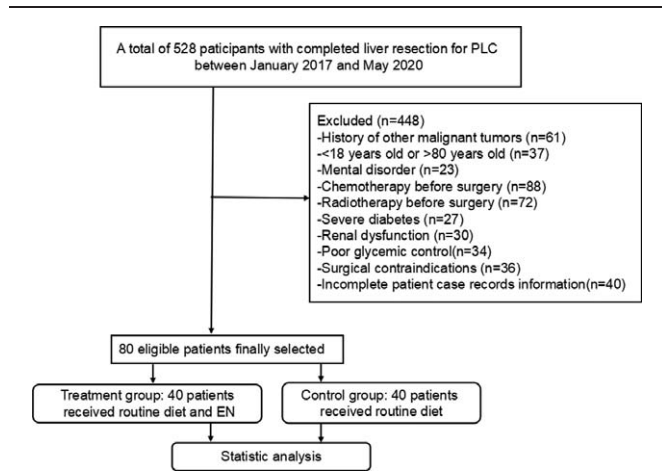

Figure 1. Flow chart of patient case records selection.

surgery (n=72), severe diabetes (n=27), renal dysfunction (n= 30), poor glycemic control (n=34), surgical contraindications (n=36), and incomplete patient case records information (n= 40). Finally, a total of 80 eligible patient case records were selected and were analyzed (Fig. 1).

Table 1

Patients' characteristic and demographic data at baseline.

Characteristics	Treatment group (n=40)	Control group (n=40)	P
Mean age, yr	56.4 (10.2)	57.1 (9.6)	.75
Gender			
Male	23 (57.5)	25 (62.5)	.65
Female	17 (42.5)	15 (37.5)	–
Race (ethnicity)			
Han	40 (100.0)	40 (100.0)	–
Occupation status			
Employed	14 (35.0)	13 (32.5)	.81
Unemployed	6 (15.0)	3 (7.5)	.30
Retired	20 (50.0)	24 (60.0)	.37
Body mass index, kg/m^2	24.3 (2.0)	24.6 (1.8)	.48
Tumor size, cm	3.9 (1.7)	3.7 (1.6)	.59
NRS2002 score	3.6 (1.8)	3.9 (1.9)	.47
Child-Pugh grade			
A	38 (95.0)	36 (90.0)	.40
B	2 (5.0)	4 (10.0)	–
Drinking history			
Yes	21 (52.5)	24 (60.0)	.50
No	19 (47.5)	16 (40.0)	–
ALT, U/L	28.9 (9.3)	28.4 (9.9)	.82
AST, U/L	28.2 (7.7)	28.0 (7.8)	.91
TB, mmol/L	14.0 (4.2)	13.6 (5.1)	.70
DB, mmol/L	4.0 (1.8)	3.8 (2.1)	.65
INR	1.07 (0.04)	1.05 (0.06)	.08
Type of hepatectomy (segments)			
≥4	6 (15.0)	5 (12.5)	.75
2–3	15 (37.5)	13 (32.5)	.64
1	19 (47.5)	22 (55.0)	.50

Data are present as mean ± standard deviation or number (%).
ALT = alanine aminotransferase, AST = aspartate aminotransferase, AKP = alkaline phosphatase, DB = direct bilirubin, INR = international normalized ratio, TB = total bilirubin.

Table 2

Comparison of immune factors after surgery between 2 groups.

Immune factors	Treatment group (n = 40)	Control group (n = 40)	P
CD4+	31.9 (2.1)	28.3 (1.8)	<.01
CD8+	30.5 (1.6)	27.7 (1.9)	<.01
CD4+/CD8+	1.05 (0.15)	1.02 (0.13)	.34

Data are present as mean ± standard deviation.

3.2. Demographics and clinical characteristics

A total of 80 cases were enrolled in this retrospective study. The characteristics and demographics of all patients are summarized in Table 1. There were not significant differences in all those values between 2 groups (P > .05, Table 1).

3.3. Laboratory findings

Laboratory results for all admitted patients with PLC after surgery are presented in Tables 2 and 3. The patients in the treatment group showed better enhancement of immune factors (CD4+, P < .01; CD8+, P < .01; Table 2) and inflammatory factors (IL-1, P < .01; IL-6, P < .01; and TNF-α, P < .01; Table 3), than those of patients in the control group. However, we did not identify significant difference in CD4+/CD8+ between 2 groups (P = .34, Table 2).

3.4. Clinical findings

Although there were not significant differences of postoperative hospital stay (day) (P = .39, Table 4), and time to first bowel sounds (hour) (P = .17, Table 4) between 2 groups, patients in the treatment group still achieved shorter time to first flatus (day) (P < .01, Table 4) and time to first defecation (day) (P < .01, Table 4), than those of patients in the control group.

3.5. Complications

All recorded complications are presented in Table 5. No significant differences of all complications were found between 2 groups (P > .05; Table 5).

4. Discussion

PLC is a very common malignant disorder,[1–4] which often causes leading mortality and morbidity.[5–7] Patients with this condition are often reported to experience malnutrition, especially for patients with LCS. EN has reported to benefit patients with LCS in improving liver function, and impacting the

Table 4

Comparison of secondary outcomes after surgery between 2 groups.

Secondary outcomes	Treatment group (n = 40)	Control group (n = 40)	P
Postoperative hospital stay, d	16.9 (3.0)	17.5 (3.3)	.39
Time to first bowel sounds, h	10.3 (4.5)	11.8 (5.2)	.17
Time to first flatus, d	1.4 (0.4)	2.2 (0.6)	<.01
Time to first defecation, d	3.2 (0.8)	2.1 (0.5)	<.01

Data are present as mean ± standard deviation.

success of LCS.[15–18] Previous studies have reported that EN has a stronger immune improvement effect and can reduce the concurrent infection rate.[22,23] In addition, EN also exerts a regulatory effect on immune function, which mainly based on the cellular immunity.[22,23] The other study has reported that EN can enhance patients' nutritional statuses and regulate their inflammation during the perioperative period.[24] There is limited study on immune and inflammatory factors after LCS. Thus, this retrospective study investigated the effect of EN on immune and inflammatory factors after LCS.

Previous study has found that increase in levels of CD4+, CD8+ can help promote the recovery of postoperative immune function and improve the status of immunosuppression, which helps to prevent postoperative infection.[25] The other studies have reported that decrease in levels of IL-1, IL-6, and TNF-α can lower inflammatory reaction, and reduce postoperative infection.[26–28] The results of this retrospective study showed that EN can not significantly improve CD4+/CD8+, postoperative hospital stay (day), and time to first bowel sounds (hour) for patients with LCS. However, EN can significantly enhance immune factors (CD4+, CD8+), inflammatory factors (IL-1, IL-6, and TNF-α); and shorten time to first flatus (day) and time to first defecation (day) for patients with LCS. Laboratory findings showed that immune factors (CD4+, CD8+) were increased, and inflammatory factors (IL-1, IL-6, and TNF-α) were lowered in the treatment group, which indicates EN may benefit patients after LCS during the recovery period. With respect to the complications, there were not significant differences in all complications between 2 groups. It means that EN may have safe profile for the management of patients after LCS.

Several limitations may exist in this retrospective study. At first, this study only inspected the short-term effect of EN on patients with LCS. So, further studies should focus on its longer term effect. Secondly, this retrospective study could not utilize randomization and blinding, which may increase the selection bias. Finally, it was retrospectively designed based on a relatively small sample size, thus, it may affect the findings of this study.

Table 3

Comparison of inflammatory factors after surgery between 2 groups.

Inflammatory factors	Treatment group (n = 40)	Control group (n = 40)	P
IL-1, pg/mL	50.3 (9.5)	61.6 (10.4)	<.01
IL-6, pg/mL	97.7 (13.6)	155.4 (30.7)	<.01
TNF-α, pg/mL	53.2 (8.8)	65.0 (10.3)	<.01

Data are present as mean ± standard deviation.
IL-1 = interleukin-1, IL-6 = interleukin-6, TNF-α = tumor necrosis factor-α.

Table 5

Comparison of complications between 2 groups.

Complications	Treatment group (n = 40)	Control group (n = 40)	P
Lung infection	1 (2.5)	0 (0)	.50
Ascites	0 (0)	1 (2.5)	.50
Postoperative hemorrhage	2 (5.0)	0 (0)	.29
Hepatic failure	0 (0)	1 (2.5)	.50

Data are present as number (%).

5. Conclusion

This study found that EN may benefit patients with LCS. Further prospective studies are still encouraged to warrant the present findings.

Author contributions

Conceptualization: Yao Xu, Feng-xiang Wei.
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