A nomogram based on Psoas muscle index and prognostic nutritional index predicts the prognosis of intrahepatic cholangiocarcinoma after surgery: a multi-center cohort study

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Research article

Keywords: Psoas muscle index, Prognostic nutritional index, Intrahepatic Cholangiocarcinoma, nomogram

DOI: https://doi.org/10.21203/rs.3.rs-753676/v1

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Abstract

Background

Intrahepatic cholangiocarcinoma (ICC) is a malignant neoplasm with a poor prognosis. Prediction of prognosis is critical for the individualized clinical management of patients with ICC. The purpose of this study is to establish a nomogram based on the psoas muscle index (PMI) and prognostic nutritional index (PNI) to identify the high risk-patient with ICC after curative resection.

Methods

ICC Patients after hepatectomy in multi-hospital from August 2012 to October 2019 were enrolled. The overall survival (OS) and recurrence-free survival (RFS) rates were analyzed by Kaplan-Meier. The independent factors were identified by univariate and multivariate Cox regression analyses. A nomogram based on independent factors was established to predict ICC patient prognosis.

Results

178 ICC patients were included. The OS was worst in the patients with a combination of low PMI combined low PNI ($p<0.01$). PMI, PNI, lymph node metastasis and tumor differentiation were the independent prognostic risk factors; these factors were used to establish the nomogram was established by it. The calibration curve revealed that the nomogram survival probability prediction model was in good agreement with the actual observation results. The nomogram has good reliability in predicting ICC patient prognosis (OS C-index = 0.692). The area under the receiver operating characteristic curve (AUC) for the nomogram’s 3-year predicted survival was 0.752. Based on the stratified by nomogram, the median survival for low-risk patients was 59.8 months, compared with 16.2 months for high-risk patients ($p<0.001$).

Conclusion

The nomogram based on the PMI and PNI can identify patients with the highest risk of poor prognosis after curative hepatectomy. It is a good decision-making tool for individualized treatment.

Background

Intrahepatic cholangiocarcinoma (ICC) is a malignant tumor of the bile duct, which originates from the intrahepatic bile duct epithelial cells[1]. In the past decade, the global incidence rate of ICC has increased significantly. Because of its insidious onset, high heterogeneity, and invasiveness, its prognosis is very poor. Radical surgery is the best choice for cure ICC[2]. However, the postoperative recurrence rate is about 50%-70[3, 4]. Previous studies revealed 5-year recurrence-free survival (RFS) and 5-year overall survival (OS) rates of patients with ICC after curative resection of 2–39% and 5–56%[5], respectively. However, the factors affecting the long-term survival after surgical resection are unclear. Therefore, prognostic model for outcome prediction and implementation of appropriate treatment strategies is required for these patients.

According to previous studies, the psoas muscle index (PMI) is a simple and measurable measure of sarcopenia[6–8]. Previous studies suggested that sarcopenia as a valuable prognostic factor in several malignant tumor, including lung
cancer[9], liver cancer[10], renal cancer[11], colorectal cancer[12], and cholangiocarcinoma[13–16]. The prognostic nutritional index (PNI) is a marker of the host’s nutritional status and inflammation levels[17]. PNI proved to be a prognostic factor for some cancers, including nasopharyngeal cancer, small cell lung cancer, esophageal cancer, pancreatic cancer[18–21], and ICC after hepatectomy[22, 23]. Previous studies have explored the individual prognosis role of sarcopenia or PNI in ICC. However, the prognostic value of a combination of sarcopenia and PNI has not been demonstrated.

In this multicenter retrospective study, we established a nomogram based on PMI and PNI to identify patients at high-risk with ICC after radical surgery.

**Methods**

**Patients selection**

The data of 251 patients with ICC who underwent radical resection in the First Affiliated Hospital of Wenzhou Medical University (Wenzhou, China) and Qilu Hospital of Shandong University (Jinan, China) from August 2012 to October 2019 were extracted from the hospital’s electronic database. After excluding 73 patients, 178 patients were included in our study (Fig. 1).

**Baseline characteristics**

The variables of interest included: (1) demographic characteristics (age, sex, body mass index, American Society of Anesthesiologists score), (2) variables from laboratory investigations (Child-Pugh grade, carcinoembryonic antigen (CEA) levels, α-fetoprotein levels, carbohydrate antigen 19–9 (CA19-9) levels, albumin (ALB) levels, platelet/lymphocyte ratio (PLR), neutrophil/lymphocyte ratio (NLR), and lymphocyte/monocyte ratio [LMR]), (3) comorbidities (diabetes, hypertension, liver cirrhosis, and portal hypertension), (4) tumor-related variables (tumor number, tumor diameter, tumor differentiation, lymph node metastasis, microvascular invasion, and perineural invasion).

Psoas muscle index and prognostic nutritional index

PMI was calculated as the total area of the psoas muscle in the horizontal axial imaging of the L3 vertebral body divided by the square of the body height[6–8]. PNI was calculated as 10×serum albumin (g/dL) + 0.005×total lymphocyte count (per mm³)[24]. To determine the PMI and PNI cutoff values, with the most significant difference, the survminer package in R was applied to find the optimal stratification. According to optimal cutoff values, all patients were divided into four subgroups: the high-PMI, low-PMI, high-PNI and low-PNI subgroups. Therefore, the patients were stratified into four subgroups: the high-PMI with high-PNI (HH-P), high-PMI with low-PNI (HL-P), low-PMI with high-PNI (LH-P), low PMI with low PNI (LL-P) subgroups.

**Postoperative follow-up strategy**

Postoperative follow-up of the cohort was conducted at each hospital. Follow-up strategies were as follows: once in every 3 months in the first year after surgery, once in every 6 months up to 3 years after surgery, and once a year after surgery. OS was defined as from the date of surgery to the date of patient’s death or the last follow-up date. The RFS considers it from the date of surgery to the date of the first recurrence or last follow-up. The last follow-up date for this cohort was May 2020.

**Statistical analysis**
Statistical analyses were performed with R (version: 3.6.1). Baseline characteristics of patients are summarized using frequency and percentage as categorical variables, and continuous variables are expressed by mean ± standard deviation or median (range). Continuous variables were compared using Student's t-test or Mann–Whitney U test. Categorical variables were compared using the χ² test or Fisher's exact test. Survival analysis between formations was performed using Kaplan-Meier method (K-M) and log-rank test. Univariate and multivariable Cox regression analyses were used to identify the risk factors of OS and RFS. A nomogram was established using the R package. The validation and accuracy of the nomogram was performed by measuring Harrell's concordance index (C-index) and area under the curve (AUC). A p-value < 0.05 was considered statistically significant.

**Results**

**Baseline characteristics**

A comparison of the baseline characteristics is illustrated in Table 1. The median follow-up time for the cohort was 28.7 months, and the 1-, 3-, and 5-year OS rates were 70.5%, 32.4%, and 18.2%, respectively; The 1-, 3- and 5-year RFS rates were 53.8%, 23.9%, and 15.9%, respectively. According to the optimal cut-off value of PMI, female patient with PMI ≤ 6.04 cm²/m² and male PMI ≤ 8.60 cm²/m² were considered to sarcopenia (Supplementary Fig. 1-A, 1-B). The optimal cut-off value of PNI was 43.6 (Supplementary Fig. 1-C), PNI was classified as low PNI and high PNI. As can be seen from the baseline data table, there were significant differences between the high PMI group and low PMI group in body mass index, tumor size, and tumor differentiation. And there were significant differences in Child-Pugh class, diabetes, NLR, PLR, and albumin between high-PNI group and low-PNI group.
| Characteristics | Total (n = 178) | PMI-low (n = 64) | PMI-high (n = 114) | P value | PNILow (n = 48) | PNI-high (n = 130) | P value |
|-----------------|----------------|------------------|-------------------|---------|----------------|-------------------|---------|
| Sex, n (%)      |                |                  |                   |         |                |                   |         |
| Female          | 93(52.3)       | 35(54.7)         | 58(50.9)          | 0.63    | 22(45.8)       | 71(54.6)          | 0.298   |
| Male            | 85(47.7)       | 29(45.3)         | 56(49.1)          |         | 26(54.2)       | 59(45.4)          |         |
| Age, year, mean ± SD | 63.57 ± 9.82 | 63.59 ± 9.62 | 63.56 ± 9.96 | 0.98   | 67.13 ± 10.52 | 62.26 ± 9.24 | 0.003 |
| BMI, kg/m², mean ± SD | 22.77 ± 3.15 | 21.98 ± 2.59 | 23.21 ± 3.35 | 0.01   | 22.72 ± 3.09 | 22.78 ± 3.17 | 0.896 |
| PMI, median (IQR) | 8.10(6.20-10.06) | 5.79(5.08-6.69) | 9.55(7.84-11.22) | 0.001 | 87(6.4-10.1) | 7.83(6.15-9.97) | 0.43   |
| PNI, mean ± SD | 47.48 ± 6.59 | 47.20 ± 5.93 | 47.63 ± 6.96 | 0.68   | 39.08 ± 3.49 | 50.58 ± 4.39 | 0.001 |
| Lymphocyte, median (IQR) | 1.5(1.17-1.91) | 1.35(1.10-1.85) | 1.53(1.24-1.93) | 0.19   | 1.15(0.82-1.38) | 1.64(1.33-2.0) | 0.001 |
| Albumin, g/l, median (IQR) | 40(36.8-43.7) | 39.8(36.8-43.4) | 40(36.9-44.1) | 0.86   | 33.7(30.6-36.6) | 42.1(39.4-44.8) | 0.001 |
| AFP, µg/L, median (IQR) | 2.76(2.01-3.89) | 3.15(2.40-4.89) | 2.56(1.90-3.70) | 0.01   | 2.55(1.91-3.43) | 2.97(2.03-3.94) | 0.306 |
| CEA, µg/L, median (IQR) | 2.80(1.7-5.52) | 3.2(1.70-7.99) | 2.58(1.70-4.38) | 0.28   | 2.5(1.7-5.05) | 2.90(1.7-5.83) | 0.624 |
| CA199, µg/L, median (IQR) | 93.0(21.0-589.8) | 117.7(23.8-823.5) | 69.5(19.9-559.2) | 0.61   | 178.9(40.4-1000) | 64.8(5.0-559.2) | 0.052 |
| PLR, median (IQR) | 142.4(103.7-194.8) | 143.4(101.3-179.6) | 141.8(106.7-197.1) | 0.71   | 187.7(113.6-251.8) | 130.6(100.8-213.2) | 0.001 |
| NLR, median (IQR) | 2.66(1.89-4.27) | 3.14(1.99-4.49) | 2.58(1.85-3.85) | 0.22   | 4.34(2.67-6.36) | 2.43(1.66-3.41) | 0.001 |
| LMR, median (IQR) | 3.13(2.14-4.25) | 2.95(1.94-5.46) | 2.35(2.21-5.46) | 0.33   | 2.16(1.33-3.2) | 3.39(2.48-4.38) | 0.001 |
| ASA grade, n (%) |                |                  |                   | 0.21    |                |                   | 0.154   |
| 1 ~ 2           | 167(93.8)      | 62(96.9)         | 105(92.1)         |         | 43(89.6)       | 124(95.4)         |         |
| 3 ~ 4           | 11(6.2)        | 2(3.1)           | 9(7.9)            |         | 5(10.4)        | 6(4.6)            |         |
| Diabetes, n (%) |                |                  |                   | 0.65    |                |                   | 0.039   |
| No              | 150(84.3)      | 55(85.9)         | 95(83.3)          |         | 36(75.0)       | 114(87.7)         |         |

\(P<0.05\) was considered statistically significant. Abbreviation: PMI, Psoas muscle index; PNI, Prognostic nutritional index; SD, standard deviation; BMI, body mass index; CEA, carcinoembryonic antigen; IQR, interquartile range; CA19-9, carbohydrate antigen 19-9; HBsAg, hepatitis B surface antigen; AFP, alpha-fetoprotein; ASA, American Society of Anesthesiologists grade score; TNM, tumor node metastasis; NLR, neutrophil to lymphocyte ratio; LMR, lymphocyte to monocyte ratio; PLR, platelet to lymphocyte ratio.
| Characteristics                        | Total (n = 178) | PMI-low (n = 64) | PMI-high (n = 114) | P value | PN-How (n = 48) | PNI-high (n = 130) | P value |
|---------------------------------------|----------------|------------------|-------------------|---------|----------------|--------------------|---------|
| Yes                                   |                |                  |                   |         |                |                    |         |
| Live Cirrhosis, n (%)                 |                |                  |                   | 0.31    | 0.276          |                    |         |
| No                                    | 143 (80.3)     | 54 (84.4)        | 89 (78.1)         |         | 36 (75.0)      | 107 (82.3)         |         |
| Yes                                   | 35 (19.7)      | 10 (15.6)        | 25 (21.9)         | 12 (25.0) | 23 (17.7)     |                    |         |
| HBsAg, n (%)                          |                |                  |                   | 0.87    | 0.341          |                    |         |
| Negative                              | 121 (68.0)     | 44 (68.8)        | 77 (67.5)         | 30 (62.5) | 91 (70.0)     |                    |         |
| Positive                              | 57 (32.0)      | 20 (31.2)        | 37 (32.5)         | 18 (37.5) | 39 (30.0)     |                    |         |
| Child-Pugh grade, n (%)               |                |                  |                   | 0.42    | 0.001          |                    |         |
| A                                     | 155 (87.1)     | 101 (88.6)       | 54 (84.4)         | 35 (72.9) | 120 (92.3)    |                    |         |
| B                                     | 23 (12.9)      | 13 (11.4)        | 10 (15.6)         | 13 (27.1) | 10 (7.7)      |                    |         |
| Portal hypertension, n (%)            |                |                  |                   | 0.85    | 0.007          |                    |         |
| No                                    | 173 (97.2)     | 111 (97.4)       | 62 (96.9)         | 44      | 129            |                    |         |
| Yes                                   | 5 (2.8)        | 3 (2.6)          | 2 (3.1)           | 4       | 1              |                    |         |
| TNM Stage, n (%)                      |                |                  |                   | 0.26    | 0.269          |                    |         |
| -                                     | 126 (70.8)     | 42 (65.6)        | 84 (73.7)         | 31 (64.6) | 95 (73.1)     |                    |         |
| +                                     | 52 (29.2)      | 22 (34.4)        | 30 (26.3)         | 17 (35.4) | 35 (26.9)     |                    |         |
| Tumor differentiation, n (%)          |                |                  |                   | 0.01    |                |                    |         |
| Well/Moderately                       | 135 (75.8)     | 41 (64.1)        | 94 (82.5)         | 36 (75.0) | 99 (76.2)     |                    | 0.873   |
| Poor                                  | 43 (24.2)      | 23 (35.9)        | 20 (17.5)         | 12 (25.0) | 31 (23.8)     |                    |         |
| Tumor size, n (%)                     |                |                  |                   | 0.02    | 0.564          |                    |         |
| ≤ 5.0 cm                              | 99 (55.6)      | 28 (43.8)        | 71 (62.3)         | 25 (52.1) | 74 (56.9)     |                    |         |
| > 5.0 cm                              | 79 (44.4)      | 36 (56.2)        | 43 (37.7)         | 23 (47.9) | 56 (43.1)     |                    |         |
| Tumor number, n (%)                   |                |                  |                   | 0.45    | 0.935          |                    |         |
| Single                                | 160 (89.9)     | 59 (92.2)        | 101 (88.6)        | 43 (89.6) | 117 (90.0)    |                    |         |

P < 0.05 was considered statistically significant. Abbreviation: PMI, Psoas muscle index; PNI, Prognostic nutritional index; SD, standard deviation; BMI, body mass index; CEA, carcinoembryonic antigen; IQR, interquartile range; CA19-9, carbohydrate antigen 19-9; HBsAg, hepatitis B surface antigen; AFP, alpha-fetoprotein; ASA, American Society of Anesthesiologists grade score; TNM, tumor node metastasis; NLR, neutrophil to lymphocyte ratio; LMR, lymphocyte to monocyte ratio; PLR, platelet to lymphocyte ratio.
| Characteristics                              | Total (n = 178) | PMI-low (n = 64) | PMI-high (n = 114) | P value | PNI-low (n = 48) | PNI-high (n = 130) | P value |
|---------------------------------------------|----------------|-----------------|-------------------|---------|-----------------|-------------------|---------|
| Multiple                                    | 18(10.1)       | 5(7.8)          | 13(11.4)          | 5(10.4) | 13(10.0)        |                   | 0.84    |
| Lymph node metastasis, n (%)                |                |                 |                   |         |                 |                   | 0.138   |
| No                                          | 146(82.0)      | 52(81.3)        | 94(82.5)          | 36(75.0)| 110(84.6)       |                   |         |
| Yes                                         | 32(18.0)       | 12(18.7)        | 20(17.5)          | 12(25.0)| 20(15.4)        |                   | 0.34    |
| Vascular invasion, n (%)                    |                |                 |                   |         |                 |                   | 0.13    |
| No                                          | 143(80.3)      | 49(76.6)        | 94(82.5)          | 35(72.9)| 108(83.1)       |                   |         |
| Yes                                         | 35(19.7)       | 15(23.4)        | 20(17.5)          | 13(27.1)| 22(16.9)        |                   | 0.08    |
| Perineural invasion, n (%)                  |                |                 |                   |         |                 |                   | 0.3     |
| No                                          | 143(80.3)      | 47(73.4)        | 96(84.2)          | 41(85.4)| 102(78.5)       |                   |         |
| Yes                                         | 35(19.7)       | 17(26.6)        | 18(15.8)          | 7(14.6)| 28(21.5)        |                   |         |

P < 0.05 was considered statistically significant. Abbreviation: PMI, Psoas muscle index; PNI, Prognostic nutritional index; SD, standard deviation; BMI, body mass index; CEA, carcinoembryonic antigen; IQR, interquartile range; CA19-9, carbohydrate antigen 19 – 9; HBsAg, hepatitis B surface antigen; AFP, alpha-fetoprotein; ASA, American Society of Anesthesiologists grade score; TNM, tumor node metastasis; NLR, neutrophil to lymphocyte ratio; LMR, lymphocyte to monocyte ratio; PLR, platelet to lymphocyte ratio.

Comparisons of long-term OS and RFS

The K-M curve analysis demonstrated that the OS and RFS of the low-PMI group were worse than those of the high-PMI group (log-rank p < 0.05) (Fig. 2A, 2B). The median OS and RFS of low PMI was 16.5 and 11.6 months, respectively; and in high PMI group was 40.2 and 28.4 months, respectively. The OS and RFS of the low-PNI group were worse than those of the high-PNI group (log-rank p < 0.05) (Fig. 2C, 2D). The median OS and RFS of low PNI was 15.9 and 12.2 months, respectively; and in high PNI group was 37.2 and 36.0 months, respectively. Therefore, this implied that patients with ICC with low PMI or low PNI have poorer prognosis.

The K-M curve analysis revealed that the LL-P group had a significantly worst OS than the HH-P, HL-P, LH-P groups (p < 0.001). The median OS of LL-P, HH-P, HL-P, LH-P groups was 10.6 months versus 59.8 months versus 24.1 versus 20.7 months, respectively (Fig. 2E). RFS was similar with this (p < 0.001). The median RFS of LL-P, HH-P, HL-P, LH-P groups was 8.5 months versus 41.3 months versus 17.8 versus 16.6 months, respectively (Fig. 2F). Therefore, this implied that the patients with ICC who had a combination of low PMI and low PNI have the worst prognosis.

Identification of prognostic factors with univariable and multivariable analysis
The univariable analysis shown that PMI, PNI, tumor differentiation, TNM stage, lymph node metastasis, CEA, CA19-9, PLR, NLR and LMR were risk factors for OS and RFS (Fig. 3A, Fig. 4A). The multivariate analysis demonstrated that PMI (HR, 2.28; 95% CI, 1.46 to 3.58; \( p < 0.0001 \)), PNI (HR, 1.7; 95% CI, 1.02 to 2.82; \( p = 0.042 \)), lymph node metastasis (HR,2.34; 95% CI, 1.07 to 5.12; \( P = 0.033 \)), and tumor differentiation (hazard ratio [HR], 1.67; 95% CI, 1.03 to 2.71; \( p = 0.037 \)) were independent prognostic factors for OS (Fig. 3B). PMI (HR, 2.2; 95% CI, 1.4 to 3.46; \( p = 0.001 \)), CA19-9 (HR, 1.79; 95% CI, 1.06 to 3.02; \( p = 0.029 \)) and lymph node metastasis (HR, 2.82; 95% CI, 1.29 to 6.16; \( p = 0.009 \)) were independent prognostic factors (Fig. 4B) for RFS.

**Establishment and validation of the OS nomogram**

PMI, PNI, tumor differentiation and lymph node metastasis were independent prognostic factors for OS in the multivariable analysis, we used it established a nomogram for OS (Fig. 5A). For internal validation, there was an acceptable consistency between the 3-year postoperative survival predicted by the actual observation and the nomogram (Fig. 5B). The C-index was 0.692 (95%CI, 0.634–0.750). The area under the receiver operating characteristic curve (AUC) for the nomogram’s 3-year predicted survival was 0.752 (Fig. 5C). All the patients with ICC were stratified based on the median risk score of the nomogram. K-M survival analysis was used to verify the reliability of nomogram predictive ability, the median survival for low-risk patients was 59.8 months, compared with 16.2 months for high-risk patients. The difference between high-risk and low-risk patients was statistically significant (\( p < 0.001 \)) (Fig. 5D).

**Discussion**

The relationship between cancer and nutritional status has been of increasing concern[25]. The predictive effects of nutritional markers, for instance PNI and body mass index is related to cancer[26, 27]. The main treatment for patients with ICC is hepatectomy, after surgery, it is very important to evaluate the prognostic indicators or models effectively. In our cohort study, we established a nomogram based on PMI and PNI to identify patients with the highest risk of mortality after radical hepatectomy. We found that PMI and PNI were independent prognostic factors for OS and RFS in these patients. Meanwhile, the patients with the worst OS and RFS were those with a combination of low PMI and low PNI. Our established nomogram had a very good predictive ability for the postoperative survival of these patients. The prognostic value of combined PMI and PNI in predicting patients undergoing radical hepatectomy in ICC has not been reported, our cohort study is the first report.

PNI is a classic immune and nutrition marker[28], which is measured using serum albumin levels and peripheral lymphocyte counts. Albumin is usually used to evaluate the nutritional status of patients. Patients with malnutrition often have a poor prognosis[29] [30]. Lymphocytes are responsible for regulating the body’s immune function against tumor attacks[31]. Several studies have confirmed the prognostic value of lymphocytes in patients with ICC[32, 33]. PNI is a new indicator to synthesize albumin and lymphocyte. And it is a comprehensive indicator to reflect the nutritional status, systemic inflammatory response and immunity function of patients[34]. In our cohort study, we also found that PNI was an independent factor affecting the OS of ICC patients, which was the same as previous reports[22, 27].

There are many factors that cause sarcopenia, such as neuromuscular dysfunction, trauma, hormones, inflammation, decreased physical activity, and genetic factors; Malnutrition is also an important cause of sarcopenia[35]. Moreover, some study have found that serum albumin level in patients without sarcopenia is significantly higher than that of patients with sarcopenia [36]. Similarly, sarcopenia can also cause decreased appetite and insufficient nutritional intake; thereby, further increasing the risk of malnutrition. Therefore, sarcopenia and malnutrition are mutually causal,
and can form a vicious circle. Several studies have found that sarcopenia is an independent poor prognostic factor for patients with ICC after hepatectomy[6–8, 37]. Our findings are consistent with those of previous reports.

Nomograms have been developed for some cancers. Several studies have shown that nomograms have a better predictive accuracy than traditional staging systems[38–40]. Many studies have assessed a single biomarker, while few have assessed the effect of multiple comprehensive markers on prognosis. We established a nomogram composed of multiple marks that can significantly improve prognosis prediction in these patients. Our nomogram’s better predictive power (compared to single marks) was proven by the C-index and calibration curve. Several studies demonstrated that the C-index for prediction of postoperative survival for patients with ICC is 0.64–0.67 for the traditional staging system, and 0.74 for the nomogram C-index; this has been validated in multiple centers[38]. Compared with the TNM staging system, the nomogram prognostic evaluation system has a personalized function and can provided important reference for individualized treatment of patients, which deserves to be promoted in clinical practice.

In our nomogram, we found that PMI and PNI play an important role in the score and were significant affecting the prognosis. Therefore, the role of PNI and PMI in influencing the prognosis of ICC patients should not be ignored in clinical practice. Based on our established nomogram, improving the nutrition of patients with both a low PNI and low PMI can improve the prognosis to an extent. Supportive care centered on nutrition and exercise can benefit patients with ICC. Multiple studies have shown that exercise and the intake of certain nutrients (such as proteins, vitamin D, antioxidants, and long-chain polyunsaturated fatty acids) are beneficial in patients with ICC having sarcopenia, and can positively improve the prognosis[41][42, 43]. Therefore, preoperative correction of hypoproteinemia and reduction of inflammation in patients, which can significantly increase the muscle mass of patients, may improve their prognosis. This should be confirmed with more prospective studies.

The potential limitations should be considered in this study. First, as a retrospective study, it has its own flaws. Second, the results of this cohort study may be limited by a small sample size, requiring a larger sample size to be confirmed. Third, the nomogram was created using data collected from two-institutions, and its accuracy needs to be verified in multiple single-center or multi-center studies. Finally, prospective multicenter cohort studies are needed to determine the clinical utility of our nomogram.

**Conclusions**

The nomogram based on PMI and PNI can identify ICC patients who underwent curative hepatectomy and had the highest risk of poor prognosis. This nomogram is a good therapeutic decision-making tool. It can help in individualized treatment, which can help surgeons make clinical decisions for adjuvant therapy.

**Abbreviations**

ICC, intrahepatic cholangiocarcinoma; PMI, psoas muscle index; PMA, psoas muscle mass area; PNI prognostic nutritional index; SD, standard deviation; BMI, body mass index; CEA, carcinoembryonic antigen; CI, confidence interval; IQR, interquartile range; CA19-9, carbohydrate antigen 19-9; AFP, alpha-fetoprotein; ASA, American Society of Anesthesiologists grade score; LNM, lymph node meta metastasis; NLR, neutrophil to lymphocyte ratio; RFS, recurrence-free survival; HBsAg, hepatitis B surface antigen; TNM, tumor node metastasis; LMR, lymphocyte to monocyte ratio; OS, overall survival; PLR, platelet to lymphocyte ratio; AUC, the area under the receiver operating characteristic curve.
Declarations

Ethics approval and consent to participate

The study was approved by the Research Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University and Qilu Hospital Shandong University.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

This study is financially supported by the National Natural Science Foundation of China. (82072685). Note that the funder play no role in study design, data collection, analysis, interpretation of data and protocol reporting.

Authors’ contributions

Conception/design: LMD, GC. Provision of material or patients: ZXL, CMZ, JGZ, BJH, ZHL. Data analysis and interpretation: JHY, HTY, ZPY, BJ, JGZ, LMD. Manuscript writing: WMB, LMD, YW. Final approval of manuscript: GC. All authors critically reviewed many revisions of the manuscript and contributed important intellectual content.

Acknowledgements

Not applicable.

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Figures

Patients who underwent curative resection for ICC from August 2012 to October 2019 at two hospitals (n=251)

Exclusion
- Perioperative mortality on three months (n=22)
- Undergoing palliative resecection (n=8)
- Missing data on PMA (n=23)
- Lost to follow-up (n=14)
- Received adjuvant therapy (n=2)
- Combined HCC-cholangiocarcinoma (n=4)

178 patients included in the analysis

Figure 1
The cohort study flow chart.

Figure 2

Comparisons of OS and RFS between the groups stratified by PMI and PNI. The OS (A, C) and RFS (B, D) for the group stratified by PMI and PNI, respectively. OS (E) and RRS (F) of the 4 groups stratified by PMI and PNI.
Figure 3

Univariable and multivariable Cox regression analysis of OS were carried out on the forest plot. (A) Univariate analysis: the indicators highlighted in red represent the indicators that have an impact on OS ($p < 0.05$). (B) Multivariable analysis: the indicators highlighted in red represent the indicators that have an impact on OS ($p < 0.05$).
Figure 4

Univariable and multivariable Cox regression analysis of RFS were carried out on the forest plot. (A) Univariable analysis: the indicators highlighted in red represent the indicators that have an impact on RFS (p < 0.05). (B) Multivariable analysis: the indicators highlighted in red represent the indicators that have an impact on RFS (p < 0.05).
Figure 5

nomogram predicts the OS of patients with ICC. (A) The nomogram predicts the 1-, 3-, and 5-year OS for patients with ICC. (B) The calibration curve for predicting the patient’s 3-year survival. (C) AUC of OS was 0.752. (D) The OS of the cohort by risk stratification for patients with ICC.

Supplementary Files

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- SFig1.tif