

Research Paper

Surgical Treatment of Combined Hepatocellular-Cholangiocarcinoma is as Effective in Elderly Patients as it is in Younger Patients: A Propensity Score Matching Analysis

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Abstract

Aims: To compare the long-term prognosis of younger and elderly patients with combined hepatocellular-cholangiocarcinoma (CHC) who underwent curative resection between 1993 and 2014 at our center.

Methods: Two hundred and thirteen patients who underwent liver resection for CHC were enrolled in our study. The overall survival (OS) and disease-free survival (DFS) of elderly patients (age \geq 60, n=52) and younger patients (age $<$ 60, n=161) were compared by multivariate analysis and propensity score matching (PSM) analysis.

Results: Among the 213 CHC patients, the elderly patients had a higher rate of worse Child-Pugh grade (P=0.027), abnormal serum albumin (P<0.001) and lymphoid metastases (P=0.024). The proportion of HBV-positive CHC patients (74.6%, 159/213) was much higher than that observed in healthy cohorts. Younger patients had a higher rate of hepatitis B virus (HBV) infection compared to older patients (83.9% vs 46.2%, P<0.001). OS and DFS of the elderly and younger patients before and after propensity score matching were comparable.

Conclusion: Elderly and younger patients who underwent liver resection for CHC have comparable long-term OS and DFS.

Key words: Combined Hepatocellular-Cholangiocarcinoma, Hepatic resection, age, Propensity score matching

Introduction

Hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC) constitute the most common primary liver malignancies^[1]. CHC is a rare type of primary liver cancer that shares the histopathologic characteristics of both cholangiocarcinoma (CC) and HCC^[2]. According to the latest WHO classification of the digestive system, CHC is divided

into two histological types: a classical type and subtypes with stem cell features^[3].

The imaging characteristics of HCC and ICC have been widely investigated by contrast-enhanced MRI or CT. CHC may share typical features with HCC and ICC, such as arterial enhancement and portal washout, whereas the remaining tumor regions may

show a delayed enhancement and biliary ductal dilation[2, 4]. Taken together, the preoperative diagnosis of CHC remains a challenge. Some clinicians suggest that the discordance between imaging features and the elevation of tumor marker levels could indicate CHC[2, 4, 5].

Due to the low prevalence of CHC, the clinical characteristics of this disease are poorly understood. Some studies indicated that CHC may show clinical characteristics resembling HCC, but the OS was more similar to that of ICC[6]. Surgical resection remains the treatment of choice for CHC patients and yields better survival benefits than other treatment options[1, 6, 7].

In retrospective studies, the propensity score analysis has been widely used to reveal the true treatment effect by balancing the confounders between younger patients and elderly patients^[8-10]. Several studies have demonstrated by PSM analysis that HCC and ICC have comparable long-term OS and DFS in younger and elder ^[11-15]. However, to date, no study has evaluated the effect of age after hepatectomy in CHC patients. In the present study, the prognostic factors that influence OS and DFS was analyzed. Thereby, PSM analysis was adopted to remove bias caused by these factors in order to reveal the true effect of age.

Patients and Methods

Study Population and Data Collection

Between March 1993 and December 2014, 269 patients diagnosed with pathologically confirmed CHC were recruited at the Department of Liver Surgery, Zhongshan Hospital. Surgical techniques for liver resection were described elsewhere^[16], and the pathology of CHC was diagnosed according to World Health Organization criteria^[3]. Preoperative imaging examinations including chest X-ray, abdominal ultrasonography, contrast-enhanced computer tomography (CT) or magnetic resonance imaging (MRI), were performed routinely. Serum biochemical and prothrombin time data and the presence of ascites were used to assess liver function. Patients with Child A cirrhosis, and early Child B cirrhosis were considered for resection: the former were offered resections up to 50%, while the latter were offered up to 25%^[17]. Eight patients were excluded for other therapeutic modalities, 11 patients were excluded due to missing data, 25 patients were excluded for preoperative therapy, four patients were excluded due to recurrence within one month after surgery, and eight patients dropped out of the study. Overall, 213 patients were included in the study. The patients were categorized into two groups, the “younger” group

(age <60, n=161) and the “elderly” group (age ≥60, n=52). The study was approved by the Institutional Review Board of the Zhongshan Hospital and complied with the standards of the Declaration of Helsinki and current ethical guidelines.

Follow up

Patients were followed up every 3 months until death or dropping out of the follow-up program. Abdominal ultrasound, liver function tests, serum alpha-fetoprotein (AFP) levels, carcinoembryonic antigen (CEA) levels and carbohydrate antigen 19-9 (CA19-9) levels were analyzed every 3 months, and abdominal magnetic resonance imaging (MRI) was performed every 6 months. The end-point of the study was overall survival (OS), which was defined as the interval between the date of surgery and the date of the patient’s death or final follow-up.

The diagnosis of recurrence was based on MRI imaging findings, increased serum AFP and CA19-9 levels. Extrahepatic recurrence was also examined by chest CT and bone scintigram. Based on the recurrence pattern and the liver function reserve, the patients were managed with different therapeutic modalities, including radiofrequency ablation (RFA), repeated resection for resectable recurrence, TACE, percutaneous ethanol injection (PEI), and chemotherapy for patients with extrahepatic metastatic disease.

Statistical Analysis

Demographic, clinical and tumor characteristics are described as summary statistics, which were obtained using established methods. In both younger and elderly cohorts, continuous data were presented as the mean and the 25th-75th percentile range and analyzed using the Mann-Whitney U test. The categorical variables were described as absolute and relative frequencies and compared using Pearson χ^2 analysis or the Fisher exact test. OS and DFS were compared using the Kaplan-Meier method, and the survival differences between the two groups were compared using the log-rank test.

Logistic regression was used for the propensity score matching analysis to estimate the propensity score (from 0 to 1), which contains information on the variates selected. To create a reliable propensity score model, the variables chosen for matching should include all the potential confounders. ^[8-10] Instead, the variables should contain all the independent prognostic factors of CHC. The Cox proportional hazards model was used to identify the independent prognostic factors. Then, the statistically significant variables ($P < 0.1$) obtained from the univariate analysis were used in the multivariate analysis. The variables entered in the final propensity model were

gender, the serum level of carcinoembryonic antigen, γ -glutamyl transpeptidase (GGT), macroscopic vascular invasion (MVI), portal lymph node invasion and extrahepatic metastases. The model used the one-to-one match without replacement between younger and elderly patients using the nearest-neighbor matching algorithm. The caliper value was set to 0.01, and the balance between the two groups after matching was evaluated by the standardized mean difference (<0.1).

All tests using a two-tailed P -value <0.05 were considered to be statistically significant. All statistical analyses were performed using the SPSS 22.0 statistical package (SPSS Incorporated, Chicago, Illinois, USA) and the design and survival packages. This project was approved by our institutional review board.

Results

Demographic and Clinicopathological Characteristics

The demographic and clinicopathological characteristics are shown in **Table 1**. The mean age of the entire cohort was 52.4 years. One quarter of the patients were ≥ 60 years old ($n=52$, 24.3%), whereas the remaining patients were <60 years old ($n=161$, 75.7%). A higher proportion of the younger patients had HBV infection ($P<0.001$). In contrast, the elderly patients had a poor liver function ($P=0.027$), a high occurrence of abnormal serum albumin ($P<0.001$) and the presence of ascites ($P=0.011$). For the tumor characteristics, the elderly patients showed a high occurrence of portal lymph node invasion ($P=0.024$).

The prognostic factors of combined hepatocellular carcinoma-cholangiocarcinoma

To identify the potential confounders, the Cox proportional hazards model was used to analyze the risk factors of CHC (**Table 2**). With regard to OS, the following 12 variates determined by the univariate analysis were included in the multivariate analysis: gender (male), the Child-Pugh grade, CEA, CA19-9, albumin, GGT, tumor number, tumor size, MVI, portal lymph node invasion, and extrahepatic metastases. The multivariate analysis revealed that CEA, GGT, MVI, lymphoid metastases, and extrahepatic metastases were independent prognostic factors of OS. For DFS, the following 4 variates determined by univariate analysis were included in the multivariate analysis: gender, GGT, MVI and portal lymph node invasion. The multivariate analysis indicated that gender, MVI, and portal lymph node invasion were independent risk factors for predicting a poor DFS. Age was not an independent factor for OS ($P=0.190$) or DFS ($P=0.292$) in either the univariate or multivariate analyses.

Table 1. Comparison of Demographic Data and Outcomes Between Younger (≤ 60 Years of Age) and Elderly (>60 Years of Age) Patients With CHC

| | Total (n=213) | Younger patients (n=161) | Elderly patients (n=52) | P value |
|--------------------------------|----------------|--------------------------|-------------------------|----------|
| Age (yrs.) | 52.4 \pm 8.7 | 47.4 \pm 8.7 | 67.7 \pm 4.9 | <0.001 |
| Gender: Male | 161 (75.6%) | 123 (76.4%) | 38 (73.1%) | 0.682 |
| HBV: Positive | 159 (74.6%) | 135 (83.9%) | 24 (46.2%) | <0.001 |
| HCV: Positive | 5 (2.3%) | 3 (1.9%) | 2 (3.8%) | 0.597 |
| Child-Pugh Class | | | | |
| A | 202 (94.8%) | 156 (96.9%) | 46 (88.5%) | 0.027 |
| B | 11 (5.2%) | 5 (3.1%) | 6 (11.5%) | |
| AFP (ng/ml) | | | | |
| ≤ 20 | 99 (46.5%) | 76 (47.2%) | 23 (44.2%) | 0.622 |
| >20 | 114 (53.5%) | 85 (52.8%) | 29 (55.8%) | |
| CEA (ng/ml) | | | | |
| ≤ 5 | 174 (81.7%) | 132 (82%) | 42 (80.8%) | 0.911 |
| >5 | 39 (18.3%) | 29 (18%) | 10 (19.2%) | |
| CA199 (U/ml) | | | | |
| ≤ 37 | 140 (65.7%) | 106 (65.8%) | 34 (65.4%) | 0.862 |
| >37 | 73 (34.3%) | 55 (34.2%) | 18 (34.6%) | |
| TB (μ mol/L): >17 | 41 (18.8%) | 29 (17.6%) | 12 (22.6%) | 0.674 |
| ALB (g/L): <40 | 73 (33.5%) | 45 (27.3%) | 28 (52.8%) | 0.001 |
| ALT (U/L): >35 | 90 (41.3%) | 72 (43.6%) | 18 (34%) | 0.213 |
| GGT (U/L): >40 | 155 (71.1%) | 114 (69.1%) | 41 (77.4%) | 0.248 |
| Ascites (ml) | | | | |
| No | 193 (90.6%) | 151 (93.8%) | 42 (80.8%) | 0.011 |
| Yes | 20 (9.4%) | 10 (6.2%) | 10 (19.2%) | |
| Tumor nodularity | | | | |
| Single | 159 (74.6%) | 118 (73.3%) | 41 (78.8%) | 0.423 |
| Multiple | 54 (25.4%) | 43 (26.7%) | 11 (21.2%) | |
| Tumor Diameter (cm) | 6.4 (3.5-8.0) | 6.4 (3.5-8.0) | 6.4 (3.3-7.7) | 0.852 |
| Macroscopic VI | | | | |
| No | 200 (93.9%) | 151 (93.8%) | 49 (94.2%) | 1.000 |
| Yes | 13 (6.1%) | 10 (6.2%) | 3 (5.8%) | |
| Microscopic VI | | | | |
| No | 167 (78.4%) | 124 (77%) | 43 (82.7%) | 0.309 |
| Yes | 46 (21.6%) | 37 (23%) | 9 (17.3%) | |
| Lymphoid Metastases | | | | |
| No | 188 (88.3%) | 147 (91.3%) | 41 (78.8%) | 0.024 |
| Yes | 25 (11.7%) | 14 (8.7%) | 11 (21.2%) | |
| Extrahepatic Metastases | | | | |
| No | 206 (96.7%) | 156 (96.9%) | 50 (96.2%) | 0.678 |
| Yes | 7 (3.3%) | 5 (3.1%) | 2 (3.8%) | |

Propensity score matching for younger and elderly patients

The distributions of the risk factors and demographic characteristics differ between the younger and elderly groups. To reduce confounding and to reflect the true effect of age, a propensity score matching model was built based on the analysis of the risk factors above. Considering OS and DFS, seven variates contributed to the model: gender, CEA, and γ -GT, MVI, lymphoid metastases and extrahepatic metastases. Therefore, 46 pairs of elderly patients and younger patients were finally matched. The comparisons between the two groups are shown in **Table 3**.

Table 2. Prognostic Analysis of Overall Survival and Disease-free Survival Before Propensity Score Matching

| Variables | Overall survival | | | | Disease-free survival | | | |
|--------------------------------------|--------------------------|--------|-------------------------|--------|-----------------------|--------|------------------------|--------|
| | Univariate | | Multivariate | | Univariate | | Multivariate | |
| | HR (95%CI) | P | HR (95%CI) | P | HR (95%CI) | P | HR (95%CI) | P |
| Age (yrs.): >60 vs ≤60 | 1.326 (0.869-2.023) | 0.190 | | | 1.306 (0.795-2.145) | 0.292 | | |
| Gender: Male vs Female | 1.507 (0.955-2.378) | 0.078 | 1.501 (0.917-2.456) | 0.106 | 1.928 (1.101-3.375) | 0.022 | 2.453 (1.339-4.495) | 0.004 |
| Child-Pugh Class: B vs A | 1.942 (0.940-4.015) | 0.073 | 1.523 (0.691-3.357) | 0.296 | 0.846 (0.267-2.688) | 0.777 | | |
| Comorbid illness: Yes vs No | 1.336 (0.921-1.937) | 0.127 | | | 1.083 (0.706-1.661) | 0.715 | | |
| HBV: Positive vs Negative | 0.962 (0.644-1.437) | 0.849 | | | 1.477 (0.868-2.512) | 0.150 | | |
| HCV: Positive vs Negative | 2.502 (0.784-7.983) | 0.121 | | | 0.818 (0.113-5.907) | 0.842 | | |
| AFP (ng/ml): >20 vs ≤20 | 0.879 (0.614-1.259) | 0.482 | | | 0.832 (0.544-1.272) | 0.396 | | |
| CEA (ng/ml): >5 vs ≤5 | 1.597 (1.050-2.428) | 0.029 | 1.628 (1.045-2.538) | 0.031 | 0.825 (0.465-1.464) | 0.512 | | |
| CA199 (U/ml): >37 vs ≤37 | 1.514 (1.053-2.176) | 0.025 | 1.117 (0.763-1.635) | 0.571 | 1.004 (0.639-1.578) | 0.985 | | |
| TB (μ mol/L): >17 vs ≤17 | 0.938 (0.599-1.471) | 0.781 | | | 1.000 (0.593-1.685) | 1.000 | | |
| ALB (g/L): <40 vs ≥40 | 1.318 (0.909-1.911) | 0.145 | | | 1.213 (0.771-1.909) | 0.405 | | |
| ALT (U/L): >35 vs ≤35 | 1.285 (0.900-1.834) | 0.168 | | | 1.644 (1.074-2.516) | 0.022 | 1.394 (0.896-2.169) | 0.141 |
| GGT (U/L): >40 vs ≤40 | 2.711 (1.700-4.323) | <0.001 | 2.069 (1.228-3.485) | 0.006 | 1.866 (1.125-3.095) | 0.016 | 1.367 (0.801-2.332) | 0.251 |
| Ascites: Yes vs No | 1.410 (0.809-2.458) | 0.226 | 1.799 (0.971-3.333) | 0.062 | 0.501 (0.187-1.342) | 0.169 | | |
| Tumor Nodularity: Multiple vs Single | 1.557 (1.055-2.298) | 0.026 | 1.484 (0.986-2.233) | 0.059 | 1.224 (0.758-1.976) | 0.408 | | |
| Tumor Diameter (cm): >5 vs ≤5 | 2.424 (1.665-3.530) | <0.001 | 1.320 (0.870-2.002) | 0.192 | 1.429 (0.929-2.196) | 0.104 | | |
| Macroscopic VI: Yes vs No | 3.805 (2.070-6.993) | <0.001 | 3.211 (1.765-5.841) | <0.001 | 5.089 (2.371-10.922) | <0.001 | 3.602 (1.647-7.879) | 0.001 |
| Microscopic VI: Yes vs No | 1.437 (0.944-2.188) | 0.090 | 1.542 (0.994-2.394) | 0.053 | 1.192 (0.708-2.007) | 0.508 | | |
| Lymphoid Metastases: Yes vs No | 2.822 (1.699-4.686) | <0.001 | 2.481 (1.358-4.530) | 0.003 | 2.454 (1.342-4.486) | 0.004 | 3.297 (1.710-6.357) | <0.001 |
| Extrahepatic Metastases: Yes vs No | 11.186 (4.900-25.536) | <0.001 | 5.060 (2.026-12.639) | 0.001 | 2.987 (0.710-12.566) | 0.135 | | |

Table 3. Characteristics of Patients before and after Propensity Score Matching

| | Before Matching | | | After Matching | | |
|-------------------------|-----------------------------|----------------------------|-------------------------|----------------------------|----------------------------|-------------------------|
| | Younger patients (n=161) | Elderly patients (n=52) | Std. Mean Difference | Younger patients (n=46) | Elderly patients (n=46) | Std. Mean Difference |
| Age (yrs.) | 47.6±8.6 | 67.7±5.0 | 2.872 | 47.0±8.2 | 67.5±5.1 | 3.015 |
| Gender | | | | | | |
| Female | 38 (23.6%) | 14 (26.9%) | 0.076 | 8 (17.4%) | 8 (17.4%) | 0.000 |
| Male | 123 (76.4%) | 38 (73.1%) | 0.076 | 38 (82.6%) | 38 (82.6%) | 0.000 |
| CEA (ng/ml): | | | | | | |
| >5 | 132 (82%) | 42 (80.8%) | 0.031 | 39 (84.8%) | 39 (84.8%) | 0.000 |
| ≤5 | 29 (18%) | 10 (19.2%) | 0.031 | 7 (15.2%) | 7 (15.2%) | 0.000 |
| GGT (U/L) | | | | | | |
| >40 | 50 (31.1%) | 12 (23.1%) | 0.180 | 11 (23.9%) | 11 (23.9%) | 0.000 |
| ≤40 | 111 (68.9%) | 40 (76.9%) | 0.180 | 35 (76.1%) | 35 (76.1%) | 0.000 |
| Macroscopic VI | | | | | | |
| No | 151 (93.8%) | 49 (94.2%) | 0.019 | 44 (95.7%) | 44 (95.7%) | 0.000 |
| Yes | 10 (6.2%) | 3 (5.8%) | 0.019 | 2 (4.3%) | 2 (4.3%) | 0.000 |
| Lymphoid Metastases | | | | | | |
| No | 147 (91.3%) | 41 (78.8%) | 0.355 | 39 (84.8%) | 39 (84.8%) | 0.000 |
| Yes | 14 (8.7%) | 11 (21.2%) | 0.355 | 7 (15.2%) | 7 (15.2%) | 0.000 |
| Extrahepatic Metastases | | | | | | |
| No | 156 (96.9%) | 50 (96.2%) | 0.040 | 45 (97.8%) | 45 (97.8%) | 0.000 |
| Yes | 5 (3.1%) | 2 (3.8%) | 0.040 | 1 (2.2%) | 1 (2.2%) | 0.000 |

Note: Values in n (%), mean ± standard deviation.
Std. mean difference: standardized mean difference

OS and DFS

The median survival of the entire cohort was 25 months, and the overall cumulative survival rates at 1, 3 and 5 years were 73.2%, 39.0%, and 28.3%, respectively. Stratified by age, the median overall survival of the elderly patients was lower than that of the younger patients (18.0 months vs 27.16 months). The cumulative survival rates of the elderly patients at 1, 3 and 5 years were 70.3%, 40.0% and 22.2%, whereas in younger patients, they were 75.2%, 42.5% and 30.3%, respectively. The OS rates were comparable between the younger and elderly patients (**Figure 1A**). After propensity score matching, the median OS was higher in the younger patients than in the elderly patients (24 months vs 18 months). The survival rates of 1, 3 and 5 years in younger patients were 78.7%, 32.5% and 20.3%, whereas in elderly patients they were 74.0%, 31.7% and 23.8%, respectively. However, the OS between the younger and elderly patients remains comparable (**Figure 1B**). Regarding the DFS, the median disease-free survival of the entire cohort was 32 months. The DFS was comparable between the younger and elderly patients before and after propensity score matching (**Figure 1 C & D**).

Discussion

CHC is a rare primary liver tumor that constitutes only 2.4% to 14.2% of all primary hepatic malignancies^[1, 2, 18-20]. The CHC had a dual differentiation of both bile duct epithelia and hepatocytes within the same tumor^[1, 2]. The biological and pathological behaviors of these tumors are complex, and aggressive liver resection may provide a better prognosis^[1]. The effect of age on the long-term prognosis of hepatic resection with in patients diagnosed with HCC or ICC has been extensively studied, but the results are conflicting. Propensity score matching, a new statistical method, revealed that long-term OS and DFS in elderly and younger patients with either HCC or ICC are comparable^[11-15]. Although previous studies noted that CHC was more common in male patients older than 65 years^[21], the effect of age on the long-term prognosis of patients with CHC who underwent curative surgery had not been studied. Thus, a total of 269 patients who underwent hepatic resection for CHC at a single center was examined and analyzed OS and DFS by propensity score analysis and multivariate analysis. Due to a lack of typical imaging characteristics, preoperative diagnosis of CHC remains difficult. Thus, most patients with CHC were misdiagnosed

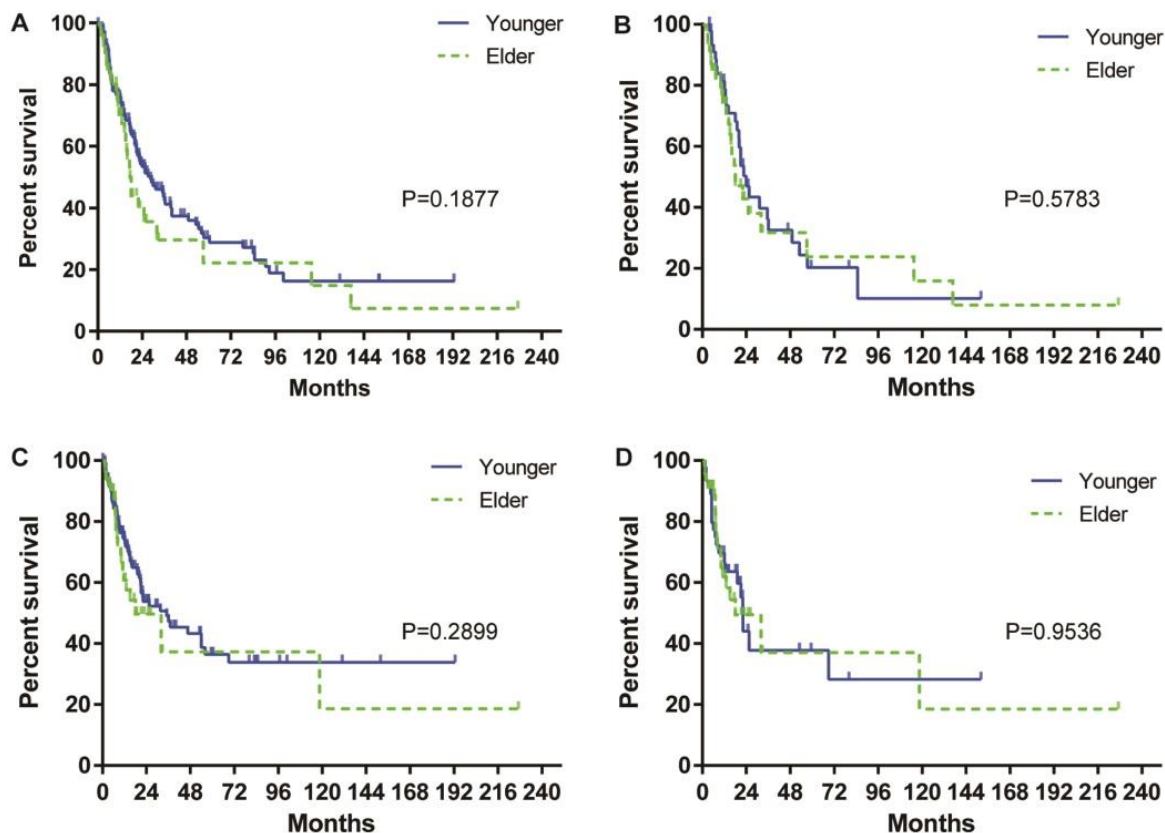


Figure 1. OS of elderly and younger patients with CHC before (A) and after (B) propensity score matching. DFS of patients with CHC before (C) and after (D) propensity score matching.

either as having HCC or CC before the surgery^[4, 22]. Surgical resection remains the main treatment for primary liver tumors; however, whether elderly patients may benefit from aggressive surgical treatment has not been agreed upon. Previous studies have noted that, compared to younger patients, elderly patients with HCC or ICC have a comparable OS and DFS after hepatectomy as revealed by propensity score matching^[11-15]. Consistent with these studies, the OS and DFS were not significantly different between younger and elderly patients. Although elderly patients are more likely to have a worse liver function reserve and lymphoid metastases, the effect of age on the long-term prognosis was not obvious after adjusting the main confounding factors using propensity score matching or multivariate analysis. To date, the present study represents the first study to assess the effect of age on the long-term prognosis of patients who underwent resection for CHC.

To further reveal the true effect of age on the long-term prognosis of surgical patients with CHC, the confounding factors must be balanced between the younger and elderly patients. In the propensity score matching analysis, regardless of whether the included variates differed between the two groups before matching, the distributions of the selected variates were comparable between the matched pairs selected by the model. Thus, a multivariate analysis of the prognosis was performed in the entire cohort to identify the independent risk factors of CHC. Consistent with previous studies^[6, 21, 23-26], age was not identified as an independent factor in the multivariate analysis. Moreover, consistent with the multivariate analysis OS and DFS did not differ significantly between the younger and elderly patients after propensity score matching, suggesting that the younger and elderly patients with CHC and similar demographic characteristics and clinicopathological features had comparable long-term prognoses. Taken together, these findings suggest that hepatic resection surgery should be considered as a potential treatment in elderly patients, as elderly patients can achieve long-term survivals that are comparable to those of younger patients.

There is a clear consensus that a high prevalence of chronic HBV infection is the most common etiological factor of HCC^[27], and HBV infection has been related to an increased risk of CC^[28]. HBV can integrate into the host genome, disrupt the expression of host genes and cause hepatocarcinogenesis even without hepatic fibrosis or cirrhosis^[29]. Recently, it has been shown that HBV infection and heavy alcohol consumption may contribute to the development of CHC^[30]. Consistent with the previous studies, the

percentage of HBV-positive patients with CHC (74.6%, 159/213) is much higher than normal population in our study^[31]. The younger patients have a higher rate of HBV infection when compared to elderly patients (83.9% vs 46.2%, $P < 0.001$), suggesting that CHC may partially share a similar mechanism with HCC -- HBV infection often occurs in early childhood, and the hepatocarcinogenesis can often be observed under the influence of decades of HBV infection. However, in the subsequent study, multivariate analysis indicated that HBV infection was not an independent risk factor associated with OS or DFS. It suggesting that HBV infection was not a solid contributor to CHC prognosis, as CHC also shares the histopathologic characteristics of cholangiocarcinoma^[23, 30].

Several limitations of the current study may have influenced the results. Given the nature of the retrospective study, there could be potential unmeasurable confounders between the two groups. Additionally, due to the low prevalence of this tumor, even though the research population is largest so far, the sample size is still relatively small and may affect the statistical power. In recent years, given the technical advancement of hepatectomy, the selection criteria have broadened, especially for elderly patients, which resulted in shorter follow-up times in the elderly group.

In conclusion, the long-term OS and DFS in younger and elderly patients who underwent liver resection for CHC are comparable. Moreover, tumor characteristics, such as MVI and extrahepatic metastases, are more powerful predictors of an unfavorable prognosis. In summary, an aggressive resection strategy could be recommended for elderly patients who have tumor characteristics that are like younger patients.

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Competing Interests

The authors have declared that no competing interest exists.

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