Original Article

Clinicopathological and Prognostic Significance of OCT4 Expression in Hepatocellular Carcinoma: An Immunohistochemical Study

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Abstract

Background: OCT4 is a pluripotency-associated transcription factor implicated in tumour stemness, progression and recurrence, but its clinicopathological and prognostic significance in hepatocellular carcinoma requires further evaluation. The objective is to evaluate OCT4 expression in hepatocellular carcinoma and determine its association with clinicopathological and prognostic outcomes, thereby assessing its potential role as a biomarker of tumour aggressiveness and prognosis. **Material and Methods:** This single-centre observational analytical study included 55 histopathologically confirmed cases of hepatocellular carcinoma from the Department of Pathology, Fathima Institute of Medical Sciences, Kadapa, Andhra Pradesh, India. **Results:** The mean age was 55.8 ± 11.4 years, with male predominance (76.4%). HBsAg positivity was present in 56.4%, cirrhosis in 61.8%, and AFP >400 ng/mL in 41.8%. The mean tumour size was 5.9 ± 2.4 cm; 54.5% had tumours >5 cm, 34.5% had multiple tumours, and vascular invasion was present in 40.0%. High OCT4 expression was observed in 37 patients (67.3%). It was significantly associated with tumour size >5 cm (67.6% vs 27.8%, p=0.009), multiple tumours (45.9% vs 11.1%, p=0.015), vascular invasion (p=0.019), poor differentiation (p=0.030), and advanced TNM stage (p=0.014). High OCT4 was associated with recurrence (56.8% vs 22.2%, p=0.022), lower 3-year OS (50.4% vs 88.5%), and lower 3-year RFS (41.7% vs 74.7%). **Conclusion:** High OCT4 expression was significantly associated with aggressive clinicopathological features, recurrence, and poorer survival outcomes, suggesting its potential utility as a prognostic biomarker in hepatocellular carcinoma.

Keywords: Hepatocellular carcinoma, OCT4, immunohistochemistry, tumour aggressiveness, recurrence-free survival, overall survival.

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Introduction

Hepatocellular carcinoma (HCC) is the dominant histological form of primary liver cancer and accounts for approximately 90% of liver cancer cases worldwide. Liver cancer continues to be a major global oncological problem, with GLOBOCAN 2022 estimating 866,136 new liver cancer cases and 758,725 deaths globally, reflecting a high mortality-to-incidence ratio of 0.86.[1,2] The clinical relevance of HCC is further emphasized by projections suggesting that annual new liver cancer cases may increase by 55.0% between 2020 and 2040, reaching nearly 1.4 million new diagnoses by 2040 if current trends continue.[3] The burden of HCC is closely related to chronic liver disease, particularly hepatitis B virus infection, hepatitis C virus infection, alcohol-related liver disease and metabolic dysfunction-associated steatotic liver disease. Llovet et al. stated that HBV and HCV infection remain the major global risk factors for HCC, while non-alcoholic steatohepatitis associated with metabolic syndrome and diabetes is becoming increasingly important in Western populations.[1] This etiological diversity is clinically important because HCC frequently develops in cirrhotic liver, where prognosis is influenced not only by tumour burden but also by hepatic functional reserve. Current AASLD guidance therefore emphasizes an integrated approach to HCC prevention, diagnosis, staging and treatment, reflecting the dual challenge of malignancy and chronic liver disease.[4]

Despite improvements in surveillance and treatment, prognosis remains heterogeneous. Curative-intent options such as resection, ablation and transplantation are feasible only in selected patients, and recurrence after apparently curative therapy remains a major clinical problem. Herrero et al. reported that up to 70% of patients may develop recurrence after liver resection, while recurrence after liver transplantation may occur in approximately 20% of patients.[5] Therefore, conventional clinicopathological variables such as tumour size, tumour multiplicity, vascular invasion, differentiation and TNM stage are valuable, but additional biomarkers are needed to refine risk stratification. Cancer stem-cell biology has provided an important framework for understanding aggressive HCC behaviour. Liver tumour-propagating cells, also referred to as liver cancer stem cells, have been implicated in tumour initiation,

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metastasis, chemoresistance, intrahepatic recurrence and overall survival.[6] OCT4, encoded by the POU5F1 gene, is a pluripotency-associated transcription factor that regulates self-renewal and differentiation, and has been increasingly studied as a marker of tumour stemness. Ye et al. identified OCT4 as a common upstream regulator of multiple HCC signature genes and observed OCT4 expression in HCC tumour tissues but not in adjacent peritumoural tissues, supporting its potential biological role in hepatocarcinogenesis.[7] Villodre et al. also described OCT4 as a regulator involved not only in embryogenesis but also in tumourigenesis and cancer therapy resistance.[8] Against this background, the present study aimed to evaluate OCT4 expression in hepatocellular carcinoma and determine its association with clinicopathological and prognostic outcomes, thereby assessing its potential role as a biomarker of tumour aggressiveness and prognosis.

Materials and Methods

This was a single-centre, hospital-based, observational, analytical study conducted in the Department of Pathology, Fathima Institute of Medical Sciences, Kadapa, Andhra Pradesh, India over a period of six months, from December 2025 to May 2026. The study was initiated after obtaining approval from the Institutional Human Ethics Committee (IHEC). Histopathologically confirmed cases of hepatocellular carcinoma with adequate formalin-fixed paraffin-embedded tissue blocks and available clinicopathological details were included in the study. Cases with insufficient tissue for immunohistochemical evaluation, poorly preserved tissue blocks, recurrent tumours, metastatic liver tumours, non-hepatocellular primary hepatic malignancies, and cases with incomplete clinical or follow-up data were excluded from the study.

The sample size for the present study was calculated based on Wang et al,[9] which evaluated OCT4 expression in hepatocellular carcinoma and reported high OCT4 expression in 36 of 53 patients (67.9%). In that study, high OCT4 expression was significantly associated with tumour size, TNM stage, vascular invasion, and poorer overall and recurrence-free survival. Assuming an expected proportion of high OCT4 expression of 67.9%, a 95% confidence level, and an absolute precision of 12.5%, the sample size was calculated using the formula $n = Z^2pq/d^2$, where $Z = 1.96$, $p = 0.679$, $q = 0.321$, and $d = 0.125$. The calculated sample size was rounded up, and the final sample size for the present study was fixed as 55 patients with hepatocellular carcinoma; enrolled using nonprobability sampling technique – convenience sampling/complete enumeration. Demographic, clinical, biochemical, histopathological and follow-up details were collected in a predesigned proforma, including age, sex, hepatitis B surface antigen status, presence of liver cirrhosis, serum alpha-fetoprotein level, tumour size, number of tumour nodules, tumour encapsulation, histological differentiation/grade, vascular invasion, TNM stage, treatment details, recurrence status, date of diagnosis or surgery, date of recurrence, date of last follow-up or death, overall survival and disease-free/recurrence-free survival.[10]

Formalin-fixed paraffin-embedded tissue blocks with adequate representative tumour tissue were retrieved, and corresponding haematoxylin and eosin-stained sections were reviewed to confirm the diagnosis, assess tumour morphology and select appropriate blocks for immunohistochemistry. Sections were then subjected to OCT4 immunohistochemical staining, and tumour-cell immunoreactivity was assessed semi-quantitatively. OCT4 expression was graded based on the percentage of positive tumour cells as Grade 0 for no positive tumour cells, Grade 1 for <10% positive tumour cells, Grade 2 for 10–50% positive tumour cells, and Grade 3 for >50% positive tumour cells. Staining intensity was scored as 0 for no staining, 1 for weak staining, 2 for moderate staining and 3 for strong staining. A final immunoreactivity score was calculated by multiplying the percentage grade by the intensity score, yielding possible scores of 0, 1, 2, 3, 4, 6 and 9; scores ≤4 were considered low OCT4 expression, whereas scores ≥6 were considered high OCT4 expression.[11]

Statistical analysis: Data were entered in Microsoft Excel and analyzed using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean and standard deviation, while categorical variables were expressed as frequencies and percentages. The association between total OCT4 expression and clinicopathological variables was assessed using the chi-square test or Fisher's exact test, as appropriate. Survival outcomes were evaluated using Kaplan–Meier survival analysis, and differences in overall survival and recurrence-free survival between OCT4 expression groups were compared using the log-rank test. Univariable Cox proportional hazards regression analysis was performed to estimate hazard ratios with 95% confidence intervals for predictors of overall survival and recurrence-free survival. A p-value of <0.05 was considered statistically significant.

Results

The mean age of the study population was 55.8 ± 11.4 years, with the largest proportion belonging to the 50–60 years age group (23, 41.8%), followed by those aged >60 years (17, 30.9%). There was a clear male predominance, with 42 males (76.4%) and 13 females (23.6%). With regard to etiological and liver-related factors, HBsAg positivity was observed in 31 patients (56.4%), while anti-HCV positivity was seen in 5 patients (9.1%). A significant alcohol history was present in 22 patients (40.0%), and cirrhosis was documented in 34 patients (61.8%). Serum AFP levels >400 ng/mL were noted in 23 patients (41.8%). Most patients belonged to Child-Pugh class A (36, 65.5%), followed by class B (16, 29.1%) and class C (3, 5.5%). The mean tumour size was 5.9 ± 2.4 cm, and slightly more than half of the patients had tumours measuring >5 cm (30, 54.5%). Most cases had a solitary tumour (36, 65.5%), while multiple tumours were present in 19 patients (34.5%). Complete tumour encapsulation was observed in 30 cases (54.5%), whereas absent or incomplete encapsulation was noted in 25 cases (45.5%). Vascular invasion was present in 22 patients (40.0%), indicating a substantial proportion with aggressive pathological features. Histologically, poorly differentiated tumours were the most frequent (23, 41.8%), followed by moderately differentiated

tumours (22, 40.0%) and well-differentiated tumours (10, 18.2%). TNM staging showed that 17 patients (30.9%) were in stage I, 15 (27.3%) in stage II, 16 (29.1%) in stage III, and 7 (12.7%) in stage IV. OCT4 IHC assessment demonstrated that more than half of the hepatocellular carcinoma cases showed extensive tumour-cell positivity, with Grade 3 expression seen in 31 patients (56.4%), while Grade 2 expression was observed in 14 patients (25.5%). Grade 0 and Grade 1 expression were each seen in 5 patients (9.1%). In terms of staining intensity, strong OCT4 staining was the most common pattern, observed in 32 cases (58.2%), followed by moderate staining in 10 cases (18.2%) and weak staining in 8 cases (14.5%); no staining was seen in 5 cases (9.1%). The mean final OCT4 immunoreactivity score was 6.0 ± 3.4. Overall, high OCT4 expression was observed in 37 patients (67.3%).

A greater proportion of patients with high OCT4 expression had tumour size >5 cm compared with the low-expression group (67.6% vs 27.8%, p=0.009). Multiple tumours were also more frequent in the high OCT4 group (45.9% vs 11.1%, p=0.015), and vascular invasion was significantly higher among patients with high OCT4 expression (51.4% vs 16.7%, p=0.019). Histological differentiation showed a significant association with OCT4 expression, with poorly differentiated tumours being more common in the high-expression group (54.1% vs 16.7%, p=0.030). Similarly, advanced TNM stage was more frequent among patients with high OCT4 expression, as stage III and IV disease together accounted for 56.7% of the high-expression group compared with 11.2% of the low-expression group (p=0.014). Prognostic outcomes were poorer among patients with high OCT4 expression. Recurrence occurred in 21 patients (56.8%) with high OCT4 expression compared with 4 patients (22.2%) with low expression, and this difference was statistically significant (p=0.022). Death during follow-up was more frequent in the high OCT4 group (43.2% vs 16.7%), although this did not reach statistical significance (p=0.072). The mean observed overall survival time was significantly lower among patients with high OCT4 expression than among those with low expression (27.8 ± 11.3 months vs 37.2 ± 5.4 months, p<0.001). Similarly, recurrence-free survival was shorter in the high OCT4 group (23.7 ± 12.6 months vs 36.6 ± 8.5 months, p<0.001). Kaplan–Meier analysis showed lower 3-year overall survival in the high OCT4 group (50.4% vs 88.5%, p=0.018) and lower 3-year recurrence-free survival (41.7% vs 74.7%, p=0.006). In univariable Cox proportional hazards analysis, high OCT4 expression was a significant predictor of poorer overall survival, with patients showing high expression having approximately four times higher risk of death compared with those with low expression (HR 4.02, 95% CI 1.16–13.97; p=0.028). Vascular invasion was also strongly associated with reduced overall survival (HR 5.15, 95% CI 1.94–13.66; p<0.001), while poor differentiation was associated with a nearly three-fold higher risk of death (HR 2.88, 95% CI 1.13–7.33; p=0.027). TNM stage III/IV and tumour size >5 cm were not significant predictors of overall survival in the univariable model. For recurrence-free survival, high OCT4 expression was significantly associated with increased risk of recurrence or progression (HR 4.04, 95% CI 1.37–11.91; p=0.011). Vascular invasion (HR 2.86, 95% CI 1.28–6.39; p=0.010), TNM stage III/IV (HR 2.97, 95% CI 1.32–6.69; p=0.009) and poor differentiation (HR 2.30, 95% CI 1.04–5.08; p=0.039) were also significant predictors of shorter recurrence-free survival, whereas tumour size >5 cm was not statistically significant.

Table 1: Baseline demographic and clinical profile of the study population (N=55)

	Value
Age (years), Mean +/- SD	55.8 +/- 11.4
Age (years)	
<50 years	15 (27.3)
50-60 years	23 (41.8)
>60 years	17 (30.9)
Sex	
Male	42 (76.4)
Female	13 (23.6)
HBsAg positive	31 (56.4)
Anti-HCV positive	5 (9.1)
Significant alcohol history	22 (40.0)
Cirrhosis present	34 (61.8)
Serum AFP >400 ng/mL	23 (41.8)
Child-Pugh class	
A	36 (65.5)
B	16 (29.1)
C	3 (5.5)

Table 2: Tumour and pathological characteristics of hepatocellular carcinoma cases (N=55)

	Value
Tumour size (cm), Mean +/- SD	5.9 +/- 2.4
Tumour size (cm)	
<=5 cm	25 (45.5)
>5 cm	30 (54.5)
Tumour number	
Solitary	36 (65.5)
Multiple	19 (34.5)
Tumour encapsulation	

Complete	30 (54.5)
Absent/incomplete	25 (45.5)
Vascular invasion	
Absent	33 (60.0)
Present	22 (40.0)
Histological differentiation	
Well differentiated	10 (18.2)
Moderately differentiated	22 (40.0)
Poorly differentiated	23 (41.8)
TNM stage	
Stage I	17 (30.9)
Stage II	15 (27.3)
Stage III	16 (29.1)
Stage IV	7 (12.7)

Table 3: OCT4 immunohistochemical grading, intensity and final expression score (N=55)

	Value
OCT4 IHC grading by percentage of positive tumour cells	
Grade 0 (no positive tumour cells)	5 (9.1)
Grade 1 (<10% positive cells)	5 (9.1)
Grade 2 (10-50% positive cells)	14 (25.5)
Grade 3 (>50% positive cells)	31 (56.4)
OCT4 staining intensity	
No staining	5 (9.1)
Weak staining	8 (14.5)
Moderate staining	10 (18.2)
Strong staining	32 (58.2)
OCT4 final immunoreactivity score, Mean +/- SD	6.0 +/- 3.4
Total OCT4 expression	
Low expression (score <=4)	18 (32.7)
High expression (score >=6)	37 (67.3)

Table 4: Association between clinicopathological variables and total OCT4 expression

		High OCT4 (n=37)	Low OCT4 (n=18)	p-value
Age (years)	<50 years	9 (24.3)	6 (33.3)	0.779
	50-60 years	16 (43.2)	7 (38.9)	
	>60 years	12 (32.4)	5 (27.8)	
Sex	Male	30 (81.1)	12 (66.7)	0.314
	Female	7 (18.9)	6 (33.3)	
HBsAg	Yes	23 (62.2)	8 (44.4)	0.255
	No	14 (37.8)	10 (55.6)	
Cirrhosis	Yes	24 (64.9)	10 (55.6)	0.563
	No	13 (35.1)	8 (44.4)	
AFP	>400 ng/mL	18 (48.6)	5 (27.8)	0.160
	<=400 ng/mL	19 (51.4)	13 (72.2)	
Tumour size (cm)	>5 cm	25 (67.6)	5 (27.8)	0.009*
	<=5 cm	12 (32.4)	13 (72.2)	
Tumour number	Multiple	17 (45.9)	2 (11.1)	0.015*
	Solitary	20 (54.1)	16 (88.9)	
Tumour encapsulation	Absent/incomplete	18 (48.6)	7 (38.9)	0.572
	Complete	19 (51.4)	11 (61.1)	
Vascular invasion	Present	19 (51.4)	3 (16.7)	0.019*
	Absent	18 (48.6)	15 (83.3)	
Histological differentiation	Well differentiated	5 (13.5)	5 (27.8)	0.030*
	Moderately differentiated	12 (32.4)	10 (55.6)	
	Poorly differentiated	20 (54.1)	3 (16.7)	
TNM stage	I	8 (21.6)	9 (50.0)	0.014*
	II	8 (21.6)	7 (38.9)	
	III	15 (40.5)	1 (5.6)	
	IV	6 (16.2)	1 (5.6)	

Table 5: Prognostic outcomes according to total OCT4 expression

Outcome	High OCT4 (n=37)	Low OCT4 (n=18)	p-value
Recurrence, n (%)	21 (56.8)	4 (22.2)	0.022*
Death during follow-up, n (%)	16 (43.2)	3 (16.7)	0.072
Observed OS time (months), Mean +/- SD	27.8 +/- 11.3	37.2 +/- 5.4	<0.001*
Observed RFS time (months), Mean +/- SD	23.7 +/- 12.6	36.6 +/- 8.5	<0.001*
1-year OS, Kaplan-Meier estimate	86.5%	100.0%	

3-year OS, Kaplan-Meier estimate	50.4%	88.5%	0.018*
1-year RFS, Kaplan-Meier estimate	83.8%	100.0%	
3-year RFS, Kaplan-Meier estimate	41.7%	74.7%	0.006*

Table 6: Univariable Cox proportional hazards analysis for overall and recurrence-free survival

Outcome	Predictor	Hazard ratio (95% CI)	p-value
Overall survival	High OCT4 expression (vs low)	4.02 (1.16-13.97)	0.028*
	Vascular invasion present (vs absent)	5.15 (1.94-13.66)	<0.001*
	TNM stage III/IV (vs I/II)	1.19 (0.48-2.97)	0.705
	Tumour size >5 cm (vs <=5 cm)	1.04 (0.42-2.57)	0.929
	Poor differentiation (vs well/moderate)	2.88 (1.13-7.33)	0.027*
Recurrence-free survival	High OCT4 expression (vs low)	4.04 (1.37-11.91)	0.011*
	Vascular invasion present (vs absent)	2.86 (1.28-6.39)	0.010*
	TNM stage III/IV (vs I/II)	2.97 (1.32-6.69)	0.009*
	Tumour size >5 cm (vs <=5 cm)	1.16 (0.53-2.57)	0.705
	Poor differentiation (vs well/moderate)	2.30 (1.04-5.08)	0.039*

Discussion

The present study demonstrated that hepatocellular carcinoma occurred predominantly in middle-aged and older adults, with a mean age of 55.8 ± 11.4 years and the highest proportion of cases in the 50–60-year age group. The marked male predominance (76.4%) and high frequency of HBsAg positivity (56.4%), cirrhosis (61.8%) and significant alcohol history (40.0%) are biologically plausible, as HCC is strongly linked to chronic viral hepatitis, alcohol-related liver disease and cirrhosis. This pattern is also consistent with Amin et al. (2025), in which HCC is reported to be substantially more common in males, and HBV, HCV, alcohol-related liver disease and steatotic liver disease are major etiological contributors.[12] The tumour profile in the present study reflected a clinically meaningful burden of aggressive disease. The mean tumour size was 5.9 ± 2.4 cm, with more than half of the patients having tumours >5 cm (54.5%), and 34.5% having multiple tumours. Vascular invasion was present in 40.0% of cases, poorly differentiated morphology was seen in 41.8%, and 41.8% of patients were in TNM stage III or IV. These findings indicate that a substantial proportion of cases had adverse pathological features at presentation. Such features are important because tumour size, multifocality, vascular invasion, differentiation and stage are well-recognised determinants of recurrence and survival in HCC, and they form the clinical background against which any prognostic biomarker such as OCT4 should be interpreted.[13,14] OCT4 expression was frequent in the present cohort, with Grade 3 staining in 56.4%, strong staining intensity in 58.2%, and high total OCT4 expression in 67.3% of patients. This high prevalence is close to the proportion reported by Wang et al., who found high OCT4 expression in 36 of 53 patients with HCC, corresponding to 67.9%.[9] In the same study, OCT4 expression was higher in HCC tissues than in corresponding non-malignant liver tissues, supporting the concept that OCT4 reactivation is part of hepatocarcinogenesis.[9]

The association between high OCT4 expression and larger tumour size in the present study was statistically significant, with tumours >5 cm observed in 67.6% of the high-expression group compared with 27.8% of the low-expression group (p=0.009). This is consistent with Wang et al., who reported that high OCT4 expression was significantly associated with tumour size >5 cm (p=0.031),[9] and with the meta-analysis by Liang et al., which included 10 trials and 985 patients and found that positive OCT4 expression was associated with larger tumour size.(10) This supports the interpretation that OCT4 may contribute to proliferative capacity and tumour expansion in HCC. Tumour multiplicity was also significantly associated with OCT4 expression in the present analysis, with multiple tumours seen in 45.9% of patients with high OCT4 expression compared with 11.1% of those with low expression (p=0.015). Liang et al. similarly reported that OCT4 positivity was associated with tumour number in HCC, suggesting that OCT4-expressing tumours may have a greater capacity for intrahepatic dissemination, field cancerisation or multicentric tumour development.[10] Although tumour multiplicity can also reflect the background liver disease, the strong association with OCT4 suggests that tumour biology may have contributed to the observed pattern.

The significant association between high OCT4 expression and vascular invasion is particularly important. In the present study, vascular invasion was present in 51.4% of high-OCT4 cases compared with only 16.7% of low-OCT4 cases (p=0.019). Wang et al. also found a significant relationship between high OCT4 expression and vascular invasion (p=0.010), and their experimental results suggested that OCT4 was involved in HCC cell viability and motility.[9] Mechanistically, OCT4 may promote invasion through cancer stem-cell-like behaviour and epithelial–mesenchymal transition, as Yin et al. showed that coexpression of OCT4 and NANOG initiated stem-cell characteristics in HCC and promoted epithelial–mesenchymal transition through STAT3/Snail activation.[15] Histological differentiation also showed a significant relationship with OCT4 expression in the present study, as poorly differentiated tumours were more common in the high-expression group than in the low-expression group (54.1% vs 16.7%, p=0.030). This finding is biologically coherent because OCT4 is a pluripotency-associated transcription factor, and its re-expression in malignant tissue may indicate dedifferentiation and acquisition of stem-cell-like properties. Liang et al. reported that OCT4 expression was associated with tumour differentiation in HCC,[10] while Dong et al. specifically reported that increased OCT4 expression was associated with low differentiation and tumour recurrence in human HCC.[16]

Advanced TNM stage was significantly more frequent among patients with high OCT4 expression, with stage III/IV disease

accounting for 56.7% of the high-expression group compared with 11.2% of the low-expression group (p=0.014). This mirrors the findings of Wang et al., who observed a significant association between OCT4 expression and TNM stage (p=0.029),[9] and Liang et al., who found that OCT4 expression was associated with TNM stage.(10) The present findings therefore reinforce the view that OCT4 is not merely a marker of tumour presence but is linked to biologically advanced disease. The prognostic analysis further strengthened the clinicopathological observations. Recurrence occurred in 56.8% of patients with high OCT4 expression compared with 22.2% of patients with low expression (p=0.022), while the mean observed recurrence-free survival was markedly shorter in the high-expression group (23.7 ± 12.6 months vs 36.6 ± 8.5 months, p<0.001). Kaplan–Meier analysis also showed a lower 3-year recurrence-free survival rate in the high OCT4 group (41.7% vs 74.7%, p=0.006). Wang et al. similarly demonstrated that patients with OCT4-high HCC had significantly shorter recurrence-free survival (p=0.0182), supporting the role of OCT4 as a recurrence-associated biomarker.[9] Overall survival was also poorer among patients with high OCT4 expression. The mean observed survival was 27.8 ± 11.3 months in the high-expression group compared with 37.2 ± 5.4 months in the low-expression group (p<0.001), and the 3-year overall survival estimate was substantially lower in the high-expression group (50.4% vs 88.5%, p=0.018). In Cox analysis, high OCT4 expression was associated with approximately four-fold higher risk of death (HR 4.02, 95% CI 1.16–13.97; p=0.028) and recurrence or progression (HR 4.04, 95% CI 1.37–11.91; p=0.011). These findings are in agreement with Wang et al., who showed poorer overall survival in OCT4-high HCC (p=0.023),[9] and with Liang et al., who reported that OCT4 expression predicted poorer 3-year and 5-year overall survival and disease-free survival.[10]

The prognostic effect of OCT4 should also be interpreted alongside conventional adverse factors. In the present study, vascular invasion was a strong predictor of both overall survival (HR 5.15, p<0.001) and recurrence-free survival (HR 2.86, p=0.010), while poor differentiation predicted worse overall survival (HR 2.88, p=0.027) and recurrence-free survival (HR 2.30, p=0.039). TNM stage III/IV significantly predicted recurrence-free survival (HR 2.97, p=0.009) but not overall survival in the univariable model. This suggests that OCT4 identifies a biologically aggressive HCC phenotype that overlaps with, but may not be fully explained by, established pathological risk factors. Wang et al. similarly observed that OCT4 overexpression was associated with poor prognosis, although advanced TNM stage and vascular invasion remained highly important determinants in survival modelling.[9]

The present study had certain limitations. The study was conducted at a single tertiary care centre, and therefore the findings may not be fully generalizable to the wider population of patients with hepatocellular carcinoma. The sample size was relatively small, which may have limited the statistical power, particularly for subgroup analysis across different TNM stages, etiological factors and survival outcomes. As the study involved immunohistochemical assessment of OCT4 expression, the results may have been influenced by pre-analytical variables such as tissue fixation, processing and antigen preservation, as well as by the semi-quantitative nature of IHC scoring. Although clinicopathological and follow-up data were analyzed, the duration and completeness of follow-up may have affected the accuracy of survival and recurrence estimates. In addition, only OCT4 expression was evaluated, while other cancer stem cell markers and molecular pathways involved in hepatocarcinogenesis were not assessed.

Conclusion

The present study demonstrated that OCT4 was frequently overexpressed in hepatocellular carcinoma, with high OCT4 expression observed in a substantial proportion of cases. High OCT4 expression showed significant association with adverse clinicopathological features, including larger tumour size, tumour multiplicity, vascular invasion, poor histological differentiation and advanced TNM stage. Patients with high OCT4 expression also had significantly higher recurrence rates and shorter overall and recurrence-free survival compared with those with low OCT4 expression. In Cox proportional hazards analysis, high OCT4 expression emerged as a significant predictor of poor overall survival and recurrence-free survival, along with established adverse factors such as vascular invasion and poor differentiation. These findings suggest that OCT4 may serve as a useful biomarker of tumour aggressiveness and adverse prognosis in hepatocellular carcinoma, and its assessment may help in risk stratification and prognostic evaluation of patients with HCC.

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Conflicts of interest

There are no conflicts of interest.

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