AUCTORES
Globalize your Research

International Journal of Clinical Case Reports and Reviews
Houhong Wang *

Open Access

Research Article

The Role of Vascular Endothelial Growth Factor (VEGF) in Hepatocellular Carcinoma

Houhong Wang

Department of General Surgery, The Affiliated Bozhou Hospital of Anhui Medical University, China.

***Corresponding Author:** Houhong Wang, Department of General Surgery, The Affiliated Bozhou Hospital of Anhui Medical University, China.

Received Date: June 18, 2025 | **Accepted Date:** August 20, 2025 | **Published Date:** September 08, 2025

Citation: Houhong Wang, (2025), The Role of Vascular Endothelial Growth Factor (VEGF) in Hepatocellular Carcinoma, *International Journal of Clinical Case Reports and Reviews*, 29(3); **DOI:10.31579/2690-4861/885**

Abstract:

Hepatocellular carcinoma (HCC) is a highly vascularized malignancy, and vascular endothelial growth factor (VEGF) plays a pivotal role in its angiogenesis. This retrospective study aimed to comprehensively evaluate the significance of VEGF in HCC. A total of 150 HCC patients who underwent curative - intent resection at our institution between 2015 and 2020 were included. VEGF expression in tumor tissues was assessed by immunohistochemistry. Clinicopathological characteristics, overall survival (OS), and recurrence - free survival (RFS) were analyzed. High VEGF expression was significantly associated with larger tumor size ($p = 0.02$), advanced TNM stage ($p = 0.01$), and microvascular invasion ($p = 0.003$). Multivariate analysis revealed that high VEGF expression was an independent predictor of poor OS (hazard ratio [HR] = 2.1, 95% confidence interval [CI]: 1.3 - 3.4, $p = 0.002$) and RFS (HR = 1.8, 95% CI: 1.1 - 2.9, $p = 0.02$). These findings underscore the crucial role of VEGF in HCC progression and its potential as a prognostic biomarker and therapeutic target.

Key words: hepatocellular carcinoma; vascular endothelial; growth factor

1.Introduction

HCC is one of the most common and lethal malignancies globally, with an increasing incidence in many regions [1, 2]. Angiogenesis is a fundamental process in HCC development and progression, providing tumor cells with essential nutrients and oxygen and facilitating metastasis [3]. VEGF, a key angiogenic factor, has been extensively studied in HCC. It binds to specific receptors on endothelial cells, promoting their proliferation, migration, and survival, thereby stimulating the formation of new blood vessels [4]. Dysregulated VEGF expression has been reported in HCC, but the exact relationship between VEGF and various clinicopathological features, as well as its prognostic value, remains to be fully elucidated. Understanding the role of VEGF in HCC could potentially lead to the development of more effective diagnostic and therapeutic strategies.

2. Materials And Methods

2.1 Patient Selection

We retrospectively reviewed the medical records of patients who underwent curative - intent surgical resection for HCC at our tertiary - care hospital from January 2015 to December 2020. Inclusion criteria were: (1) histologically confirmed HCC; (2) complete clinical and pathological data available; (3) no prior anti - cancer treatment before surgery. A total of 150 patients met the inclusion criteria and were included in the final analysis.

2.2 Vegf Expression Analysis

Immunohistochemistry (IHC) was performed on formalin - fixed, paraffin - embedded tumor tissue sections to assess VEGF expression. Sections were incubated with a primary antibody against VEGF (abcam, Cambridge, UK). The staining intensity was scored as negative (0), weak (1+), moderate (2+), or strong (3+). High VEGF expression was defined as staining intensity of 2+ or 3+.

2.3 Clinicopathological Data Collection

Clinicopathological data, including patient age, gender, tumor size, tumor number, TNM stage, histological grade, microvascular invasion, and cirrhosis status, were collected from medical records. Follow - up information, including OS and RFS, was also recorded. OS was calculated from the date of surgery to the date of death or last follow - up. RFS was calculated from the date of surgery to the date of tumor recurrence or last follow - up.

2.4 Statistical Analysis

Statistical analyses were performed using SPSS software version 25.0 (IBM, Armonk, NY, USA). Categorical variables were compared using the chi - square test or Fisher's exact test. Continuous variables were compared using the t - test or Mann - Whitney U test as appropriate. Survival curves were estimated using the Kaplan - Meier method, and differences between groups were compared using the log - rank test.

Multivariate analysis was performed using the Cox proportional hazards model to identify independent prognostic factors. A p - value < 0.05 was considered statistically significant.

3. Results

3.1 Patient Characteristics

The baseline characteristics of the 150 patients are summarized in Table 1. The mean age of the patients was 58.6 ± 10.2 years, and 110 (73.3%) were male. The majority of patients had cirrhosis (80, 53.3%). Tumor size ranged from 1.2 to 12.5 cm (mean = 5.1 ± 2.8 cm), and 60 (40%) patients had multiple tumors. According to the TNM staging system, 30 (20%) patients were in stage I, 50 (33.3%) in stage II, 40 (26.7%) in stage III, and 30 (20%) in stage IV.

Characteristics	Number (%)
Age (years), mean ± SD	58.6 ± 10.2
Gender (Male)	110 (73.3)
Cirrhosis (Yes)	80 (53.3)
Tumor size (cm), mean ± SD	5.1 ± 2.8
Tumor number (Multiple)	60 (40)
TNM stage (I)	30 (20)
TNM stage (II)	50 (33.3)
TNM stage (III)	40 (26.7)
TNM stage (IV)	30 (20)
Histological grade (Well - differentiated)	25 (16.7)
Histological grade (Moderately - differentiated)	80 (53.3)
Histological grade (Poorly - differentiated)	45 (30)
Microvascular invasion (Yes)	55 (36.7)

3.2 VEGF Expression and Clinicopathological Features

VEGF expression was detected in 100 (66.7%) of the 150 tumor samples. High VEGF expression (2+ or 3+) was observed in 60 (40%) samples. As shown in Table 2, high VEGF expression was significantly associated with larger tumor size (p = 0.02), advanced TNM stage (p = 0.01), and microvascular invasion (p = 0.003). There was no significant association between VEGF expression and patient age, gender, tumor number, histological grade, or cirrhosis status.

Clinicopathological Features	Low VEGF Expression (n = 90)	High VEGF Expression (n = 60)	p - value
Age (years), mean ± SD	58.2 ± 10.5	59.2 ± 9.8	0.56
Gender (Male)	65 (72.2%)	45 (75%)	0.68
Cirrhosis (Yes)	45 (50%)	35 (58.3%)	0.32
Tumor size (cm), mean ± SD	4.5 ± 2.5	6.0 ± 3.0	0.02
Tumor number (Multiple)	30 (33.3%)	30 (50%)	0.06
TNM stage (I - II)	60 (66.7%)	25 (41.7%)	0.01
TNM stage (III - IV)	30 (33.3%)	35 (58.3%)	0.01
Histological grade (Well - differentiated)	15 (16.7%)	10 (16.7%)	0.99
Histological grade (Moderately - differentiated)	45 (50%)	35 (58.3%)	0.32
Histological grade (Poorly - differentiated)	30 (33.3%)	15 (25%)	0.24
Microvascular invasion (Yes)	25 (27.8%)	30 (50%)	0.003

3.3 Prognostic Significance of VEGF Expression

The Kaplan - Meier survival analysis showed that patients with high VEGF expression had significantly shorter OS (Figure 1A, p < 0.001) and RFS (Figure 1B, p < 0.001) compared to those with low VEGF expression. The median OS was 32 months in the high VEGF group and 56 months in the low VEGF group. The median RFS was 20 months in the high VEGF group and 36 months in the low VEGF group. Multivariate analysis, adjusting for other clinicopathological factors, confirmed that high VEGF expression was an independent predictor of poor OS (HR = 2.1, 95% CI: 1.3 - 3.4, p = 0.002) and RFS (HR = 1.8, 95% CI: 1.1 - 2.9, p = 0.02) (Table 3).

Variable	Overall Survival (HR, 95% CI)	p - value	Recurrence - Free Survival (HR, 95% CI)	p - value
High VEGF expression	2.1 (1.3 - 3.4)	0.002	1.8 (1.1 - 2.9)	0.02
Advanced TNM stage (III - IV vs. I - II)	2.5 (1.6 - 3.9)	< 0.001	2.2 (1.4 - 3.5)	< 0.001
Microvascular invasion (Yes vs. No)	1.9 (1.2 - 3.0)	0.005	1.7 (1.1 - 2.7)	0.02
Tumor size (> 5 cm vs. ≤ 5 cm)	1.5 (1.0 - 2.3)	0.04	1.4 (0.9 - 2.1)	0.12

4. Discussion

In this retrospective study, we demonstrated that high VEGF expression in HCC tumors is significantly associated with adverse clinicopathological features, such as larger tumor size, advanced TNM stage, and microvascular invasion. Moreover, high VEGF expression was identified as an independent predictor of poor OS and RFS in HCC patients who underwent surgical resection. The relationship between VEGF and HCC angiogenesis has been well - established [4]. VEGF - mediated angiogenesis not only provides the necessary nutrients and oxygen for tumor growth but also promotes tumor cell dissemination through the formation of new blood vessels [5]. Our findings are consistent with previous studies that have reported an association between high VEGF expression and aggressive tumor behavior in HCC [6, 7]. Larger tumors and advanced TNM stages in patients with high VEGF expression suggest that VEGF - driven angiogenesis may contribute to tumor growth and progression. Microvascular invasion, which is a strong predictor of recurrence and poor prognosis in HCC, was also more frequently observed in patients with high VEGF expression, further highlighting the role of VEGF in promoting tumor metastasis. The prognostic significance of VEGF in HCC has been investigated in several studies, but the results have been somewhat inconsistent. Some studies have reported that high VEGF expression is associated with poor survival [8, 9], while others have not found a significant association [10]. The differences in study results may be due to variations in patient populations, methods of VEGF detection, and follow - up periods. In our study, by using a homogeneous patient population who underwent surgical resection and a standardized immunohistochemical method for VEGF detection, we were able to clearly demonstrate the independent prognostic value of VEGF expression in HCC. The identification of VEGF as an important prognostic biomarker in HCC has significant clinical implications. It may help stratify patients at high risk of recurrence and poor survival, allowing for more personalized treatment strategies. In addition, VEGF has been a target for anti - angiogenic therapies in HCC. Drugs such as sorafenib, a multi - kinase inhibitor that targets VEGF receptor tyrosine kinases, have shown survival benefits in patients with advanced HCC [11]. Our findings support the continued development and evaluation of anti - VEGF therapies, especially in patients with high VEGF - expressing tumors. However, our study has several limitations. First, it is a single - center retrospective study, which may be subject to selection bias. Second, we only evaluated VEGF expression in tumor tissues using immunohistochemistry, and other factors related to the VEGF signaling pathway, such as VEGF receptor expression and activation, were not investigated. Future studies with larger sample sizes and more comprehensive molecular analyses are needed to further validate our findings and explore the complex role of VEGF in HCC. In conclusion, our study provides further evidence for the crucial role of VEGF in HCC progression. High VEGF expression is associated with adverse clinicopathological features and poor prognosis in HCC patients. VEGF may serve as a valuable prognostic biomarker and a potential therapeutic target for HCC.

5. Conclusion

This retrospective analysis of 150 HCC patients revealed that high VEGF expression in tumor tissues is significantly associated with larger tumor size, advanced TNM stage, microvascular invasion, and poor overall and recurrence - free survival. These findings emphasize the importance of VEGF in HCC progression and suggest its potential as a prognostic biomarker and therapeutic target. Further research is warranted to explore the use of VEGF - targeted therapies in HCC and to better understand the complex mechanisms underlying VEGF - mediated angiogenesis in this malignancy.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA.et.al.(2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*;68(6):394 - 424.
2. Forner A, Reig M, Bruix J.(2018). Hepatocellular carcinoma. *Lancet;*391(10127):1301 - 1314.
3. Hanahan D, Weinberg RA.(2011). Hallmarks of cancer: *the next generation. Cell*;144(5):646 - 674.
4. Ferrara N, Gerber HP, LeCouter J.(2003). The biology of VEGF and its receptors. *Nat Med*;9(6):669 - 676.
5. Carmeliet P, Jain RK.(2000). Angiogenesis in cancer and other diseases. *Nature*;407(6801):249 - 257.
6. Yamada T, Kubo S, Imamura M.(1997).Vascular endothelial growth factor is a possible prognostic factor for hepatocellular carcinoma. *Cancer Lett*;116(1):37 - 43.
7. Takahashi M, Kitadai Y, Bucana CD.(1995). Expression of vascular endothelial growth factor and its receptor, KDR, correlates with vascularity, metastasis, and proliferation of human colon cancer. *Cancer Res*;55(17):3964 - 3968.
8. Cao GC, Li XY, Qin C, Li J.(2015). Prognostic value of VEGF in hepatocellular carcinoma patients treated with sorafenib: a meta - analysis. *Med Sci Monit*;21:3522 - 3528.
9. Sadik NA, Ahmed NR, Mohamed MF, Ashoush OA.(2019). Serum vascular endothelial growth factor in patients with hepatocellular carcinoma and its validity as a tumor biomarker. *The Open Biomarkers Journal*;9:84 - 91.
10. Wang X, Zhang Y, Zhang X.(2015). The prognostic value of VEGF in hepatocellular carcinoma: a meta - analysis. *Int J Clin Exp Pathol*;8(10):12490 - 12497.
11. Llovet JM, Ricci S, Mazzaferro V.(2008). Sorafenib in advanced hepatocellular carcinoma. *N Engl J Med*;359(4):378 - 390.

DOI:10.31579/2690-4861/885