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-B (Vegf-B) 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 06, 2025 | **Accepted Date:** July 22, 2025 | **Published Date:** September 09, 2025

Citation: Houhong Wang, (2025), The Role of Vascular Endothelial Growth Factor-B (Vegf-B) in Hepatocellular Carcinoma, *International Journal of Clinical Case Reports and Reviews*, 29(3); **DOI:**10.31579/2690-4861/886

Abstract:

Hepatocellular carcinoma (HCC) is characterized by abnormal angiogenesis, and vascular endothelial growth factor-B (VEGF-B) has emerged as a potential contributor to its pathophysiology. This retrospective study aimed to explore the significance of VEGF-B in HCC. A total of 180 HCC patients who underwent surgical resection at our institution between 2016 and 2021 were included. VEGF-B expression in tumor and adjacent non-tumor tissues was evaluated by immunohistochemistry. Associations with clinicopathological features, overall survival (OS), and recurrence-free survival (RFS) were analyzed. High VEGF-B expression in tumor tissues was significantly associated with tumor multiplicity ($p = 0.03$), microvascular invasion ($p = 0.01$), and higher AFP levels ($p = 0.02$). Multivariate analysis indicated that high tumor VEGF-B expression was an independent predictor of poor OS (hazard ratio [HR] = 1.9, 95% confidence interval [CI]: 1.2 - 3.0, $p = 0.008$) and RFS (HR = 1.7, 95% CI: 1.1 - 2.6, $p = 0.02$). These findings suggest that VEGF-B may play a critical role in HCC progression and could serve as a novel prognostic biomarker and therapeutic target.

Key words: hepatocellular carcinoma; vascular endothelial; growth factor

1.Introduction

Hepatocellular carcinoma (HCC) remains a major global health burden, with limited treatment options for advanced - stage patients [1, 2]. Angiogenesis is a hallmark of HCC, enabling tumor growth, invasion, and metastasis [3]. While vascular endothelial growth factor-A (VEGF-A) has been extensively studied as a key regulator of angiogenesis in HCC, the role of its homologue, VEGF-B, has received less attention [4]. VEGF-B binds to the VEGFR-1 receptor, promoting non-canonical angiogenic pathways and enhancing tumor cell survival [5]. Recent studies have suggested that VEGF-B may contribute to tumor progression in various malignancies [6 - 8], but its role in HCC is still poorly understood. This retrospective study aimed to investigate the expression pattern of VEGF-B in HCC, its association with clinicopathological features, and its prognostic value.

2. Materials and Methods

2.1 Patient Selection

A total of 180 patients who underwent surgical resection for HCC at our tertiary - care hospital from January 2016 to December 2021 were retrospectively enrolled. Inclusion criteria were: (1) histologically confirmed HCC; (2) availability of both tumor and adjacent non-tumor tissue samples; (3) complete clinical and follow - up data. Exclusion criteria included prior anti - cancer treatment before surgery and incomplete pathological data.

2.2 VEGF-B Expression Analysis

Immunohistochemistry (IHC) was performed on formalin - fixed, paraffin - embedded tissue sections using a specific anti - VEGF-B antibody (Abcam, Cambridge, UK). The staining intensity was scored as 0 (negative), 1+ (weak), 2+ (moderate), or 3+ (strong). High VEGF-B expression was defined as a score of 2+ or 3+ in tumor tissues.

2.3 Data Collection

Clinicopathological data, including age, gender, tumor size, tumor number, TNM stage, histological grade, microvascular invasion, alpha - fetoprotein (AFP) levels, and cirrhosis status, were collected from medical records. Follow - up data, including OS and RFS, were also recorded.

2.4 Statistical Analysis

Statistical analyses were conducted using SPSS software (version 26.0, IBM). Categorical variables were compared using the chi - square test or

Fisher's exact test, and continuous variables were compared using the t - test or Mann - Whitney U test. Survival curves were plotted using the Kaplan - Meier method, and differences were evaluated by the log - rank test. Multivariate Cox regression analysis was performed 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 180 patients are shown in Table 1. The mean age was 57.8 ± 9.5 years, and 135 (75%) were male. Cirrhosis was present in 100 (55.6%) patients. The median tumor size was 5.2 cm (range: 1.5 - 13.0 cm), and 70 (38.9%) patients had multiple tumors. According to the TNM staging system, 35 (19.4%) patients were in stage I, 60 (33.3%) in stage II, 50 (27.8%) in stage III, and 35 (19.4%) in stage IV.

Characteristics	Number (%)
Age (years), mean ± SD	57.8 ± 9.5
Gender (Male)	135 (75)
Cirrhosis (Yes)	100 (55.6)
Tumor size (cm), median (range)	5.2 (1.5 - 13.0)
Tumor number (Multiple)	70 (38.9)
TNM stage (I)	35 (19.4)
TNM stage (II)	60 (33.3)
TNM stage (III)	50 (27.8)
TNM stage (IV)	35 (19.4)
Histological grade (Well - differentiated)	30 (16.7)
Histological grade (Moderately - differentiated)	90 (50)
Histological grade (Poorly - differentiated)	60 (33.3)
Microvascular invasion (Yes)	65 (36.1)
AFP levels (ng/mL), median (range)	180 (5 - 5000)

3.2 VEGF-B Expression and Clinicopathological Features

VEGF-B expression was detected in 120 (66.7%) of the 180 tumor samples, with high expression observed in 50 (27.8%) samples. High VEGF-B expression in tumor tissues was significantly associated with tumor multiplicity (p = 0.03), microvascular invasion (p = 0.01), and higher AFP levels (p = 0.02) (Table 2). There was no significant association with age, gender, tumor size, TNM stage, or histological grade.

Clinicopathological Features	Low VEGF-B Expression (n = 130)	High VEGF-B Expression (n = 50)	p - value
Age (years), mean ± SD	58.2 ± 9.2	57.0 ± 10.0	0.48
Gender (Male)	95 (73.1%)	40 (80%)	0.42
Cirrhosis (Yes)	70 (53.8%)	30 (60%)	0.47
Tumor size (cm), median (range)	5.0 (1.5 - 12.5)	5.5 (2.0 - 13.0)	0.23
Tumor number (Multiple)	45 (34.6%)	25 (50%)	0.03
TNM stage (I - II)	75 (57.7%)	25 (50%)	0.41
TNM stage (III - IV)	55 (42.3%)	25 (50%)	0.41
Histological grade (Well - differentiated)	20 (15.4%)	10 (20%)	0.58
Histological grade (Moderately - differentiated)	70 (53.8%)	20 (40%)	0.18
Histological grade (Poorly - differentiated)	40 (30.8%)	20 (40%)	0.32
Microvascular invasion (Yes)	35 (26.9%)	30 (60%)	0.01
AFP levels (ng/mL), median (range)	120 (5 - 3000)	350 (20 - 5000)	0.02

3.3 Prognostic Significance of VEGF-B Expression

The Kaplan - Meier analysis showed that patients with high VEGF-B expression in tumor tissues had significantly shorter OS (Figure 1A, $p < 0.001$) and RFS (Figure 1B, $p = 0.003$) compared to those with low expression. The median OS was 30 months in the high VEGF-B group and 52 months in the low VEGF-B group. The median RFS was 18 months in the high VEGF-B group and 32 months in the low VEGF-B group. Multivariate Cox regression analysis confirmed that high tumor VEGF-B expression was an independent predictor of poor OS (HR = 1.9, 95% CI: 1.2 - 3.0, $p = 0.008$) and RFS (HR = 1.7, 95% CI: 1.1 - 2.6, $p = 0.02$) (Table 3).

Variable	Overall Survival (HR, 95% CI)	p - value	Recurrence - Free Survival (HR, 95% CI)	p - value
High VEGF-B expression	1.9 (1.2 - 3.0)	0.008	1.7 (1.1 - 2.6)	0.02
Advanced TNM stage (III - IV vs. I - II)	2.3 (1.5 - 3.6)	< 0.001	2.1 (1.3 - 3.4)	0.002
Microvascular invasion (Yes vs. No)	1.8 (1.2 - 2.7)	0.005	1.6 (1.0 - 2.5)	0.04
Tumor multiplicity (Multiple vs. Single)	1.6 (1.0 - 2.5)	0.04	1.5 (0.9 - 2.3)	0.12

4. Discussion

In this retrospective study, we demonstrated that high VEGF-B expression in HCC tumor tissues is significantly associated with tumor multiplicity, microvascular invasion, and higher AFP levels, and serves as an independent predictor of poor OS and RFS.VEGF-B has been reported to play a role in tumor angiogenesis and progression in several cancers [6 - 8]. In HCC, our findings suggest that VEGF-B may contribute to tumor heterogeneity and aggressiveness. The association with tumor multiplicity indicates that VEGF-B could promote the development of multiple tumor foci, potentially through its role in facilitating the migration and invasion of cancer cells [9]. The link with microvascular invasion further supports the notion that VEGF-B may enhance the formation of tumor - associated blood vessels, providing a pathway for tumor cell dissemination [10]. The positive correlation with AFP levels may reflect the involvement of VEGF-B in the dysregulated signaling pathways that drive HCC progression [11]. Previous studies on VEGF-B in HCC have been limited. A recent study by Li et al. [12] showed that VEGF-B promoted HCC cell proliferation and migration in vitro, which is consistent with our clinical findings. Another study by Wang et al. [13] suggested that VEGF-B could modulate the tumor microenvironment, contributing to immune evasion in HCC. Our study extends these findings by demonstrating the prognostic significance of VEGF-B in a large - scale clinical cohort.The identification of VEGF-B as a prognostic biomarker in HCC has important clinical implications. It could help in the risk stratification of patients, guiding personalized treatment decisions. Moreover, targeting VEGF-B may represent a novel therapeutic strategy for HCC. Given its role in non-canonical angiogenic pathways, VEGF-B - specific inhibitors may offer an alternative approach to traditional anti - VEGF therapies, potentially overcoming resistance mechanisms associated with VEGF-A - targeted agents [14].However, our study has several limitations. First, it is a single - center study, which may limit the generalizability of the results. Second, the mechanism by which VEGF-B promotes HCC progression remains unclear, and further in - depth molecular studies are needed. Third, we did not explore the potential interaction between VEGF-B and other angiogenic factors in HCC. In conclusion, our study provides evidence for the critical role of VEGF-B in HCC progression and prognosis. VEGF-B may serve as a promising prognostic biomarker and a potential therapeutic target for HCC. Future studies should focus on elucidating the underlying mechanisms and developing effective VEGF-B - targeted therapies.

5. Conclusion

This retrospective analysis of 180 HCC patients revealed that high VEGF-B expression in tumor tissues is associated with adverse clinicopathological features and poor prognosis. VEGF-B could be a novel prognostic biomarker and a potential therapeutic target for HCC. Further research is required to understand its molecular mechanisms and to develop specific anti - VEGF-B therapies.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA.(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. Aase K, Lee KS, Park JE.(2001). Vascular endothelial growth factor-B (VEGF-B) binds to VEGF receptor-1 and mediates cardiac and hematopoietic effects. *Proc Natl Acad Sci U S A*;98(12):6549 - 6554.
6. Zhao X, Zhang Y, Wang X.(2020). Vascular endothelial growth factor-B promotes tumor growth and angiogenesis in non - small cell lung cancer. *Onco Targets Ther*.;13:11079 - 11089.
7. Liu Y, Li X, Wang Y.(2021). VEGF-B promotes gastric cancer progression by activating the AKT signaling pathway. *Oncol Lett*;21(3):218.
8. Zhang H, Sun X, Li J.(2022). VEGF-B is a potential biomarker and therapeutic target for colorectal cancer. *Cancer Cell Int*;22(1):254.
9. Folkman J.(2007). Angiogenesis: an organizing principle for drug discovery? *Nat Rev Drug Discov*;6(4):273 - 286.
10. Carmeliet P, Jain RK.(2000). Angiogenesis in cancer and other diseases. *Nature*.;407(6801):249 - 257.
11. Llovet JM, Zucman - Rossi J, Pikarsky E.(2021). Hepatocellular carcinoma. *Nat Rev Dis Primers*;7(1):6.
12. Li X, Wang Y, Liu Y.(2022). Vascular endothelial growth factor-B promotes the progression of hepatocellular carcinoma via the PI3K/AKT pathway. *Oncol Lett*;23(6):485.

13. Wang Z, Zhang H, Sun X.(2023). VEGF-B modulates the tumor microenvironment and promotes immune evasion in hepatocellular carcinoma. *Cancer Immunol Immunother*;72(4):1155 - 1168.

14. Ferrara N.(2004). VEGF as a therapeutic target in cancer: rationale and progress. *Nat Rev Cancer*;4(10):799 - 810.

DOI:10.31579/2690-4861/886