

How to Cite:

Divya J, D. J., Prathipaa R, P. R., & Keerthini G, K. G. (2022). Expression of VEGF in breast cancer. *International Journal of Health Sciences*, 6(S7), 6396-6400. Retrieved from <https://sciencescholar.us/journal/index.php/ijhs/article/view/13532>

Expression of VEGF in breast cancer

Dr. Divya J

Assistant Professor Department of Pathology, A.C.S Medical College and Hospital
Velappanchavadi, Chennai

Dr. Prathipaa R

Assistant Professor Department of Pathology, A.C.S Medical College and Hospital,
Velappanchavadi, Chennai
Corresponding Author

Dr. Keerthini G

Assistant Professor Department of Pathology, A.C.S Medical College and Hospital,
Velappanchavadi, Chennai.

Abstract---Background: To evaluate the expression of Vascular Endothelial Growth Factor in breast cancer patients. Materials & methods: A total of 40 patients were enrolled. Mean age of the patients was 47.5 years. Biopsy specimens were obtained and were subjected with H and E staining. For VEGF marker, IHC staining was done. Segregation of subjects was done on the basis of VEGF expression. Univariate analysis was done for assessing the factors associated with positive expression of VEGF in breast cancer. All the results were recorded and were analysed using SPSS software. Results: A total of 40 patients were enrolled. Mean BMI was 25.5 kg/m². Majority had a positive expression of VEGF. Positive smoking history with positive VEGF was 20 and showed significant p- value. Positive family history of cancer and mean tumour size were also significant. Conclusion: Breast cancer patients are associated with enhanced expression of VEGF.

Keywords---breast cancer, VEGF.

Introduction

Breast cancer is the most frequent type of cancer among women worldwide, with increasing incidence rates in the majority of countries. ¹ In Thailand, breast cancer is also the most common type of cancer among women. ² Genetic alteration is one of the key factors involved in breast cancer initiation and progression. Human epidermal growth factor receptor 2 (HER2), an oncogene that is amplified and overexpressed in breast cancer, has been correlated with more aggressive

characteristics, including negative estrogen receptor (ER) and progesterone receptor (PR) status, higher histological grading, lymph node involvement and resistance to chemotherapy.

In addition to oncogene alterations, angiogenesis, the formation of new blood vessels, is of particular significance in the process of cancer growth, invasion and metastasis.^{3,4} The most important key modulator in this complex process is vascular endothelial growth factor (VEGF). The expression of VEGF has been correlated with the presence of higher microvessel density (MVD), lymphovascular invasion (LVI) and shorter disease-free survival (DFS) and overall survival (OS).

Vascular endothelial growth factor (VEGF), a potent angiogenic factor, plays a critical role in tumor growth and metastasis.^{5,6} VEGF signaling in cancer cells is responsible for their resistance to apoptotic stimuli and their migration and invasion.⁷ VEGF is highly up-regulated in breast cancer. Compared with normal or benign breast tissues, breast cancer showed higher levels of VEGF transcripts.⁸ Approximately 72–98% of breast cancer is positive for VEGF by immunohistochemistry (IHC).⁹ VEGF expression in breast tumors is correlated with large size, high histologic grade, estrogen receptor (ER) negativity, progesterone receptor (PR) negativity, human epidermal growth factor receptor-2 (HER2) over-expression, and lymph node metastasis.¹⁰ In animals, anti-VEGF therapy inhibits the growth of breast tumors, reduces tumor microvessel density, and limits the infiltration of tumor-associated macrophages.¹¹ Anti-VEGF therapy with bevacizumab, a humanized monoclonal antibody against VEGF, shows an improvement in progression-free survival in combination with chemotherapy for women with metastatic breast cancer.¹² Increased VEGF expression is implicated in acquired anti-estrogen resistance in vitro.¹³ Hence, this study was conducted to evaluate the expression of Vascular Endothelial Growth Factor in breast cancer patients.

Materials & methods

A total of 40 patients were enrolled. Mean age of the patients was 47.5 years. Biopsy specimens were obtained and were subjected with H and E staining. For VEGF marker, IHC staining was done. Segregation of subjects was done on the basis of VEGF expression. Univariate analysis was done for assessing the factors associated with positive expression of VEGF in breast cancer. All the results were recorded and were analysed using SPSS software.

Results

A total of 40 patients were enrolled. Mean BMI was 25.5 kg/m². Majority had a positive expression of VEGF. Positive smoking history with positive VEGF was 20 and showed significant p-value. Positive family history of cancer and mean tumour size were also significant.

Table 1: Associative factors

Variable	VEGF Positive	VEGF negative	p- value
Mean age (years)	46.3	48.8	0.14
Mean BMI (Kg/m ²)	25.3	25.8	0.78
Positive Smoking history (n)	20	2	0.001*
Positive family history of cancer	15	5	0.01*
Mean tumour size (cm)	6.2	2.8	0.01*

* : significant

Discussion

The correlation of VEGF with established pathological markers for breast cancer prognosis has been reported.¹¹ However, little is known about whether VEGF is differentially expressed by intrinsic subtypes of breast cancer. The analysis of plasma VEGF levels in metastatic breast cancer patients receiving bevacizumab demonstrated that VEGF levels >32.6 pg/ml were associated with shorter time-to-progression.¹⁴ The evaluation of VEGF in a randomized control trial on HER2-negative metastatic breast cancer revealed that the pretreatment plasma concentration of VEGF was correlated with a greater treatment effect. In addition, patients with higher VEGF concentrations exhibited lower hazard ratio (bevacizumab + docetaxel vs. placebo + docetaxel).¹⁵ In this study, a total of 40 patients were enrolled. Mean BMI was 25.5 kg/m². Majority had a positive expression of VEGF. Positive smoking history with positive VEGF was 20 and showed significant p- value. Positive family history of cancer and mean tumour size were also significant.

A study by Sa Nguanraksa D et al, showed that Vascular endothelial growth factor (VEGF), the key modulator of angiogenesis, has been implicated in breast cancer susceptibility and aggressiveness. VEGF expression was determined in 99 breast cancer tissue samples using reverse transcription-polymerase chain reaction and the human epidermal growth factor receptor 2 (HER2) status was determined by immunohistochemistry. Subsequently, the associations of VEGF, HER2 and hormone receptor status with clinicopathological data were evaluated. High VEGF expression was found to be significantly correlated with the presence of lymphovascular invasion. In hormone receptor-positive/HER2-positive, HER2-positive and triple-negative breast cancer, high VEGF expression was correlated with the presence of axillary nodal metastasis and lower overall survival rates. Therefore, the assessment of the VEGF status along with the hormone receptor and HER2 status may help identify high-risk patients who may benefit from anti-VEGF treatment.¹⁶

Another study by Liu Y et al, they showed by using immunostaining of tissue microarray sections, VEGF expression was determined in 1,788 primary invasive breast cancers identified from the Nurses' Health Study cohort. Overall, 72.5% of breast cancers were positive for VEGF. VEGF expression was correlated with

intrinsic subtypes ($P < 0.0001$), with higher frequency in luminal B, HER2, and basal-like types versus luminal A type. Although VEGF expression was not significantly related to worse survival when all cases were considered together, it was significantly associated with increased risks for breast cancer-specific mortality (BCSM) (HR = 1.41, 95% CI = 1.01, 1.97) and distant recurrence (HR = 1.49, 95% CI = 1.07, 2.07) among women with luminal A tumors. In 262 women untreated systemically, VEGF expression was significantly associated with BCSM (HR = 5.58, 95% CI = 1.17, 26.66). In 902 women receiving adjuvant hormonal therapy, VEGF expression did not significantly predict clinical outcomes. The VEGF-associated increased risk of BCSM is limited to luminal A tumors. VEGF expression is a prognostic but not predictive marker of hormonal response in non-metastatic invasive breast cancer.¹⁷

Conclusion

Breast cancer patients are associated with enhanced expression of VEGF.

References

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin*. 2011;61:69–90. doi: 10.3322/caac.20107.
2. National Cancer Institute: Information Technology Division, corp-author. [Nov 1;2014]. http://www.nci.go.th/th/cancer_record/cancer_rec1.html Accessed.
3. Folkman J. What is the evidence that tumors are angiogenesis dependent? *J Natl Cancer Inst*. 1990;82:4–6. doi: 10.1093/jnci/82.1.4.
4. Folkman J. Tumor angiogenesis: Therapeutic implications. *N Engl J Med*. 1971;285:1182–1186. doi: 10.1056/NEJM197111182852108.
5. Folkman J. The role of angiogenesis in tumor growth. *Semin Cancer Biol*. 1992;3:65–71.
6. Weidner N, Semple JP, Welch WR, Folkman J. Tumor angiogenesis and metastasis—correlation in invasive breast carcinoma. *N Engl J Med*. 1991;324:1–8.
7. Rice A, Quinn CM. Angiogenesis, thrombospondin, and ductal carcinoma in situ of the breast. *J Clin Pathol*. 2002;55:569–574.
8. De Paola F, Granato AM, Scarpi E, Monti F, Medri L, Bianchi S, Amadori D, Volpi A. Vascular endothelial growth factor and prognosis in patients with node-negative breast cancer. *Int J Cancer*. 2002;98:228–233.
9. Bando H, Weich HA, Brokelmann M, Horiguchi S, Funata N, Ogawa T, Toi M. Association between intratumoral free and total VEGF, soluble VEGFR-1, VEGFR-2 and prognosis in breast cancer. *Br J Cancer*. 2005;92:553–561.
10. Ribeiro-Silva A, Ribeiro do Vale F, Zucoloto S. Vascular endothelial growth factor expression in the basal subtype of breast carcinoma. *Am J Clin Pathol*. 2006;125:512–518.
11. Roland CL, Dineen SP, Lynn KD, Sullivan LA, Dellinger MT, Sadegh L, Sullivan JP, Shames DS, Brekken RA. Inhibition of vascular endothelial growth factor reduces angiogenesis and modulates immune cell infiltration of orthotopic breast cancer xenografts. *Mol Cancer Ther*. 2009;8:1761–1771.

12. Miller K, Wang M, Gralow J, Dickler M, Cobleigh M, Perez EA, Shenkier T, Cella D, Davidson NE. Paclitaxel plus bevacizumab versus paclitaxel alone for metastatic breast cancer. *N Engl J Med*. 2007;357:2666–2676.
13. Kim MR, Choi HS, Yang JW, Park BC, Kim JA, Kang KW. Enhancement of vascular endothelial growth factor-mediated angiogenesis in tamoxifen-resistant breast cancer cells: role of Pin1 overexpression. *Mol Cancer Ther*. 2009;8:2163–217
14. Burstein HJ, Chen YH, Parker LM, et al. VEGF as a marker for outcome among advanced breast cancer patients receiving anti-VEGF therapy with bevacizumab and vinorelbine chemotherapy. *Clin Cancer Res*. 2008;14:7871–7877. doi: 10.1158/1078-0432.CCR-08-0593
15. Miles DW, de Haas SL, Dirix LY, et al. Biomarker results from the AVADO phase 3 trial of first-line bevacizumab plus docetaxel for HER2-negative metastatic breast cancer. *Br J Cancer*. 2013;108:1052–1060. doi: 10.1038/bjc.2013.69
16. Sa-Nguanraksa D, Chuangsuwanich T, Pongpruttipan T, O-Charoenrat P. High vascular endothelial growth factor gene expression predicts poor outcome in patients with non-luminal A breast cancer. *Mol Clin Oncol*. 2015 Sep;3(5):1103–1108. doi: 10.3892/mco.2015.574. Epub 2015 Jun 9. PMID: 26623059; PMCID: PMC4534845.
17. Liu Y, Tamimi RM, Collins LC, Schnitt SJ, Gilmore HL, Connolly JL, Colditz GA. The association between vascular endothelial growth factor expression in invasive breast cancer and survival varies with intrinsic subtypes and use of adjuvant systemic therapy: results from the Nurses' Health Study. *Breast Cancer Res Treat*. 2011 Aug;129(1):175–84. doi: 10.1007/s10549-011-1432-3. Epub 2011 Mar 9. PMID: 21390493; PMCID: PMC3640508.