The Effect of Bevacizumab-Related Hypertension on the Prognosis of Patients with Colorectal Cancer and Non-Small Cell Lung Cancer

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To study and analyze the effect of bevacizumab-related hypertension on the prognosis of patients with colorectal cancer and non-small cell lung cancer. The study randomly selected 100 colorectal cancer patients and 100 non-small cell lung cancer patients who received therapy in our hospital from October 2019 to October 2021. Among them, adopted intervention for 100 colorectal cancer patients with bevacizumab combined with cytotoxic drug chemotherapy and adopted intervention for 100 non-small cell lung cancer patients with bevacizumab combined with standard chemotherapy. Bevacizumab treatment has better therapeutic effect of hypertension on colorectal cancer patients than non-small cell lung cancer patients. Compared with colorectal cancer patients who received bevacizumab treatment, non-small cell lung cancer patients under bevacizumab treatment caused more adverse reactions. Among 100 colorectal cancer patients, the number of patients with bevacizumab-related hypertension in grade 1, grade 2 and grade 3 were 45, 12 and 23 respectively. Among 100 non-small cell lung cancer patients, the number of patients with bevacizumab-related hypertension in grade 1, grade 2 and grade 3 were 44, 25 and 20 respectively. Bevacizumab-related hypertension can improve the prognosis and efficacy of colorectal cancer and non-small cell lung cancer patients.

Key words: Bevacizumab, hypertension, colorectal cancer, non-small cell lung cancer, prognosis

Bevacizumab is a humanized therapeutic monoclonal antibody that can be combined with Vascular Endothelial Growth Factor (VEGF) to target[1]. Bevacizumab has been widely used in treating metastatic colorectal cancer and locally advanced, recurrent or metastatic Non-Small Cell Lung Cancer (NSCLC). However, it often causes gastrointestinal perforation, delayed incision healing, bleeding, arterial thrombosis, proteinuria, congestive heart failure, etc.,[2]. The most common adverse reaction rate is 11 % to 16 %. We often use oral antihypertensive drugs to treat hypertension 1 to 2 in clinic[3]. Studies have indicated that the mechanism of bevacizumab concerns with blood pressure and, Nitrogen and Oxygen (NO). VEGF can promote NO synthesis and inhibiting VEGF can reduce NO[4]. Moreover, NO is a vasodilator, which can cause vasoconstriction, reduce Na+ renal excretion and ultimately increase blood pressure[5]. Studies have indicated that bevacizumab can prolong the progression-free survival and overall survival of hypertensive cancer patients[6]. In this study, we selected 100 colorectal cancer and 100 NSCLC patients who have received treatment in our hospital as general data. We attempt to discuss the effect of bevacizumab-related hypertension on prognosis of colorectal cancer and NSCLC patients by analyzing the post-treatment conditions of both groups. The study randomly selected 100 colorectal cancer patients and 100 NSCLC patients who received therapy in our hospital from October 2019 to October 2021. Among them, adopted intervention for 100 colorectal cancer patients with bevacizumab combined with cytotoxic drug chemotherapy; and adopted intervention for 100 NSCLC patients with bevacizumab combined with standard chemotherapy. The age and gender of 100 colorectal cancer patients: 65 males and 35 females included, ages were from 18 to 76 y old and average was about (53.2±16.32) y old. The age and gender of 100 non-small cell lung cancer patients: 73

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males and 27 females included, ages were from 19 to 75 y old and average was about (52.2±15.22) y old. Inclusion criteria include meeting the diagnostic criteria for colorectal cancer and NSCLC patients; complete clinical data; signed the voluntary informed letter. Exclusion criteria include patients symptoms such as hemoptysis, tumor invasion or adjacent large blood vessels; patients with a history of thrombosis or bleeding disorders[7]. The intervention measures taken for 100 NSCLC patients were bevacizumab combined with standard chemotherapy regimens, bevacizumab (Swiss E company, batch number: 10136082) 15 mg/kg, three times a week, combined with standard chemotherapy regimens. The intervention measures taken for 100 colorectal cancer patients were bevacizumab combined with cytotoxic drug chemotherapy, bevacizumab 5 mg/kg, first-line treatment or morphine 10 mg/kg, transfer to second-line therapy and cytotoxic chemotherapy. Moreover, performed whole-body Computed Tomography (CT) scans on 200 patients and evaluated the clinical efficacy according to the actual situation. And measure the patient's blood pressure before each treatment cycle according to the common adverse reaction 4.0 version (CTCAE V4.0) terminology standard. Hypertension is divided into three grades: Grade 1-transient and asymptomatic hypertensive patients who are not treated with antihypertensive drugs; Grade 2-patients who relapse, persist or show symptoms during bevacizumab treatment will be treated with antihypertensive drugs; Grade 3-compared with Grade 2, use one or more antihypertensive drugs to maintain treatment. Observation indicators includes analysis of patients with bevacizumab-related hypertension; analysis of adverse reactions conditons in patients; analysis of the classification of patients with hypertension; multi-factors logistic regression analysis of prognostic factors of bevacizumab associated hypertension in colorectal cancer patients and multi-factors logistic regression analysis of prognostic factors of bevacizumab associated hypertension in NSCLC patients. Adopted Statistical Package for the Social Sciences (SPSS) 20.0 software to process the data collected in this research. Used $\bar{x}\pm s$ to represent the measurement data, comparison between groups by t-test. Used χ^2 to test the comparison of enumeration data. In Table 1, among 100 colorectal cancer patients, the rate of bevacizumab-related hypertension patients was 8 %; but among 100 NSCLC patients, it was 6 %. It can be seen that bevacizumab treatment had better hypertension therapeutic effect on NSCLC patients than colorectal cancer patients. In Table 2, among 100 colorectal cancer patients, the number and proportion of patients with protein, bleeding, thromboembolism and gastrointestinal perforation were 8 (8 %), 5 (5 %), 4 (4 %) and 7 (7 %) respectively, the fatal adverse reaction rate was 1 %. Among 100 NSCLC patients, the number and proportion of patients with protein, bleeding, thromboembolism and gastrointestinal perforation were 10 (10 %), 8 (8 %), 6 (6 %) and 9 (9 %) respectively, the fatal adverse reactions rate was 2 %. It can be seen that compared with colorectal cancer patients who received bevacizumab treatment, NSCLC patients under bevacizumab treatment caused more adverse reactions. In Table 3, among 100 colorectal cancer patients, the quantity of patients with grade 1, grade 2 and grade 3 bevacizumab related hypertension were 45, 12 and 23 respectively. Among 100 NSCLC patients, the quantity of patients with grade 1, grade 2 and grade 3 bevacizumab related hypertension were 44, 25 and 20 respectively. Multi-factor logistic regression analysis of prognostic factors of bevacizumab associated hypertension in colorectal cancer patients was represented in Table 4. Multi-factor logistic regression analysis of prognostic factors of bevacizumab associated hypertension in NSCLC patients is shown in Table 5. Bevacizumab is an angiogenesis inhibitor approved by the United States Food and Drug Administration and it is often used as the first-line therapy for metastatic colorectal cancer and locally advanced, recurrent or metastatic NSCLC. However, drugs with targeted signaling pathways that affect angiogenesis often cause hypertension[8]. Studies have indicated that bevacizumab-related hypertension may be a predictor of the clinical results of cancer patients[9]. Studies have proved that lung cancer patients often develop hypertension within 1 mo after bevacizumab treatment and the long-term overall survival of bevacizumab-related hypertension is a predictor of the prognosis of lung cancer patients[10]. For example, elevated blood pressure in colorectal cancer patients 3 mo after bevacizumab treatment is common and is a factor affecting the patient's prognosis. At the same time, studies have also shown that patients with NSCLC, colorectal cancer and ovarian cancer often develop hypertension in the early stage (42 d) of bevacizumab treatment, which affects the treatment effect of bevacizumab. The results of this study indicated that among NSCLC patients treated with bevacizumab, there is an association between colorectal

cancer and early hypertension and bevacizumab-related hypertension can remarkably prolong survival. Moreover, the correlation between early bevacizumab treatment and bevacizumab did not prolong the progression free survival time and overall survival time of hypertension patients. Therefore, the correlation between bevacizumab and the prognosis of patients with hypertension is an influencing factor[11]. The multi-factor logistic regression analysis of this study indicated that the duration of bevacizumab treatment was an influencing factor in colorectal cancer and bevacizumab related hypertension patients and it was an influencing factor in NSCLC and bevacizumab related hypertension patients. Moreover, long-term bevacizumab treatment for cancer patients increases the risk of hypertension. The duration or reason of bevacizumab treatment may be related to bevacizumab related risk factors of hypertension. In summary, the association between bevacizumab and hypertension can improve the prognosis of patients to a certain extent.

TABLE 1: ANALYSIS OF BEVACIZUMAB-RELATED HYPERTENSION PATIENTS CONDITIONS (n %)

Group	Cases	Patients with bevacizumab-related hypertension (n)	Proportion (%)
Patients with colorectal cancer	100	8	8 %
Patients with non-small cell lung cancer	100	6	6 %
χ^2			1.221
p			0.048

TABLE 2: ANALYSIS OF ADVERSE REACTIONS CONDITIONS IN PATIENTS (n %)

Group	Occurrence of protein	Bleeding	Thromboembolism	Gastrointestinal perforation	Fatal adverse reactions rate
Colorectal cancer patients	8 (8 %)	5 (5 %)	4 (4 %)	7 (7 %)	1 (1 %)
Non-small cell lung cancer patients	10 (10 %)	8 (8 %)	6 (6 %)	9 (9 %)	2 (2 %)
χ^2			3.209		
p			0.047		

TABLE 3: ANALYSIS OF THE PATIENTS' HYPERTENSION CLASSIFICATIONS (n %)

Group	Cases	Patients with grade 1 bevacizumab associated hypertension (n)	Patients with grade 2 bevacizumab associated hypertension (n)	Patients with grade 3 bevacizumab associated hypertension
Colorectal cancer patients	100	45	12	23
Non-small cell-lung cancer patients	100	44	25	20
χ^2		1.889	1.675	1.432
p		0.004	0.006	0.005

TABLE 4: MULTI-FACTORS LOGISTIC REGRESSION ANALYSIS OF PROGNOSTIC FACTORS OF BEVACIZUMAB ASSOCIATED HYPERTENSION IN COLORECTAL CANCER PATIENTS

Variable	β	SE	Wald χ^2	df	p	OR (95 % CI)
Age	0.44	0.20	0.45	1	0.45	1.34 (0.56, 3.45)
Gender	0.42	0.08	0.51	1	0.67	1.27 (0.86, 2.78)
Cycle of bevacizumab treatment	0.67	0.89	1.45	1	0.32	1.34 (0.55, 2.89)
History of hypertension	0.91	1.05	3.21	1	0.09	1.87 (0.78, 7.99)
Duration of bevacizumab treatment	1.45	1.12	4.78	1	0.01	2.78 (1.78, 7.98)
Proteinuria	0.01	0.01	0.01	1	0.89	1.90 (0.45, 1.89)

TABLE 5: MULTI-FACTORS LOGISTIC REGRESSION ANALYSIS OF PROGNOSTIC FACTORS OF BEVACIZUMAB ASSOCIATED HYPERTENSION IN NON-SMALL CELL LUNG CANCER PATIENTS

Variable	β	SE	Wald χ^2	df	p	OR (95 % CI)
Age	0.05	0.01	0.12	1	0.67	1.09 (0.34, 1.78)
Gender	0.89	0.89	2.45	1	0.21	1.34 (0.78, 2.67)
Cycle of bevacizumab treatment	0.56	0.34	5.78	1	0.02	1.87 (1.12, 2.99)
History of hypertension	0.67	0.98	1.89	1	0.34	1.45 (0.56, 2.56)
Duration of bevacizumab treatment	0.02	0.01	0.09	1	0.78	0.78 (0.34, 1.78)
Proteinuria	0.45	0.07	0.56	1	0.67	1.07 (0.56, 2.54)

Conflict of interests:

The authors declared no conflicts of interest.

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