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Correlation between *H. pylori* infections and expressions of P53, Bax and FHIT in patients with gastric cancer.

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Abstract

Objective: It was designed to investigate the relationship between *H. pylori* infections in the patients with gastric cancer and P53, Bax, FHIT proteins expression.
Method: 180 patients with gastric cancer admitted in our hospital from January 2015 to December 2015 were selected to detect *H. pylori* infections and was divided into positive group and negative group according to the infection results. The expression of P53, Bax and FHIT proteins in cancer tissue of all patients was detected.
Result: in 180 patients with gastric cancer, there were 120 positives infected with *H. pylori*, 60 negatives and the positive rate was 66.67%; for patients in positive group, the positive rate of P53 protein expression was 58.3%, while for patients in negative group, it was only 15.0%, and there was statistical difference between group data (P<0.05); the positive rate of Bax protein expression for patients in positive group was 67.5%, 21.67% for those in negative group, and there was statistical difference between group data (P<0.05); the positive rate of FHIT protein expression for patients in positive group was 52.5%, 25.0% for those in negative group, and there was statistical difference between group data (P<0.05).
Conclusion: It has been concluded that P53, Bax, FHIT gene in *H. pylori* infections for patients with gastric cancer were all in high expression and the gastric cancer might be resulted from the influence of *H. pylori* on P53, Bax, FHIT.

Keywords: Gastric cancer, *H. pylori*, P53, Bax, FHIT.

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Introduction

The occurrence and progression of gastric cancer is affected by a variety of factors. At present, one of factors that are studied is *H. pylori* [1]. Researchers generally believe that the occurrence and progression of gastric cancer undergo a process: chronic gastritis-intestinal metaplasia-atypical hyperplasia-gastric cancer, and *H. pylori* is considered to be involved in the whole process, therefore, *H. pylori* infection is an important cancerigenic factor in the occurrence of gastric cancer [2,3]. P53 is a cancer suppressor gene, its mutation may result in cell malignant transformation, further promoting the development of tumors; *FHIT* gene is a group of gene encoded with FHIT; *Bax* gene is a member of bcl-2 gene family, and its main function is the same as *P53* gene, i.e., controlling cell apoptosis [4,5]. *H. pylori* infection has an important regulation on related gene variation and abnormal expression of gastric mucosal cell, especially P53, Bax, FHIT, c-myc on differentiation of apoptosis for normal gastric mucosal cell [6,7]. Therefore, the paper is designed to investigate the difference of P53, Bax and FHIT in gastric mucosa tissue between patients with gastric cancer and *H. pylori* infection and negative patients with gastric cancer and *H. pylori* infection to investigate the correlation between them. The following are the detailed contents of the study:

Data and Methods

Basic data

A Total of 180 patients with gastric cancer who were received in our hospital from January 2015 to December 2015 were selected, and they were divided into two groups: positive group and negative group according to the results of *H. pylori* infections. There were 120 cases in the positive group, including 49 female cases and 71 male cases, aged 36-73 years, mean age of (58 ± 4) years; there were 60 cases in the negative group, including 52 female cases and 67 male cases, aged 39~77 years, mean age of 62 ± 3 years. Detailed data were shown in the Table 1 below.

Inclusion criteria

All patients selected in this study must meet the following criteria prior to inclusion. (1) All patients were diagnosed with gastric cancer through pathological examination of living samples. (2) There was no significant difference in age and sex

between the two groups (P<0.05). (3) Patients in both groups received anti-Hp standardized treatment prior to the study; (4) This study has received the consent of patients themselves or their family, signed with informed consent.

Table 1. Basic data of patients in the two groups.

Group	Number of cases (n)	Sex (n)		Age (years)	
		Male	Female	Range	Mean age
Positive group	120	71	49	36~73	58 ± 4
Negative group	60	67	53	39~77	62 ± 3
t/X^2 value		1.305		0.953	
P value		0.072		0.085	

Methods

All specimens of gastric cancer resected in the operation were collected and fixed by formaldehyde solution. According to the requirements in the kit, some specimens of patients were taken for testing of *H. pylori* infections (urease kits were used for testing, purchased from Nanjing Jiancheng Biotechnology Co., Ltd.); for the remaining specimens, tissues were embedded by paraffin embedding technique, then slicing at the thickness of 0.5 μm was performed by a microtome, and then immumohistochemical staining was carried out, including main steps: dewaxing, washing, antigen labeling and repair, double antibody repair, re-staining, dehydration, sealing [5]. The bax, FHIT antibodies were human polyclonal antibodies produced by Santa.Cruz, and P53 antibody was the rat's immune antibody produced by Nanjing Jiancheng Biotechnology Co., Ltd.

Evaluation indexes

P53 expression grading criteria were as follows: the staining of P53 protein was located around the nucleus, and if the nucleus was stained brown, it was deemed as positive expression. Five high-power fields (40 × 10) were selected, and 100 cells were randomly selected from each high-power field, and then evaluation was performed according to the staining: score 0 for no color, score 10 for light yellow, score 20 for light brown, and score 30 for brown yellow. Then the scores were determined according to the positive rates of tumor cells. If the positive rate of tumor cells was below 20%, it was scored 10 points; and if the positive rate of tumor cells was 20~50%, it was scored 20 points; and if the positive rate of tumor cells was over 50%, it was scored 30 points. The above two scores were added, and if the total score was greater than or equal to 50 points, it was deemed positive expression [6]. FHIT and Bax were located in the cytoplasm. FHIT was stained brown and Bax was stained brown yellow. Its positive expression scoring standard was the same as that of P53.

The evaluation standard of positive *H. pylori* infection (urease method) was as follows: if the detection region became red after adding liquid of the test kit, it was positive *H. pylori* infections; and if the detection region did not become red or become other color after adding liquid of the test kit, it was negative *H. pylori* infections. The rates of *H. pylori* infections and the positive expression rates of P53, FHIT and Bax of patients with positive infection and negative infection were calculated.

Statistical processing

Statistical analysis of all data in this study was performed by SPSS19.0 software. For measurement data, t test was used, and chi-square χ^2 test was used for comparison between groups, a=0.05. P<0.05 was considered statistically significant.

Results

Testing of H. pylori infections

For 180 cases diagnosed with gastric cancer, testing of *H. pylori* infections in gastric tissue specimens was carried out; results showed that, there were 120 cases with positive *H. pylori* infections, and 60 cases with negative *H. pylori* infections (P=0.037), showing statistically significant difference.

Table 2. The positive expression of P53 in different types of patients.

Group	Number of cases (n)		Number of cases with positive expression (n)	Positive expression rate (%)	Total expression rate (%)
Positive infection group*	120	Male#	39	32.5	58.3
		Female	31	25.83	
		≥ 60 years#	33	27.5	
		<60 years	37	30.83	
Negative infection group	60	Male#	6	10.0	15.0
		Female	3	5.0	
		≥ 60 years#	4	6.67	
		<60 years	5	8.33	

(Note: *positive group *vs.* negative group, P=0.014, the data between groups were statistically different; #In groups of male and female, and ages, P>0.05, no statistically significant difference)

Positive expression rate of P53 in different types of patients

Among patients in the positive group, there were 70 cases of positive expression of P53, with the positive expression rate of 58.3%, including 39 male cases, 31 female cases, 33 cases elder than or equal to 60 years, and 37 cases under 60 years. Among the patients in the negative group, there were 9 cases of positive expression of P53, with the positive expression rate of 15.0%, including 6 male cases, 3 female cases, 4 cases elder than or equal to 60 years, and 5 cases under 60 years. The results were shown in the following Table 2.

Positive expression rate of Bax in different types of patients

Among patients in the positive group, there were 81 cases of positive expression of Bax, with the positive expression rate of 67.5%, including 43 male cases, 37 female cases, 35 cases elder than or equal to 60 years, and 46 cases under 60 years. Among the patients in the negative group, there were 13 cases of positive expression of Bax, with the positive expression rate of 21.67%, including 8 male cases, 5 female cases, 6 cases elder than or equal to 60 years, and 7 cases under 60 years. The results were shown in the following Table 3.

Table 3. *The positive expression of Bax in different types of patients.*

Group	Number of cases (n)		Number of cases with positive expression (n)	Positive expression rate (%)	Total expression rate (%)
Positive infection group*	120	Male#	43	35.83	67.5
		Female	37	30.83	
		≥ 60 years#	35	29.17	
		<60 years	46	38.33	
Negative infection group	60	Male#	8	13.33	21.67
		Female	5	8.33	
		≥ 60 years#	6	10.0	
		<60 years	7	11.67	

(Note: *positive group *vs.* negative group, P=0.022, the data between groups were statistically different; #In groups of male and female, and ages, P>0.05, no statistically significant difference)

Positive expression rate of FHIT in different types of patients

Among patients in the positive group, there were 63 cases of positive expression of FHIT, with the positive expression rate of 52.5 %, including 33 male cases, 30 female cases, 27 cases elder than or equal to 60 years, and 36 cases under 60 years. Among the patients in the negative group, there were 15 cases of positive expression of FHIT, with the positive expression rate of 25.0%, including 9 male cases, 6 female cases, 7 cases elder than or equal to 60 years, and 8 cases under 60 years. The results were shown in the following Table 4.

Discussion

The discovery of *H. pylori* is a major achievement in the history of studies of gastric mucosal lesions. Since its discovery in the 1980s, more and more studies on the correlation between *H. pylori* and the occurrence of a variety of gastric mucosal lesions have been carried out [7]. Gastric cancer is a malignant tumor of gastric tissues affected by a variety of factors. At present, a number of studies have shown that, the occurrence of gastric cancer was closely associated with the *H. pylori* infections, and some scholars listed the *H. pylori* as the first type of carcinogenic factor of gastric cancer [8]. *P53* gene is a more important tumor suppressor gene in the human body. Its main expression product is P53 protein. Studies have confirmed that the main function of P53 protein is to regulate the cell differentiation cycle, especially in regulation of apoptosis of dedifferentiating cells [9]. About 0.002% of the P53 protein in human body is wild-type protein, which is the normal P53 protein mutant, without normal regulatory function, causing dedifferentiating cells unable to apoptosis and canceration [10]. Therefore, the high expression of P53 protein is closely related to the occurrence of various human tumors. *Bax* gene belongs to a member of *bcl-2* gene family, and its main function, same as the *P53* gene, is to regulate cell apoptosis, so Bax protein is also closely related to the occurrence and progression of cancers [11].

Table 4. *The positive expression of FHIT in different types of patients.*

Group	Number of cases (n)		Number of cases with positive expression (n)	Positive expression rate (%)	Total expression rate (%)
Positive infection group*	120	Male#	33	27.5	52.5
		Female	30	25.0	
		≥ 60 years#	27	22.5	
		<60 years	36	30.0	
negative infection group	60	Male#	9	15.0	25.0
		Female	6	10.0	
		≥ 60 years#	7	11.67	
		<60 years	8	13.33	

(Note: *positive group *vs.* negative group, P=0.037, the data between groups were statistically different; #In groups of male and female, and ages, P>0.05, no statistically significant difference)

FHIT gene is a group of genes encoding FHIT protein, and its main structure is a group of histidine triplet, and it is a newly discovered tumor suppressor gene. With the actions of a variety of carcinogenic factors, *FHIT* gene may mutate, and after *FHIT* gene mutation, it will directly affect the expression levels of FHIT proteins. FHIT proteins, as a kind of proteins regulating the cell cycle, have important monitoring and regulatory effects on abnormal differentiating cells, therefore, the expression levels of FHIT proteins are related to the occurrence and progressions of cancers [12-14]. Based on the above, in this article, we investigated the expressions of P53 protein, Bax protein and FHIT protein in gastric cancer patients with infections of *H. pylori*. Studies showed that, among the 120 cases with *H. pylori* infections, the positive expression rates of P53, Bax and FHIT were 58.3%, 67.5% and 52.5% respectively, significantly higher than those of the patients in the *H. pylori* negative infection group (15.0%, 21.67% and 25.0% respectively, P<0.05). In the group, the expressions of

P53, Bax and FHIT were not correlated with the distributions of sex and age of the patients (P>0.05).

In summary, *H. pylori* is an important factor in the occurrence and progression of gastric cancer, and the *H. pylori* infection is strongly associated with the abnormal expressions of P53, Bax and FHIT.

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