Application Value of Combined Detection of Serum IGF-I and IGFBP-3 in the Diagnosis of Bladder Cancer

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Objective. To investigate the application value of the combined detection of serum IGF-I and IGFBP-3 in the diagnosis of bladder cancer (BC). Methods.Sixty BC patients in our hospital (January 2019-January 2020) were chosen as group A, while sixty healthy people during the same period were chosen as group B. The serum IGF- I and IGFBP-3 levels of the subjects were detected to explore the relationship between the two levels (serum IGF- I and IGFBP-3) and BC.Results.Compared with group B, the two levelsof group A were lower while IGF-I/IGFBP-3 was higher. Compared with low-grade BC group, non-muscle invasive BC (NMIBC) group and non-lymph node metastasis group, the two levels were lower in high-grade BC group, muscle-invasive BC (MIBC) group and lymph node metastasis group (P<0.05). No notable difference in IGF-I/IGFBP-3 was found among patients with high-grade or low-grade BC, with or without lymph node metastasis, andwith or without muscular invasion (P>0.05).Conclusion. The serum IGF-I and IGFBP-3 levels of BC patients are obviously different compared with healthy people, and vary in patients with different types of BC, indicating the two factors can be applied in clinical diagnosis of BC.

Keywords: serum IGF- I; IGFBP-3; diagnosis of bladder cancer (BC)

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Bladder cancer (BC), a genitourinary system tumor with the highest incidence in China, has complex pathogenic factors and a high possibility of recurrence. BC patients usually present with symptoms such as hematuresis and urinary incontinence, with poor prognosis and unsatisfactory overall survival. The special lesion sites of BC add to the difficulty in the surgical treatment of invasive bladder cancer. In addition, early diagnosis and treatment can effectively increase the success rate of surgery, and ensure the life health of patients. In recent years, tumor markers have become an important criterion for determining whether patients have cancer in clinic, in which serum IGF-I and IGFBP-3, as members of insulin-like growth factors (IGFs) family, can effectively reflect the proliferation and development of tumors[1-3]. Nowadays, some scholars have successfully confirmed the relationship between the tumor markers and cervical cancer or colon cancer by studying IGF-I and IGFBP-3 levels in tissues[4-7]. However, few studies have linked the two factors with clinical diagnosis of BC. To investigate the effect of the combined detection of the two factorson the diagnosis of BC, sixty BC patients admitted to our hospital (January 2019-January 2020) were chosen as group A, while sixty healthy people were chosen as group B at the same time in this paper.

MATERIALS AND METHODS

General Information

Sixty BC patients admitted to our hospital (January 2019-January 2020) were chosen as group A, while sixty healthy people during the same period were chosen as group B. No statistical difference in general information was shown between the two groups (P>0.05), as below.The study obtained the approval of the Hospital Ethics Committee.

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Table 1
Comparison of general data of patients

Items	Group A (n=60)	Group B (n=60)	X^2/t	P
Gender			0.036	0.850
Male	38	37		
Female	22	23		
Age (years old)				
Range	54-74	55-74		
Average age	68.21±6.20	69.23±6.21	0.900	0.370
Hypertension	10	11	0.058	0.810
Coronary heart disease (CHD)	5	4	0.120	0.729
Smoking history	24	23	0.035	0.852
Drinking history	15	16	0.044	0.835

Inclusion Criteria

(1) The patients or their families full knew the study process and signed the informed consent. (2) The patients were pathologically confirmed to have BC.

Exclusion Criteria

(1) The patients had mental problems or were unable to communicate with others. (2) The patients had other organic diseases. (3) The patients were not diagnosed with BC for the first time. (4) The lesions of

Methods

The serum IGF-I and IGFBP-3 were determined as follows. (1) 5 mL of fasting peripheral venous blood was extracted from the subjects in the morning and centrifuged at 3000r/min for 0.5h. (2) UniCel DxI800 automatic chemiluminescence analysis system and matching reagents (Beckman, USA; NMPA certified No.: 20082401894) were used for determining serum IGF-I and IGFBP-3.

Observation Criteria

The patients were grouped as below. (1) Group A of BC patients and group B of healthy people. (2) The patients in group A were divided into low-grade BC group (n=39) and high-grade BC group (n=21). Low-grade BC refers to low-grade papillary urothelial carcinoma, and high-grade BC refers to high-grade papillary urothelial carcinoma[8-11]. (3) According to the classification of muscle-invasive BC (MIBC) and non muscle-invasive BC (NMIBC), the patients in group A were divided into MIBC group (n=19) and NMIBC group (n=41). (4) The patients in group A were divided into lymph node metastasis group (n=20) and non-lymph node metastasis group (n=40) according to whether there was lymph node metastasis.

Statistical Treatment

In this study, the data were processed by SPSS20.0 software, and graphed by GraphPad Prism 7 (GraphPad Software, San Diego, USA). The data included enumeration data and measurement data, tested by X^2 and t test. The difference was statistically significant when $p < 0.05$.

RESULTS

Comparison of IGF-I and IGFBP-3 Levels between Group A and Group B

Compared with group B, the IGF-I and IGFBP-3 levels in group A were lower and IGF-I/IGFBP-3 was higher, as below.

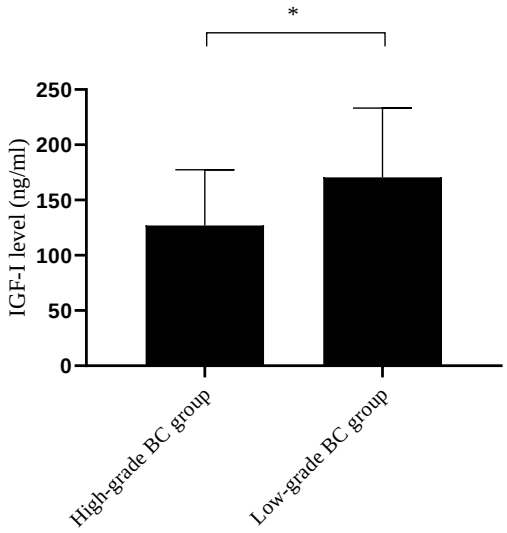
Table 2
Comparison of IGF-I and IGFBP-3 levels between group A and group B ($\bar{x}$±s)

Group	N	**IGF-I** (ng/ml)	IGFBP-3(μg/ml)	**IGF-I**/IGFBP-3
Group A	60	128.56±58.89	2.68±1.25	48.89±15.45
Group B	60	210.54±62.50	4.98±1.52	41.25±14.56
t		7.395	9.053	2.788
P		0.000	0.000	0.006

Comparison of IGF-I and IGFBP-3 Levels between High-grade and Low-grade BC Groups

The IGF-I and IGFBP-3 levels in high-grade BC group were lower compared with low-grade BC group (P<0.05), as below.

Figure 1
Comparison of IGF-I levels between high-grade and low-grade BC groups ($\bar{x}$±s, ng/ml)

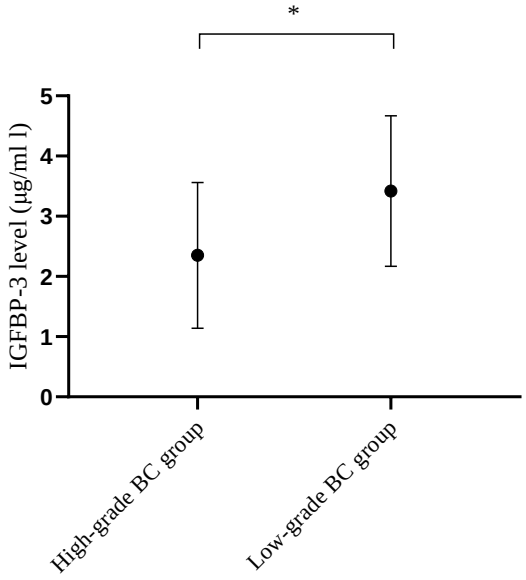


Note: In Figure 1, the abscissa from left to right represented high-grade BC group and low-grade BC group, and the ordinate represented the IGF-I level (ng/ml).

* indicated P<0.05.

The IGF-I level was (126.89±50.56) ng/ml in high-grade BC group and (170.58±62.56) ng/ml in low-grade BC group.

Figure 2
Comparison of IGFBP-3 levels between high-grade and low-grade BC groups ($\bar{x}$±s, μg/ml)

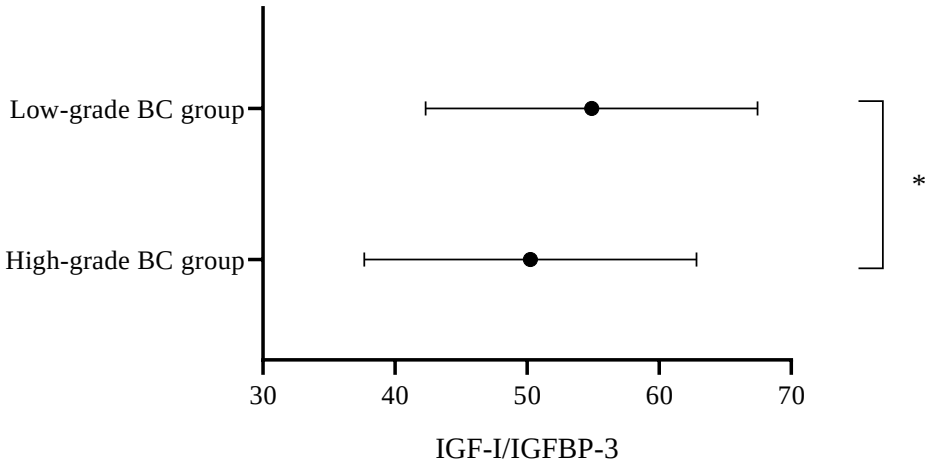


Note: In Figure 2, the abscissa from left to right represented high-grade BC group and low-grade BC group, and the ordinate represented the IGFBP-3 level (μg/ml).

* indicated P<0.05.

IGFBP-3 was (2.35±1.21) μg/ml in high-grade BC group and (3.42±1.25) μg/ml in low-grade BC group.

Figure 3
Comparison of IGF-I/IGFBP-3 between high-grade and low-grade BC groups ($\bar{x}\pm s$)



Note: In Figure 3, the ordinate from top to bottom represented low-grade BC group and high-grade BC group, and the abscissa represented IGF-I/IGFBP-3.

IGF-I/IGFBP-3 was (50.26±12.58) in high-grade BC group and (54.89±12.56) in low-grade BC group.

Comparison of IGF-I and IGFBP-3 Levels between MIBC Group and NMIBC Group

The IGF-I and IGFBP-3 levels in MIBC group were lower compared with NMIBC group (P<0.05), as below.

Table 3
Comparison of IGF-I and IGFBP-3 levels ($\bar{x}\pm s$)

Group	N	**IGF-I**(ng/ml)	IGFBP-3(μg/ml)	**IGF-I**/IGFBP-3
MIBC group	19	125.89±60.54	2.35±1.35	50.58±11.56
NMIBC group	41	185.68±59.51	3.41±1.30	55.26±12.20
t		3.601	2.903	1.405
P		0.001	0.005	0.166

Comparison of IGF-I and IGFBP-3 Levels between Lymph Node Metastasis Group and Non-lymph node Metastasis Group

The IGF-I and IGFBP-3 levels in the lymph node metastasis group were lower compared with the non-lymph node metastasis group (P<0.05), as below.

Table 4
Comparison of IGF-I and IGFBP-3 levels ($\bar{x}\pm s$)

Group	N	**IGF-I**(ng/ml)	IGFBP-3(μg/ml)	**IGF-I**/IGFBP-3
Lymph node metastasis group	20	120.89±60.21	2.21±1.01	54.56±10.58
Non-lymph node metastasis group	40	171.24±65.89	3.32±1.25	50.85±11.54
t		2.869	3.444	1.206
P		0.006	0.001	0.233

DISCUSSION

BC is a high-risk tumor in the urinary system with extremely complex biological characteristics. Although biopsy is often used for clinical diagnosis of BC in practice, its application is limited because this invasive and expensive diagnosis method and the low tolerance of patients are not conducive to its clinical promotion. In addition to biopsy, imaging examination can also be used for the diagnosis of BC. However, the sensitivity of imaging examination is not high due to the small

tumor size in the early stage of BC, resulting in missed diagnosis and delay of the best treatment opportunity of patients. Therefore, other detection methods are needed to enhance the diagnostic accuracy. With the increasing awareness of serum markers, many tumor markers have been applied in clinical examination, while there are few markers that can directly relate to BC. This paper explored the pathogenesis of BC, and selected IGF-I and IGFBP-3 as diagnostic markers because some studies have confirmed that IGFs are closely related to the disorders of malignant proliferation and apoptosis in cancer cells[12-15]. IGF-I and IGFBP-3 are members of IGF family. IGF-I, an important factor weakening the rate of cell apoptosis, is closely related to cell proliferation and division, and can bind to its receptors, thereby playing a role through autocrine and paracrine. IGFBP-3 can accelerate cell apoptosis and regulate the total IGF-Icontent.IGF-I combined with IGFBP-3 can not only control the cell proliferation and apoptosis in the body of patients, but also directly reflect BC occurrence and development[16-19].

The results showed that compared with group B, IGF-I and IGFBP-3 of group A were lower while IGF-I/IGFBP-3 was higher. This was consistent with the research results of Rexin P who found that serum IGF-I and IGFBP-3 of BC patients were (130.56±55.89) ng/ml and (2.65±1.21) μg/ml, which were notably lower compared with healthy people ($P < 0.001$)[20], suggesting that the two insulin factors in BC patients cannot be competitively combined, resulting in decreased number of complexes, weakened control function of IGFBP-3, abnormal concentration of local IGF-I, obviously reduced frequency of cell apoptosis, abnormal cell growth, and eventually the occurrence of BC[21-23].

In addition, compared with low-grade BC group, NMIBC group and non-lymph node metastasis group, IGF-I and IGFBP-3 were lower in high-grade BC group, MIBCgroup and lymph node metastasis group, revealing that the two levels are closely associated with BC occurrence and development. Navarro J has confirmed in his study that the two levels of patients with colorectal cancer and lymph node metastasis were lower than those of patients without metastasis[24]. Hanson White has found that the levels of the two insulin factors in patients with advanced cancer were higher than those in patients at early stage of cancer[25], indicating that the two factorscan change with the progression of the disease. Therefore, the two factors are of great significance in determining the degree of cancer differentiation and pathological staging of BC patients.

This study does not show the relationship between IGF-I/IGFBP-3 and the development of BC patients, presumably due to the small sample size. The effect of IGF-I/IGFBP-3 on diagnosing BC needs to be further explored.

In summary, IGF-I and IGFBP-3 are important criteria for determining whether patients have BC or not, which are closely associated withBC occurrence and development, with a high diagnostic value.

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