

Some clinical-pathological characteristics and factors related to muscle-invasion in newly diagnosed bladder cancer

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Summary

Objective: To learn about some clinical and histological characteristics of bladder cancer, as well as investigate about some factors related to muscle-invasion in newly diagnosed bladder cancer. **Subject and method:** A descriptive retrospective study was conducted on 416 patients with newly diagnosed bladder cancer who underwent transurethral resection of bladder tumor within 6 years from 2018 to 2023 at 108 Military Central Hospital. **Result:** Mean age was 66.3 ± 12.4 (16-92); male 88.7%, female 11.3%; male/female ratio was 7.8/1. Asymptomatic gross hematuria was the majority (77.9%). Papillary tumors were the majority (62.3%), commonly found in both lateral walls (53.6%), most were ≤ 3 cm in size (72.8%), and more than half of the patients had a solitary tumor (54.3%). Most bladder cancers were urothelial carcinomas (99.04%), of which 76.9% were high-grade malignancy; the rate of non-muscle-invasive tumors detected for the first time was 76.9%. The rate of muscle-invasive tumors in both sexes was similar; meanwhile, advanced age, sessile tumor characteristics, tumor size > 3 cm, number > 3 tumors, and high-grade malignancy were all statistically significant factors related to muscle-invasive tumors. **Conclusion:** The detection rate of the first diagnosed non-muscle-invasive bladder cancer was comparable to the world literature; some tumor characteristics were statistically significantly associated with the presence of muscle-invasive tumor.

Keywords: Bladder cancer, non-muscle invasion, muscle invasion.

I. BACKGROUND

Bladder cancer is the 7th most common malignancy in men and the 10th most common worldwide for both sexes, with an estimated 573,278 new cases in 2020^{1,2}. Of these, about 75% of tumors are still localized in the mucosa or submucosa without invading the muscle layer¹.

The estimated incidence of bladder cancer in Vietnam is lower than the general rate in the world, from 2.3 - 3.7 cases/100,000 people for men and 0.85 - 1.2 cases/100,000 for women². However, the disease seems to be on the rise, with 1,502 new cases and 883 deaths reported in 2018, increasing to 1,721 new cases and 902 deaths in 2020^{2,3}.

We believe that the above statistics are probably lower than the reality, given that in Vietnam there are no multi-center statistics on this disease. Therefore, there is not enough reliable data on the initial characteristics of bladder tumors, the rate of muscle invasion at the time of detection. Therefore, we conducted this study to investigate some clinical and histopathological features of bladder cancer detected for the first time, as well as to investigate some factors related to muscle-invasion at the time of initial detection.

II. SUBJECT AND METHOD

2.1. Subject

Patients with first-time bladder tumor diagnosis, undergoing transurethral resection of bladder tumor, at the Department of Urology, 108 Military

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Central Hospital, between January 1, 2018 and December 31, 2023.

Exclusion criteria included recurrent bladder cancer, cancer from other organs metastasized to the bladder, postoperative histopathology was benign, or low malignant potential urothelial papilloma.

2.2. Method

Study design was a descriptive retrospective study. Here is the summary of the diagnosis and treatment process for bladder tumors detected for the first time at 108 Military Central Hospital:

Preliminary diagnosis of bladder tumor is based on clinical symptoms (asymptomatic hematuria), or by abdominal ultrasound.

Definitive diagnosis of bladder tumors based on cystoscopy (white light, no biopsy).

Imaging: Abdominal CT scan, or bladder MRI (for VI-RADS score).

Transurethral surgery to remove bladder tumor, perform histopathological diagnosis and T-stage diagnosis.

If the post-operative histopathological results are primary bladder cancer, the patient will be assigned to do a staging diagnosis (by chest-abdominal CT-scan, bone scintigraphy), and consult with the urological cancer committee to decide on the next treatment.

Variables were age, gender, reason for examination, tumor characteristics (via cystoscopy, CT-scan/MRI), histopathology. From statistical analysis, we find out some related factors for the first-detected muscle-invasive bladder cancer.

We collected data from patients' electronic medical records; process data using SPSS 22.0 software: Calculate mean, frequency, and correlation between variables using Chi-square test.

And, this is a retrospective study, all patient information is anonymized for scientific research and not used for any other purpose.

III. RESULT

We retrospectively reviewed the records of 684 patients who transurethral resection of bladder

tumor at the Department of Urology, 108 Military Central Hospital over a 6-year period from January 1, 2018 to December 31, 2023, collecting data from 508 patients with first-time bladder tumors; postoperative histopathology showed that there were 416 cases of primary bladder cancer (81.9%), 25 cases of low-malignant potential papillomas (4.9%), 67 cases of benign lesions (13.2%) such as benign papillomas, cystic cystitis, schwannoma, paraganglioma, etc.

We analyzed data on 416 patients with first-time primary bladder cancer, and the results showed that:

The mean age was 66.3 ± 12.4 (16–92). Male 88.7%, female 11.3%; male/female ratio was 7.8/1. The rates of first primary bladder cancer in young (≤ 44 years old), middle-aged (45–59), elderly (60–74) and old age (≥ 75) were 5.8%, 16.6%, 51.4% and 26.2%, respectively; this distribution was similar in both sexes (**Figure**).

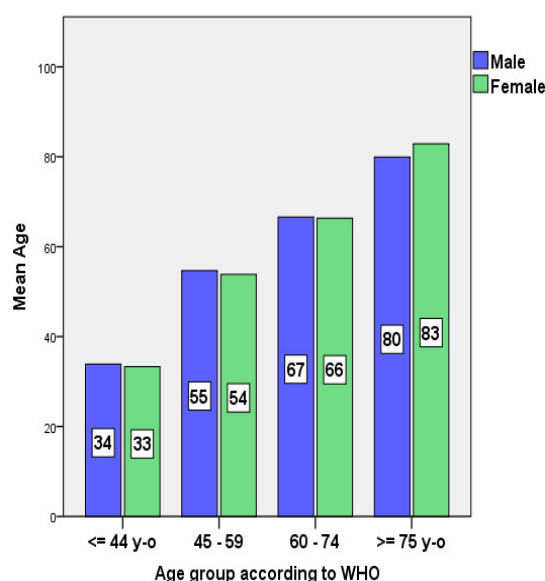


Figure 1. Age group division according to WHO⁴

The proportion of patients who came to the clinic because of asymptomatic gross hematuria was the majority (77.9%); 13.7% of patients discovered bladder tumors incidentally during ultrasound examination; other lower urinary tract symptoms that caused patients to go to the clinic were frequent urination (5%) and hesitancy (3.4%).

Table 1. Gross characteristics of bladder tumors

Gross characteristics of bladder tumors		Number of cases	Percentage %
Appearance	Papillary	259	62.3
	Sessile	157	37.7
Site	Trigone (1)	22	5.3
	Right ureteral orifice (2)	32	7.7
	Left ureteral orifice (3)	28	6.7
	Right wall (4)	109	26.2
	Left wall (5)	114	27.4
	Anterior wall (6)	13	3.1
	Posterior wall (7)	53	12.7
	Dome (8)	23	5.5
	Neck (9)	22	5.3
Size	25.3 ± 13.8 mm (5 - 74)		
	≤ 3cm	303	72.8
	> 3cm	113	27.2
Number	1 tumor	226	54.3
	2 tumors	42	10.1
	3 tumors	19	4.6
	≥ 4 tumors	129	31.0

Papillary tumors were the majority (62.3%), often found in both lateral walls (53.6%), most were ≤ 3cm in size (72.8%), and more than half of the patients had a solitary tumor (54.3%).

Table 2. Pathological features

Pathological features		Number of cases	Percentage %
Pathology	Urothelial carcinomas	412	99.04
	Squamous cell carcinoma	3	0.72
	Adenocarcinoma	1	0.24
Grade*	Low	95	23.1
	High	317	76.9
Muscle-invasion	Yes	320	76.9
	No	96	23.1

(* specific for urothelial carcinoma)

Most bladder cancers were urothelial carcinomas (99.04%), of which 76.9% were high grade malignancy; the rate of non-muscle-invasive tumors detected for the first time was 76.9%.

Table 3. Some factors related to muscle-invasion

Factors		Non-muscle invasion	Muscle invasion	p
		n (%)		
Age	≤ 44	24 (7.5)	0	< 0.05
	45 - 59	53 (16.6)	16 (16.7)	
	60 - 74	166 (51.9)	48 (50)	
	≥ 75	77 (24.1)	32 (33.3)	

Factors		Non-muscle invasion	Muscle invasion	p
		n (%)		
Sex	Male	284 (88.8)	85 (88.5)	> 0.05
	Female	36 (11.2)	11 (11.5)	
Appearance	Papillary	229 (71.6)	30 (31.2)	< 0.01
	Sessile	91 (28.4)	66 (68.8)	
Size	≤ 3cm	258 (80.6)	45 (46.9)	< 0.01
	> 3cm	62 (19.4)	51 (53.1)	
Number	≤ 3 tumors	231 (72.2)	56 (58.3)	< 0.05
	> 3 tumors	89 (27.8)	40 (41.7)	
Grade*	Low	90 (28.1)	5 (5.4)	< 0.01
	High	230 (71.9)	87 (94.6)	

(Pairwise chi-square test), (*specific for urothelial carcinoma)

The rate of first-time detection of muscle-invasive tumors in both sexes was similar; meanwhile, advanced age, sessile tumor characteristics, tumor size > 3cm, number > 3 tumors, and high-grade malignancy were all statistically significant factors related to muscle-invasive tumors.

IV. DISCUSSION

4.1. On some clinical and pathological features

Our study encountered some very young patients (youngest age 16 years old), however, in general, bladder cancer is more common in the elderly (from 60 to 74 years old) and the senile age (from 75 years old and above) ⁴, similar distribution in both sexes (Figure 1). Several previous studies also found similar age-specific incidence rates ⁵⁻⁷.

Typical clinical symptom of bladder tumor is gross hematuria, according to medical literature accounting for more than 90%. A recent report by Nguyen Minh An (2022) shows that this rate was 94.3% ⁷. However, another study by Shephard (2012) on 4915 bladder cancer patients in the UK also showed that the rate of gross hematuria was 53% ⁸. In this study, we observed a rate of 77.9% of patients with this symptom; and up to 13.7% of patients discovered bladder tumors incidentally during ultrasound examination. On the contrary, Khadra's statistics on 1930 cases of hematuria showed that the rate of bladder cancer detection was only 12% ⁹.

The above statistics show that this symptom is still the most important sign in the clinical diagnosis of bladder cancer.

Regarding the gross characteristics of the tumor, we based on the guidelines of the European Association of Urology, classifying it into 2 groups: papillary tumors and sessile tumors ¹. In fact, this classification can be reasonable and accurate when the tumor is not too large (the entire tumor can be observed in one endoscopic field, usually when the size is ≤ 3cm). The study showed that papillary tumors were the majority (62.3%), often found in both lateral walls (53.6%), most were ≤ 3cm in size (72.8%), and more than half of the patients had a solitary tumor (54.3%) (Table 1).

Regarding histopathological results, our study was similar to the literature, when the rate of urothelial carcinoma accounted for 99.04% (Table 2).

4.2. On some factors related to muscle invasion

The rate of primary non-muscle-invasive bladder cancer detected for the first time in this study was 76.9% (or the rate of muscle-invasion was 23.1%), similar to world literature¹. However, some other studies referred to have a fairly high rate of muscle invasive tumors, such as Sasikumar (2016) reported a muscle invasive rate of 35% (56/159 patients), Nguyen Van Mao (2017) 79.9% muscle invasion (47/59 patients) Nguyen Minh An (2022) 100% muscle

invasion (35/35 patients)⁵⁻⁷. We believe that this discrepancy may be due to sample selection.

Whether bladder cancer has invaded the bladder muscle at the first time of detection is the most important question, as this will determine the next directions of diagnosis and treatment for the patient. The importance of this question is reflected in the reality when the European Association of Urology or the American Urological Association have been publishing 2 separate guidelines for each situation (non-muscle invasive bladder cancer guideline, and muscle-invasive bladder cancer guideline).

The gold standard for diagnosis of muscle-invasion is pathology, with the usual procedure being endoscopic resection and separate removal of bladder muscle samples for histopathology. However, in clinical practice, there are many situations that make the procedure substandard, such as multiple tumors, large tumors, infiltrative tumors with a wide tumor base (the entire specimen is tumor without normal tissue), bladder perforation during tumor excision due to obturator jerk, and inexperienced surgeons (fear of bladder perforation so they perform superficial excision)...

In addition, although diagnostic imaging has become increasingly reliable (MRI with VIRADS score), additional prognostic factors are still needed to help assess the patient's condition more realistically.

Our study initially found that the rate of muscle-invasive tumors in both sexes was similar; meanwhile, elderly and old age, sessile tumor characteristics, tumor size > 3cm, number > 3 tumors and high-grade malignancy were all factors related to newly primary muscle-invasive bladder cancer with statistical significance (Table 3).

Nguyen Van Mao's report (2017) also had some similarities; there was a correlation between differentiation and tumor invasion level: poor differentiation had a high risk of muscle invasion; however, the author did not find a correlation between tumor size and tumor invasion level with 95% confidence (size < 3 and ≥ 3cm)⁶. Additionally, we have not found any other studies with similar analyses.

V. CONCLUSION

The results of a retrospective study on 416 patients with primary bladder cancer first detected at the 108 Military Central Hospital showed that most patients came for examination due to asymptomatic gross hematuria (77.9%); most bladder cancers were urothelial carcinomas (99.04%), of which 76.9% were high-grade malignancy; the rate of non-muscle-invasive tumors first detected was 76.9%. The rate of muscle-invasive tumors in both sexes was similar; meanwhile, advanced age, sessile tumor, tumor size > 3cm, number > 3 tumors, and high-grade malignancy were all statistically significant factors related to muscle-invasion.

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