THE VALUE OF URINARY CYTOLOGY AND HYDRONEPHROSIS TO PREDICT MUSCLE INVASIVE BLADDER CANCER

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ABSTRACT

Objective: *We evaluated the value of urinary cytology, and presence of hydronephrosis to predict muscle invasive bladder cancer.* ***Material & methods:*** *We retrospectively analyzed data of 167 patients that diagnosed bladder cancer from medical record at Sardjito General Hospital Yogyakarta, between 2004-2011. Preoperative parameters were evaluated including age, gender, number and location of bladder cancer, urinary cytology, as well as presence of hydronephrosis. The outcome was muscle invasive bladder cancer.* ***Results:*** *A total of 96 (57.5%) patients had positive urinary cytology, 80 (47.9%) had hydronephrosis, most location of tumor were in trigone 43 (25.7%). The youngest patient was 26 years and the oldest was 84 years old, male was most affected in 145 (86.8%). On bivariate analysis, positive urinary cytology and hydronephrosis were associated with muscle invasive bladder cancer (OR 0.08 CI 0.038–0.167; OR 30.24 CI 12.72–71.89, respectively, each $p < 0.05$). Combination urinary cytology and hydronephrosis incrementally improved prediction of muscle invasive bladder cancer with positive and negative predictive value were 93.9% and 71.4%, respectively. Presence of hydronephrosis was associated with tumor location in trigone ($p < 0.05$).* ***Conclusion:*** *Urinary cytology and hydronephrosis were associated with muscle invasive bladder cancer, and can be used to predict muscle invasive bladder cancer.*

Keywords: *Urinary cytology, hydronephrosis, muscle invasive bladder cancer.*

ABSTRAK

Tujuan: *Kami mengevaluasi nilai sitologi urine dan adanya hidronefrosis untuk memprediksi kanker kandung kemih muscle invasif.* ***Bahan & cara:*** *Secara retrospektif kami menganalisa data dari 167 pasien yang didiagnosa kanker kandung kemih dari rekam medis RSU Sardjito Yogyakarta, antara tahun 2004-2011. Parameter pre-operatif dievaluasi termasuk usia, jenis kelamin, jumlah & lokasi kanker kandung kemih, sitologi urine, adanya hidronefrosis. Hasilnya adalah kanker kandung kemih muscle invasif.* ***Hasil:*** *Sebanyak 96 pasien (57.5%) dengan sitologi urine positif, 80 (47.9%) dengan hidronefrosis, sebagian besar lokasi tumor di trigonum 43 (25.7%). Pasien termuda berusia 26 tahun dan tertua 84 tahun, laki-laki paling banyak terpengaruh 145 (86.8%). Pada analisa bivariate, sitologi urine positif dan hidronefrosis dihubungkan dengan kanker kandung kemih muscle invasif (OR 0.08 KI (0.038–0.167); OR 30.24 KI (12.72–71.89), setiap $p < 0.05$). Kombinasi sitologi urine dan hidronefrosis meningkatkan prediksi kanker kandung kemih muscle invasif dengan nilai prediktif positif dan negatif 93.9% dan 71.4%. Adanya hidronefrosis dihubungkan dengan lokasi tumor di trigonum ($p < 0.05$).* ***Simpulan:*** *Sitologi urine dan hidronefrosis dihubungkan dengan kanker kandung kemih muscle invasif, dapat digunakan untuk memprediksi kanker kandung kemih muscle invasif.*

Kata kunci: *Sitologi urine, hidronefrosis, kanker kandung kemih muscle invasif.*

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INTRODUCTION

Bladder cancer is a lethal disease. According to American Cancer Society, there were 68.810 case diagnosed in United State in 2007, and comprised of 3% of all deaths. The risk and grading of bladder cancer are age dependent. In general, young adults tend to develop well-differentiated non-invasive, rather than invasive bladder cancer.[1]

At initial diagnosis bladder cancer is about 70% non muscle invasive, just 30% is muscle invasive, from database patients undergo radical cystectomy about 57% is muscle invasive, and about 43% is non muscle invasive.[2] Bladder cancer is a progressive disease, 20-40% of non muscle invasive cancer develop into muscle invasive if are not given

adequate treatment.[3] The main management of non invasive bladder cancer is local resection and intravesical chemotherapy, while muscle invasive bladder cancer is radical cystectomy, so that early detection will provide more promising treatment outcomes.[4]

Urinary cytology is microscopic examination taken from voided urine or bladder washing specimens with histopathology staining. Interpretation is based on the finding of urothelial cells in voided urine or bladder washing. The study shows only 58% bladder cancer with urinary cytology positive. Urinary cytology has high sensitivity in high grade bladder cancer and CIS (carcinoma in situ) and has low sensitivity in low grade bladder cancer.[5]

Urinary cytology has specificity 95% interpreted by experience Pathologists, although the tumor are not seen on cystoscopy. Urinary cytology has low sensitivity in muscle invasive bladder cancer by 62% and positive predictive value of 44%. However, in some education centers, urinary cytology is still used for diagnostic and surveillance bladder cancer.[6]

Bladder cancer has characteristic as multifocal cancer that can infiltrate alongside urinary tract especially ureter and cause hydronephrosis. A previous study reported hydronephrosis had correlated with muscle invasive bladder.[7]

A transabdominal ultrasound bladder cancer can show size of bladder cancer, intraluminal tumor protrusion in the bladder and bladder wall thickness, presence of hydronephrosis indicated obstruction to urinary flow caused bladder cancer infiltrating or compressing the ureteral orifice. The European Association of Urology (EAU) guidelines recommend IVU or CT urography only in selected cases on suspicious bladder cancer located in trigone or muscle invasive.[8] Based on this background, we do see preoperative factor can be used to improve the predictive value muscle invasive bladder cancer.

OBJECTIVE

The aim of this study was to evaluate the value urinary cytology and hydronephrosis to predict muscle invasive bladder.

MATERIAL & METHOD

This retrospective cross sectional study between 2004-2011, patients with diagnosis of suspicious bladder cancer in Sardjito General Hospital Yogyakarta, which underwent urinary cytology, transabdominal ultrasound, IVU, and CT urography examination. Data recorded from medical files including age, gender, presence of hydronephrosis, urinary cytology, location tumor during cystoscopy, and staging bladder cancer beside on histopatological derived from biopsy or transurethral resection specimen were recorded and reviewed. The statistical analysis was carried out using SPSS software.

RESULTS

The mean age of the 167 patients was 60.69 ± 13.172 (range 26-86) years. The sex distribution revealed that the majority of the patients were male 145 (86.8%). Total number of muscle invasive bladder cancer (≥ T2) were 89 (53.3%) patients, positive urinary cytology were 96 (57.5%), and presence of hydronephrosis were 82 (49.1%) (table 1),

Table 1. Preoperative characteristic of patients.

Characteristic	Variable	N	Mean
Age	< 40 years	15 (9%)	60.69 ± 13.172 (26-86) years
	≥40 years	152 (91%)	
Gender	Male	145 (86.8%)	
	Female	22 (13.2)	
Staging	T1	78 (46.7%)	
	≥T2	89 (53.3%)	
Cytology	Positive	96 (57.5%)	
	Negative	71 (42.5%)	
Hydronephrosis	Positive	82 (49.1)	
	Negative	85 (50.9%)	

trigone is more frequent locate bladder cancer 43 (25.7%) (table 2).

The bivariate correlation with Pearson Chi-square revealed urinary cytology, hydronephrosis showed significant correlation with muscle invasive bladder cancer (OR 0.08 CI 0.038-0.167; OR 30.24 CI 12.72-71.89 respectively) $p < 0.05$. The age and gender revealed no correlation with muscle invasive bladder cancer (table 3). The hydronephrosis showed significant correlation with location of bladder cancer ($p < 0.05$) (table 2). The combination urinary cytology and hydronephrosis increased positive predictive value and negative predictive value of muscle invasive bladder cancer (93.9%; 71.4%) (table 4).

Table 2. Correlation of hydronephrosis with tumor location.

Location	N	Hydronephrosis
Lateral	19 (11.4%)	
Posterior	31 (18%)	
Anterior	26 (15.6%)	$p < 0.05$
Dome	26 (15.6%)	
Trigon e	43 (25.7%)	
Multiple	22 (132%	

DISCUSSION

This study revealed the muscle invasive bladder cancer was more frequent in age ≥ 40 years, similar to the results from with another study (Linn et al, 1998), bladder cancer tend to develop invasive and more aggressive in older age (≥40 years), as well as study by Parag et al, 2009. Unlike many other cancers, younger patients tend to develop more aggressive disease, the opposite appears to be true in bladder cancer, this is due to bladder cancer at a young age has a different biological and genetic instability in some cases.[1,9]

Male has incidence of bladder cancer more often than female, with ratio of 6:1, presumably because of an increased prevalence of smoking and exposure to environmental toxins, carcinogenic agents, which cause bladder cancer, where the majority of women in Indonesia work as

Table 3. Correlation between age, gender, urinary cytology and hydronephrosis with muscle invasive bladder cancer.

Variable		T1		≥T2		CI 95%			
		n	%	n	%	p	RO	min	max
Age	< 40	9	11.5	6	6.7	0.279	1.804	0.612	5.32
	≥40	69	88.5	83	93.3				
Gender	Male	65	83.3	80	89.9	0.211	0.563	0.226	1.398
	Female	13	16.7	9	10.1				
Urinary cytology	Positive	22	28.2	74	83.1	< 0.005	0.08	0.038	0.167
	Negative	56	71.8	15	16.9				
Hydronephrosis	Positive	9	11.5	71	79.8	< 0.005	30.24	12.72	71.9
	Negative	69	88.5	18	20.2				
Total		78	100	89	100				

Table 4. Positive, negative predictive value urinary cytology and hydronephrosis.

Variable	Positive predictive value	Negative predictive value
Hydronephrosis	88.75%	79.3
Urinary cytology	77%	78.9%
Combination	93.9%	71.4%

housewife.[1,9] However, in this study no significant correlation was observed, probably a few sample can be used as an excuse in this study.

Urinary cytology and hydronephrosis showing significant correlation with muscle invasive bladder cancer (OR 0.08 CI 0.038-0.167; OR 30.24 CI 12.72-71.89) respectively ($p < 0.05$). This means that in patients with positive urinary cytology showed a tendency to 0.08 times more likely to become muscle invasive bladder cancer, while hydronephrosis showed tendency to 30.24 times more likely to become muscle invasive, this is similar with study by James et al 2010.[7]

Location of tumor has significant correlation to the hydronephrosis, where trigone is most common. According to Hatch and Barry, obstruction on the ureteral orifice is related to muscle invasive bladder cancer, more than 90% patient transitional bladder cancer are accompanied by hydronephrosis.[10] The study conducted on 116 patients with unilateral or bilateral hydronephrosis found 85% in form of muscle invasive.[10] Unfor-tunately, in this study only few patients undergo radical cystectomy, so that the findings of histopatology of the ureter indicating infiltration of the ureter can not be confirmed.

Combination of the urinary cytology and hydronephrosis show positive predictive value 93% and negative predictive value 71.4%. This means that the probability of a person suffering muscle invasive bladder cancer when urinary cytology positive and presence hydronephrosis is 93.9%, while the probability when the negative 71.4%, similar with study by James C et al.[7,11]

CONCLUSION

Urinary cytology and hydronephrosis significantly correlated with muscle invasive bladder cancer. Patients with positive urinary cytology and hydronephrosis will increase the risk for muscle invasive bladder cancer.

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