



ORIGINAL ARTICLE

Impact of Examination of re-cut Slides on Grade and Invasion in Urothelial carcinoma of the Bladder

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ABSTRACT

Effect of pathology slide review on grading the malignancies can be a challenging and essential subject in different diagnostic pathology and oncology centers. According to the impact of different parameters on the evaluation of pathology slides, our aim was to compare the results of slides' evaluations in terms of grade and invasion of bladder urothelial carcinoma in different times and labs. The slides of 202 cases of urothelial bladder carcinoma from shahid modares hospital were re-cut, stained and reviewed by a second pathologist. The stage and grade of the initial report were determined according to the 1978 TNM classification and second revision was done according to the 1999 classification. The second review showed that the samples which had been evaluated as invasive T1 and T2 (and greater) down staged to non-invasive Ta in 49(24.2%) of cases, respectively. This discrepancy was also observed for Ta and T1 stages which were upstaged to greater stages in 4 (19.8%) of cases, respectively. The interobserver agreement between pathologists was determined for grading of bladder cancer (Coefficient kappa=0.51). Our findings reveal that reclassification of T stage and grade occur in the second review. This difference could be because of subjective modality in grading of bladder cancer between pathologists.

Keywords: Cancer, Urothelial

Received 11.05.2014

Revised 10.06.2014

Accepted 10.08.2014

INTRODUCTION

Bladder cancer is known as a heterogeneous group of malignancies [1]. Because of the cumulative exposure to a variety of carcinogens, bladder cancer shows different stages of progression [2]. Bladder cancer has been reported as the 4th and 8th most common cancer in men and women in the western world, respectively [1]. Its incidence in men is lower than women (3:1) [3].

Determining the pathological stage of bladder cancer is the most important factor for prognosis, follow up, treatment and prediction of risk of death in patients suffering from bladder cancer(4-6). According to the sixth TNM categorization of tumors, bladder cancer classified as: stage Ta (Noninvasive papillary carcinoma), Tis (Carcinoma in situ), T1 (invasion of the subepithelial connective tissue or lamina propria), papillary tumors without any grading and carcinoma *in situ* (CIS).(2, 5). Because of being subjective, there are some limitations on using the histological method for staging and grading the bladder cancer and subsequent treatment protocols(7).

According to the reports, Inter-pathologist variation points to the difference on review of tissue paraffin-embedded samples for determining the grade and stage of malignancies by two independent pathologists.(7-10)Even more, the change in the results of high risk cases such as stage T1 grade 3 of bladder cancer to the non-invasive forms after re-evaluating the samples has been occurred by Meijden and et al.(7).

Therefore, second pathological review of tumor slides is highly controversial. In the present study, we tried to investigate whether examination of the re-cut slides could change the stages and grades of previously reviewed samples of the urothelial bladder tumor.

MATERIAL AND METHODS

As a retrospective study, we studied a total of 202 stored tissue samples of urothelial bladder tumor cases evaluated by general pathologists in Shahid Modares hospital during 7 years. All specimens were prepared using TURBT(transurethral resections). Examining the new re-cuts of paraffin embedded blocks was done by a second pathologist reviewer without being aware of the initial results. For samples with more than one block, all of them were reviewed. Then, the previous and current reports were completely compared. If there were any controversy between the results of the first and the second reviewers, the slides were checked again by a third pathologist to confirm or reject the reports. In this study, the stage and grade of the initial report were determined according to the 1978 TNM classification which was a three tiered system, while the new examination was performed according to 1999 classification (?). To interpreting the results, grade I and II of the 1978 TNM classification have been considered as low and grade III as high risk cases. The same procedure for slide preparation and staining was used for the previous and current review; both were done by the same laboratory and staffs. SPSS 10.1 was used for data analyzing.

Statistical analysis

Coefficient kappa were measured. Data were evaluated by SPSS 10.1(?)

RESULTS

A total of 202 samples from bladder cancer patients who had been referred to Shahid Modares hospital were entered in this study.The clinical and laboratory features of patients' samples have been shown in Table 1.

The inter-observer agreement between pathologists was measured (Coefficient kappa) which was ?for staging and 0.51 for grading the bladder cancer..

The second review of paraffin-embedded tissue samples showed that T1 and T2 and greater down staged to Ta in 49(24.2 %) of samples. In addition, upstaging some samples from Ta and T1 to greater stage in 4(19.8%).

The second pathologist agreed to the initial pathologist in 76% cases for grading and 74% for staging.

Table no 1: Clinical and laboratory features of patients' samples

	The initial report	The review report
No of patients	202	202
Papillary feature	189	175
T category		
Ta	194	153
T1	7	48
T2 and greater	1	1
Lymphovascular invasion	2	11
Grade		
Low(I, II)	100	73
High(III)	95	123
Unknown	7	6

Table no 2: The agreement of old and new staging in bladder cancer

Old stage	New stage			Total no
	Ta	T1	T2 and greater	
Ta	145(98%)	3(2%)	0	148(73%)
T1	36(88%)	4(10%)	1(2%)	41(20%)
T2 and greater	13(100%)	0	0	13(6%)
Total	194(96%)	7(3%)	1(1%)	202

Table no 3: agreement of old and new grade scores in bladder cancer patients' samples

Old grade	New grade		Total(n)
	Low	High	
Low	62(62%)	38(38%)	100(52%)
High	9(9%)	84(91%)	93(48%)
Total	71(37%)	122(63%)	193

Table no 4: Discrepancy between old and new revision

	Down grade	up grade	down stage	up stage
No (%)	9(4.4)	38(18.8)	49(24.2)	4(19.8)

All the p values are less than 0.05

DISCUSSION

In the present study, we showed that inter-observer differences can affect the analysis of pathological samples in about 51% of cases. The second review of re-cut slides of the bladder cancer tissue samples revealed that making final decision on the grade and stage of cancer was changed as 4.4% for down-grading, 18.8% for up-grading, 24.2% for down staging and 19.8% for up staging the cases.

In several studies, intra- and inter-observer variability have been reported as the most important causes of disagreement between reviews using light microscopy [7,11,12]. Various reasons can be considered for inter-observer variability including: different protocols for grading the samples, lacking a similar terminology for classification, different levels of training and experience among pathologists [11].

As an international agreement, the TNM classification system and WHO categorization are used for bladder cancer staging and grading, respectively. Therefore, grading and T classification are assessed discretely and highly dependent on sampling by urologists [7].

The quality of slides is also important for the pathologist's interpretation due to the variation with stage and grade between the slides [7, 13]. In addition, a good and universal sampling method would be applicable in urology guidelines(13).

In this study, we reported up to 24.2 % down staging in bladder cancer while it was about 50% for stage T1 and 50% for stage T1 grade 3 cases during the second review in another study.

Moreover, Bol et al showed 12.3% and 24.6% inter-observer disagreement on stage and grade after the second review, respectively [14]. In another study, coefficient kappa was low between pathologists [15] with an inter-observer variation of 49% on grading the samples between pathologists.

Obviously, determination of accurate tumor features influence the quality and effectiveness of proper treatment [13]. The considerable aim of good grading method is to help the physicians for determining the precise diagnosis and subsequent treatment of malignancies [16].

There were some limitations on our study about of the present study including: absence enough information about the patients' survival, recurrence of non-muscle-invasive tumors, their tumor size and treatment.

CONCLUSION

Our findings reveal that reclassification of T stage and grade may occur in the second review. This discrepancy can be based on subjective modality in grading the bladder cancer between the pathologists.

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CITATION OF THIS ARTICLE

Behrang K N, Zeinab K F, Majid A A, Abbas M A, Mohammad R H A, Samira M G, Ehsan H. Impact of Examination of re-cut Slides on Grade and Invasion in Urothelial carcinoma of the Bladder. *Bull. Env. Pharmacol. Life Sci.*, Vol 3 [11] October 2014: 90-93