Expression of E-Cadherin in Malignant Epithelial Neoplasms of the Urinary Bladder

Hany Khattab, Hosni K. Salem, Mostafa Salem, Mostafa Khodeir and Maya Elserafy

Department of Pathology, Faculty of Medicine, Cairo University, Cairo, Egypt
Departement of Urosurgery, Faculty of Medicine, Cairo University, Cairo, Egypt

Abstract: Globally, bladder cancer is one of the most common malignancies and a major cause of cancer morbidity and mortality. Loss of E-cadherin expression is considered a critical factor in facilitating the progression of bladder cancer. The aim of this work is to study the immunohistochemical expression of E-cadherin in malignant epithelial neoplasms of the urinary bladder and then possible prognostic values. 52 radical cystectomy specimens; collected from the Pathology department, Faculty of medicine, Cairo University, during the period from September 2011 up to December 2012. The two 4-µm thick sections were cut from the formalin fixed, paraffin embedded tumor blocks. One was stained with H&E for histopathological reassessment and one was stained immunohistochemically by E-cadherin monoclonal antibody. The immunohistochemical demonstration of the immune markers was accomplished by using immunoperoxidase method. Results showed that loss of E-cadherin expression was found to be significantly correlated with high stages of urinary bladder carcinoma and positive lymph nodal metastasis. Also, a significant correlation was detected between E-cad expression and the histological type of the tumors. In conclusion, the application of E-cad immunohistochemical marker could be used as an independent predictor of lymph node metastasis.

Key words: Urinary Bladder Carcinoma • Immunohistochemistry • E-Cadherin • TCC • SCC • Schistosoma Infestation

INTRODUCTION

Globally, bladder cancer is one of the most common malignancies and a major cause of cancer morbidity and mortality [1]. In developing countries particularly in the Middle East and Africa, the majority of bladder cancers are squamous cell carcinomas (SCCs) and most of these cancers are secondary to Schistosoma haematobium infection. In Africa, the highest incidence of SCC has been seen in schistosomal-endemic areas, notably Sudan and Egypt, where SCC ranges from two thirds to three quarters of all malignant tumors of the bladder. Few studies from Egypt have shown a reversal of this trend due to better control of schistosomiasis in the region, whereas in other parts of Africa the association is unchanged [2, 3]. The major prognostic factors in carcinoma of the bladder are the depth of invasion into the bladder wall and the degree of differentiation of the tumor. Most superficial tumors are well differentiated. Patients in whom superficial tumors are less differentiated, large, multiple, or associated with carcinoma in situ in other areas of the bladder mucosa are at greater risk for recurrence and the development of invasive cancer [4]. The cell-cell adhesion protein E-cadherin represents a cell surface glycoprotein which accounts for a Ca-dependent homotypic adhesion. It plays a role in organization and maintenance of tissue structure [5].

Lack of E-cadherin expression may lead to diminished cellular adhesion, resulting in invasion into connective tissue and possibly to metastasis [6]. In bladder cancer, altered E-cadherin expression is associated with the degree of invasiveness, lymph node metastasis and increased risk of death from bladder cancer [7]. Loss of E-cadherin expression is considered a critical factor in facilitating the progression of bladder cancer [8].

Therefore, we conducted this study to assess the immunohistochemical expression of E-cadherin in malignant epithelial neoplasms of the urinary bladder and the possible prognostic values.
MATERIALS AND METHODS

Study Design: This is a retrospective cross sectional study. The material of this study consists of 52 radical cystectomy specimens of human urinary bladder carcinomas. All specimens were collected from the Pathology department, Faculty of medicine, Cairo University. The period of recruitment was from September 2011 up to December 2012. All the specimens were radical cystectomy specimens with pelvic lymphadenectomy. The clinical data of these patients including age and sex were taken from their pathology requisition sheets enclosed with the specimens.

Histopathological Evaluation: Hematoxylin and Eosin stained slides were evaluated for the histological type of the tumor according to World Health Organization (WHO) histological classification of tumors of the urinary tract; 2004 and for tumor grade based on AJCC/UICC TNM, 7th edition; 2010. Other architectural features were assessed as the extent of invasion, presence of vascular and/or nerve invasion, lymph node metastases and associated schistosomal infestation [9].

Immunohistochemical Staining: Sections were mounted on already coated glass slides. The slides were incubated at 37°C overnight for accurate adhesion of the section to the slide, deparaffinized by incubation in the oven at 56°C for 15 minutes and inserted in xylene for 30 minutes, rehydrated by transferring into graded ethanol, then washed in phosphate buffer saline (PBS) (pH 7.2) for 5 minutes. Slides were immersed in a solution of 90 ml methanol + 10 ml hydrogen peroxide (1.5%) for 30 minutes for blocking of endogenous peroxidase. Slides were placed in citrate buffer, then heated in a microwave oven at 100°C for three successive times, five minutes each for antigen retrieval. Tissue sections were covered immediately with 2 drops of blocking reagent (normal rabbit serum) and were left for 30 minutes in humidified chamber to suppress non-specific binding of immunoglobulins. The rabbit monoclonal anti- E-cadherin antibody of IgG type is applied to detect endogenous levels of total E-cadherin protein (Isotype: Rabbit IgG, Molecular weight: 135 KDa, #3195, stored at -20°C, dilution 1:400) (manufactured by Cell Signaling Technology, Inc.). Application of link antibody [biotinylated goat secondary anti-polyvalent {anti-mouse IgG (H+L) and anti-rabbit IgG (H+L)} catalog # TP-015-BN], then application of labeling reagent streptavidin-horseradish peroxidase complex (Catalog # TS-015-HR) is done. The antigen was finally localized by the addition of DAB chromogen (3-3 diaminobenzidine tetrahydrochloride) plus substrate (Catalog # TA-015-HSX) and DAB plus chromogen (Catalog # TA-001-HCX). Slides were immersed in Mayer’s hematoxylin for 3-5 minutes. Slides were placed in 2 changes of 95% ethanol, then 2 changes of absolute alcohol for rehydration. The sections were washed in between the successive steps by distilled water and by PBS. In each staining session, an internal control of normal urothelium was used as positive control for E-cadherin. As a negative control, a tumor tissue section was processed in the above mentioned sequence but the primary antibody was not added and instead (PBS) was used in this step. The membranous expression of E-cadherin (at the cell-cell border) immunostaining was evaluated according to Elzagheid et al. [10] as follows: (2+) more than 40% of tumor cell membranes showed staining. (1+) from 10 to 40% of tumor cell membranes showed staining. ( - ) less than 10% of tumor cell membranes showed staining Figure (1).

Fig 1: Micrograph of low grade urothelial carcinoma, E-cadherin immunostained, score 2+, (magnification x 200).
**Statistical Methods:** All analyses were done using SPSS (Statistical Package for Social Sciences) software, version 18, Chicago, IL, USA. Categorical variables were expressed as frequencies and percentages. Chi-square test was used for testing proportion independence and Fisher Exact tests if expected number of observations in 25% or more of the cells is less than 5. Kappa measured concordance of markers positivity and negativity being perfect if equal to 1.0. P value was set significant if ≤ 0.05 level.

**RESULTS**

The mean age of the cases was 60 years old, with minimum of 40 years and maximum of 80 years. Most of our cases were males (87% of all cases), with male: female ratio of 6.4:1. Most of the tumors (79%) were more than 3 cm in diameter. Seventy three percent of cases have TCC and 63% of cases were high grade. Most of TCC cases had high grade tumors (76%), while most of SCC cases had moderately differentiated tumors (71%). Most of our cases were pT 3 stage which represented 46% of all cases and tumors with extravesical mass or extension (pT3b and pT4) represented three fourth of all our cases (75% of cases). One third of our cases had lymph nodal metastasis. Thirty eight percent of our cases showed positive vascular invasion in their examined specimens. Forty two percent of our cases had Bilharzial ova in their specimens. We found a significant correlation between SCC tumors of the urinary bladder and Schistosomal infestation (71% of SCC cases were infested, in comparison to only 32% of TCC cases). Eighty one percent of all cases (42 cases out of 52 cases) showed positive E-cadherin expression.

There is no significant correlation between E-cadherin expression and either the age, sex of the patients or size of the tumors. We detected positive E-cadherin expression in 100% of SCC cases, while in only 74% of TCC cases. This correlation proved to be statistically significant. 24% of patients having high grade tumors showed loss of E-cad expression, while 11% of patients having low grade tumors showed loss of expression of the marker. Also there is a significant correlation between decreased E-cadherin expression and high stages of urinary bladder carcinoma. 100% of tumors having pT stage less than 3b (tumors confined to

<table>
<thead>
<tr>
<th><strong>Table 1:</strong> Demographic and histopathological results of the studied groups</th>
<th>E-cad Negative</th>
<th>E-cad Positive</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤50 y</td>
<td>2(4%)</td>
<td>5(10%)</td>
<td>0.500</td>
</tr>
<tr>
<td>&gt;50 y</td>
<td>8(15%)</td>
<td>37(71%)</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>2(4%)</td>
<td>5(10%)</td>
<td>0.500</td>
</tr>
<tr>
<td>Male</td>
<td>8(15%)</td>
<td>37(71%)</td>
<td></td>
</tr>
<tr>
<td><strong>Size of the tumour</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤3 cm</td>
<td>3</td>
<td>8</td>
<td>0.446</td>
</tr>
<tr>
<td>&gt;3 cm</td>
<td>7</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td><strong>Histological Type</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCC</td>
<td>0(0%)</td>
<td>14(27%)</td>
<td>0.046</td>
</tr>
<tr>
<td>TCC</td>
<td>10(19%)</td>
<td>28(54%)</td>
<td></td>
</tr>
<tr>
<td><strong>Grade</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>2</td>
<td>17</td>
<td>0.293</td>
</tr>
<tr>
<td>High</td>
<td>8</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td><strong>pT Stage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>0(0%)</td>
<td>4(7.5%)</td>
<td>0.033</td>
</tr>
<tr>
<td>2b</td>
<td>0(0%)</td>
<td>5(10%)</td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>0(0%)</td>
<td>4(7.5%)</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>9(17%)</td>
<td>11(21%)</td>
<td></td>
</tr>
<tr>
<td>4a</td>
<td>1(2%)</td>
<td>15(29%)</td>
<td></td>
</tr>
<tr>
<td>4b</td>
<td>0(0%)</td>
<td>3(6%)</td>
<td></td>
</tr>
<tr>
<td><strong>T stage</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative (≤3a)</td>
<td>0(0%)</td>
<td>13(25%)</td>
<td>0.050</td>
</tr>
<tr>
<td>Positive (&gt;3a)</td>
<td>10(19%)</td>
<td>29(56%)</td>
<td></td>
</tr>
<tr>
<td><strong>Pelvic organ invasion (T4)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>9(17%)</td>
<td>24(46%)</td>
<td>0.050</td>
</tr>
<tr>
<td>Positive</td>
<td>1(2%)</td>
<td>18(35%)</td>
<td></td>
</tr>
<tr>
<td><strong>LN</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>4(7%)</td>
<td>31(60%)</td>
<td>0.041</td>
</tr>
<tr>
<td>Positive</td>
<td>6(12%)</td>
<td>11(21%)</td>
<td></td>
</tr>
<tr>
<td><strong>Vascular invasion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>7(13%)</td>
<td>25(48%)</td>
<td>0.541</td>
</tr>
<tr>
<td>Positive</td>
<td>3(6%)</td>
<td>17(33%)</td>
<td></td>
</tr>
<tr>
<td><strong>Schistosomal infestation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>6</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>4</td>
<td>18</td>
<td>1</td>
</tr>
</tbody>
</table>
the bladder) positively expressed E-cadherin, while only 74% of cases with pT stage more than 3a (tumors
grossly invading extravesical tissue or pelvic organs) showed positive expression of the marker in a
significant correlation. There is a significant correlation between positive E-cadherin expression and
tumors with pT 4. This might be due to the fact that 90% of cases having E-
cadherin negative tumors were in the category of stage pT 3 while only one case out of nine was in the category
of stage pT 4.

Decreased E-cadherin expression correlates with positive lymph nodal metastasis. It showed that about
90% of cases with no LN metastasis showed positive E-cadherin expression, while only 65% of cases having
LN metastasis showed positive expression. No significant correlation between vascular invasion by tumor emboli
in our included specimens and E-cadherin expression.

DISCUSSION

In our present work, most of the tumors in our specimens were transitional cell carcinoma (73%), while
the rest were squamous cell carcinoma. The age of our 52 patients ranged between 40 and 80 years with the mean
age 59.8 ± 7.4 years which was in concordance with other reports from Egypt, that found that the mean age of
bladder cancer cases was 58.34 ± 12.13 years [11] and 59.0 ± 9.9 [12]. Our results were also near to those of
Salem and Mahfouz, who detected an increase of the mean patient age from 41±11.2 years to 52±8.6 years [13]
and Gouda et al. [3] who reported an increase in the median age of patients from 47.4 years to 60.5 years. Most
of our cases were males (87%), with male to female ratio 6.4:1. This is near to the results observed by El-Bolkainy
et al and Zarzour et al, where the male to female ratio was 5:1 and 5:5:1 respectively [11,14]. The male predominance
is probably attributed to the fact that males are more exposed to the established risk factors, including bilharzial
infestation, cigarette smoking and occupational exposure to chemical carcinogens [15, 16]. In discordance to our
results, Salem and Mahfouz, reported a decrease in the male to female ratio which changed from 5.6:1 to 4.2:1 [13].
This difference may be due to larger sample size and the relatively longer duration of the study.

Millan-Rodriguez et al. [17] and Rodriguez-Alonso et al. [18] recorded that tumors more than 3 cm were
associated with a greater risk of stage progression and reduced survival. This is also observed in our current
study, as most of the tumors (79%) were more than 3 cm in diameter. At the same time, 75% of the tumors were
high stages and showed extravesical mass or extension (pT3b and pT4).

In our study, about three fourth of the cases had TCC (73% of all cases) and only 27% of cases had SCC. This
is almost similar to the results of Salem and Mahfouz, who found that a significant increase occurred in the
prevalence of transitional cell carcinoma from 20% to 66%, with a significant decrease in the prevalence of squamous
cell carcinoma from 73% to 25% [13]. In concordance, Ashley et al. [19] also detected that the relative frequency
of TCC in their multi-year sample (26 years) increased from 22% in 1980 to 73% of bladder tumor diagnoses in 2005,
while SCC decreased from 78% of diagnosed bladder tumors in 1980 to 27% of diagnosed bladder tumors in
2005. It also goes with the results of Gouda et al, who reported a significant decline of the prevalence of SCC
from 75.9% to 28.4% and a significant rise in TCC from 16% to 65.8% of bladder cancers [3]. This might be
attributed to better control and treatment programs of Schistosomiasis in Egypt especially in the rural
population which was traditionally one of the most important risk factors of SCC in the urinary bladder.
This was accompanied by a change in the histological profile of tumors, with significant predominance of
transitional cell carcinoma and an increase in the age of patients, a pattern rather similar to that in western
reports [3]. Also, increased smoking habits are believed to have contributed to the shift toward
TCC in Egypt, which has a stronger smoking association [20].

Despite the use of advanced imaging techniques, regional or distant metastases may go unnoticed until
surgery or at follow-up. There is ample documentation that clinical staging is inaccurate in one third of cases,
with a tendency for underestimation of the extent of the disease. Therefore, there is a need for additional objective
information on the aggressiveness of bladder tumors [23]. This is suggested by our results as most of our cases
were pT3b (38% of all cases) and pT4a (31% of all cases). This means that many cases were understaged before
cystectomy.

Our results showed that 38% of our cases show positive vascular invasion in examined specimens. This is
quite near to the results of Thalita dos Reis et al. [22] who reported microvascular invasion in 50% of their examined
specimens.

In relation to schistosomiasis-associated carcinoma of the urinary bladder, it was found that it represented a
distinct clinico-pathological entity different from nonbilharzial carcinoma and it showed a high frequency
of squamous cell carcinoma due to squamous metaplasia and dysplasia of the transitional epithelium. Recently, however, a relative increase in the frequency of transitional cell type in schistosomiasis-associated bladder cancer has been noted [2, 24].

Our results revealed that 42% of our cases showed Bilharzial ova in their specimens. This agrees with the results of Salem and Mahfouz, who found that the incidence of associated Bilharziasis in bladder carcinoma decreased from 80% to 50% [13]. This also goes with the results of Gouda et al, who reported a significant decline of Bilharzial association in bladder carcinoma from 82.4% to 55.3% [3].

In our present study, 71% of SCC cases had Schistosomal ova in their specimens, while only 32% of TCC cases were infested. Statistical analysis showed a significant correlation between SCC tumors of the urinary bladder and Schistosomal infestation (P value= 0.01). In the same context, Rambau et al. [26] noticed that Schistosomiasis was commonly associated with squamous carcinoma compared to non squamous carcinomas. The relatively high frequency of bladder cancer in Egypt supports the etiological relationship to urinary schistosomiasis. Despite the marked decrease in prevalence of endemic schistosomiasis over the last 2 decades, Egypt is paying the toll of the previously high prevalence of the disease. Comparison of the frequency of active urinary schistosomiasis previously reported during the era of high prevalence of the disease and the age-specific incidence rate indicates a strong cohort effect Ibrahim and Khaled [26] and Jemal et al. [1], reported that the majority of bladder carcinomas associated with schistosomiasis are squamous cell carcinoma. Smoking and occupational exposures are the major risk factors in Western countries, whereas chronic infection with Schistosoma hematobium in developing countries, particularly in Africa and the Middle East, accounts for about 50% of the total burden.

Radical cystectomy is commonly the treatment of choice for patients with muscularis propria-invasive urothelial carcinoma. Unfortunately, up to 40% of patients whose disease is confined to the bladder wall will develop tumor recurrence; virtually all of them will die as a result of the disease. Thus, it is imperative that we find additional markers (clinical, pathologic, or molecular) to predict adverse clinical events in these patients [27].

Cadherin/catenin-based anchoring junctions organize and connect the microfilaments to maintain cell adhesive properties and integrate intra- and intercellular signaling, which includes regulation of nuclear functions and transcription pathways [28, 29].

Reduction in expression of cell adhesion molecules has been reported in human cancers [30]. Decreased E-cadherin expression is involved in the initial step of invasion, which involves deregulation of cell adhesiveness resulting in tumor cell detachment and dedifferentiation in human carcinomas. Therefore, the investigation of E-cadherin in cancerous tissue, using immunohistochemical technique on tissue sections, may enable early prediction of the potential of cancer cells to detach from the parent tumor and their potential aggressiveness [31, 32]. In addition, loss of E-cadherin expression is a critical factor in facilitating the progression of bladder cancer [33].

In this study, about one fifth of our cases (10 cases out of 52 cases) showed loss of E-cadherin expression. This is quite near to that observed by Szekely et al. [34] who found that E-cadherin expression was lost in 13/40 (32%) of their bladder carcinoma cases. It also keeps with Shariat et al. [35] who detected loss of normal membrane E-cadherin immunoreactivity in 17 patients with bladder carcinoma (32%). These slight differences might be due to different geographical locations and different scoring systems used.

In our study, no significant correlation was found between E-cadherin expression and either the age or the sex of the patients. This is supported by the results of Szekely et al. [34] In concordance, Thalita dos Reis et al., reported that the correlation between E-cadherin immunohistochemical expression and the sex of the patients was insignificant [22].

In our study, no significant correlation was detected between E-cadherin expression and the size of the tumors (p value = 0.4). Parallel to this finding, in a study conducted by Hu et al. [36] the abnormal expression rate of E-cadherin in bladder cancer tissues was not significantly correlated with tumor size (p value = 0.6). Thalita dosReis et al. [22] also did not detect any significant association between E-cadherin expression and the size of the tumors (p value = 0.3).

In this work, 24% of patients having high grade tumors showed loss of E-cad expression, while only 11% of patients having low grade tumors showed loss of expression of the marker, but the difference did not reach statistical significance. In the study conducted by Szekely et al. [34] they reported that there was no association between E-cadherin expression and tumor grade, age or gender of the patient. This is parallel to our results in these criteria. Similarly, Thalita dosReis et al. [22] detected insignificant relationship between E-cadherin expression and tumor grade.
Furthermore, Koksai et al. [37] also showed that abnormal E-cadherin expression had no association with the grade. Mialhe et al. [38] observed that E-cadherin expression was not correlated with the tumor grade, although it was highly correlated with the tumor stage. On the other hand, Hu et al. [36] reported that the abnormal expression rate of E-cadherin in bladder cancer tissues of the 72 cases included was significantly correlated with tumor pathological grade. Also, Iang et al. [39] detected that membranous E-cadherin expression was more decreased in tumors with high grade. This discordance may be much attributed to larger sample size used by these authors and different immunoreactivity cut-offs.

In our study, we found a significant correlation between decreased E-cadherin expression and high stages of urinary bladder carcinoma (P value < 0.009). In concordance to our results, Hu et al. [36] reported that the abnormal expression rate of E-cadherin in bladder cancer tissues was significantly correlated with tumor stage (P < 0.05).

Moreover, Clairotte et al. [39] observed a highly significant correlation between the decreased expression of E-cadherin and increased TNM stage (P value < 0.001). This is also keeping with the results of Koksai et al. [37] who reported that abnormal E-cadherin expression was associated with advanced tumor stage in their cases. This goes with the results of other studies by Byrne et al. [7] and Mialhe et al. [38] who observed that reduced expression of E-cadherin was associated with increased depth of invasion. On the other hand, Szekely et al. [34] reported no association between E-cadherin expression and tumor stage. This discordance can be explained as they conducted their study on urinary bladder carcinoma having lower pathological stages in TUR specimens.

In our present study, we detected a statistically significant correlation between decreased E-cadherin expression and positive lymph nodal metastasis (P value = 0.041). In the study done by Byrne et al. [7] they concluded that, in bladder cancer, altered E-cadherin expression was associated with lymph node metastasis (p value = 0.044). In addition, they demonstrated significant association between altered E-cadherin expression with the degree of invasiveness and increased risk of death from bladder cancer.

Also, in this study, a multivariate logistic regression analysis showed a significant correlation between loss of E-cad expression and lymph node metastasis (p value = 0.01). This means that application of E-cad immunohistochemical marker on small biopsy specimens (TUR-T) could be used as an independent predictor of lymph node metastasis in a safe, easy and relatively affordable method. This should be further proved in multicentric studies with larger series of patients.

Several publications proved that the loss of E-cadherin expression is associated with poor prognosis, high tumor grade and stage, while others did not detect these associations. These differences might be explained by the fact that the loss of E-cadherin expression is associated with disturbances at different levels (mRNA or protein), or with disturbances of the expression of the E-cadherin-associated catenins [40]. This might explain why our results were concordant with some studies and discordant with others.

In our results, a significant correlation was found between pelvic organ invasion (stage pT 4) and positive E-cad expression. Our explanation to this is that 90% of our cases having negative E-cad expression were in the category of stage pT 3b while only one case out of nine was in the category of stage pT 4. Other studies with larger sample size or with different scoring systems might be able to solve this problem.

The determination of prognosis in bladder cancer is currently based on staging methods that depend primarily on the pathological stage of a tumor which is highly subjective. That’s why we need to find more objective criteria for the determination of prognosis. Dysregulation in cell-cycle regulation markers is involved in the development and progression of bladder cancer. Individual alterations of these molecules are associated with the degree of aggressiveness of a given tumor and its impending outcome [41].

As far as we know, no other study noted the statistically significant correlation between E-cad immunohistochemical expression and the histological type of urinary bladder carcinoma (TCC versus SCC).

CONCLUSION

The use of E-cadherin in pathological specimens of urinary bladder carcinomas may have a prognostic value as it significantly correlated with each of the pathological stage of the tumors and the histological type of the tumors.

REFERENCES


