Usefulness of recurrence and progression nomograms in Mexican bladder cancer patients

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ABSTRACT

Background: Superficial bladder cancer prognosis factors have been a controversial topic and the subject matter of various medical articles over the years. Currently cystoscopy and urinary cytology are the gold standard for transitional cell carcinoma surveillance. However, cystoscopy is an expensive study, is uncomfortable for the patient and can be the cause of infection or trauma.

Materials and Methods: A retroactive review of case records of all patients presenting with superficial bladder cancer from January 1990 to January 2007 was carried out. Statistical analysis was calculated by measures of central tendency and dispersion: range, mean, median, mode, standard deviation, proportion or percentage.

Results: Seventy patients diagnosed with superficial bladder cancer were analyzed. Sixty of them, 44 men (73%) and 16 women (26.6%), met the inclusion criteria and ranged in age from 19 to 91 years (mean age 59.2 years).

Highest recurrence at one year presented in the intermediate risk group (77.7%) with a score of 5-9 points. Disease progression for the high risk group was 85.7%, presenting at 2 to 14 months. After 14

RESUMEN

Introducción: Los factores pronóstico en pacientes con cáncer superficial de vejiga han sido un tema de controversia y motivo de varias publicaciones a lo largo de los años. Actualmente, la cistoscopia y las citologías urinarias representan el gold standard para la vigilancia del carcinoma de células transicionales. Sin embargo, la cistoscopia representa un estudio de alto costo, molestias para el enfermo y la posibilidad de complicaciones tales como infección o trauma.

Material y métodos: Revisamos los expedientes de todos los pacientes con cáncer superficial de vejiga de entre enero de 1990 a enero de 2007. El análisis estadístico se realizó con medidas de tendencia central y de dispersión: rango, media, mediana, moda, desviación estándar, proporciones o porcentaje.

Resultados: Se analizaron 70 pacientes con diagnóstico de cáncer superficial de vejiga, de los cuales 60 cumplieron con criterios de inclusión: 44 (73%) hombres y 16 (26.6%) mujeres, con rangos de edad de entre 19 a 91 años, media de 59.2.

La mayor recurrencia al año se presentó en pacientes con grupo de riesgo intermedio (77.7%), con puntuación de 5-9 (66.6%). A 5 años recurrieron los pacientes de riesgo...
months there was no recurrence. The most important recurrence factors were tumor size and number.

**Conclusions:** Nomograms for predicting recurrence and progression are useful tools in the Mexican population, though they should be used merely as guides. It is necessary to evaluate a larger number of patients and a longer follow-up.

**Key words:** Nomograms, urothelium, recurrence, progression.

**INTRODUCTION**

Prognostic factors in patients presenting with superficial bladder cancer have been a controversial topic and the subject matter of various publications over the years. According to tumor characteristics after transurethral resection, 70% of patients present with superficial tumors (Ta, T1) at the time of diagnosis with a recurrence from 15-70% at one year and a 7-40% progression at five years (1,2).

Although factors relating to prognosis have been extensively analyzed over the years, there is a great difference in the variables studied, each of which is important and has a correlation with other factors (3).

Today cystoscopy and urinary cytology represent the gold standard for transitional cell carcinoma surveillance. However, cystoscopy is expensive, unpleasant for the patient and can be the possible cause of complications such as infection or trauma. Cystoscopy is complemented with urinary cytology that has a high sensitivity for high grade tumors but the disadvantage of low sensitivity for low grade tumors (1,4).

Patients are generally divided into groups of good, intermediate and poor prognosis, especially after transurethral resection of the bladder (TURB), and treatment is decided accordingly. Establishing recurrence and progression risk preoperatively in patients presenting with superficial tumors is somewhat difficult since risk is established for both factors using the same parameters even though these two factors are completely different (5, 7).

To avoid this situation, the use of nomograms that divide and calculate the probability of a certain event in a determined period of time has been suggested. For example, homogeneous parameters, rather than simply the experience of each surgeon, are used to determine which patients will present with recurrence or progression. Although tumor markers have currently been used to predict recurrence by establishing risk, they are not routinely used in clinical practice.

In a study involving 2596 patients, the European Organization for Research on Treatment of Cancer (EORTC) published criteria for dividing patients into risk groups by which it is possible to predict recurrence and progression in 1 and 5 years. This helps the urologist choose the most adequate adjuvant treatment whether it be intravesical therapy or early cystectomy and in some cases reduce the frequency of follow-up studies. Presently there are no studies in the Mexican medical literature that evaluate the usefulness of these nomograms in our population. Because of significant differences between Mexican and Anglo populations we consider it important to determine if these nomograms are a useful tool in the evaluation of the Mexican patient (2, 3, 5).

The objective of the present study is to analyze the usefulness of recurrence and progression EORTC nomograms in the Mexican population.

**MATERIALS AND METHODS**

Case records of all patients diagnosed with superficial urothelial carcinoma (Ta, T1) attended to at the urology service of the second level General Hospital Dr. Manuel Gea González in Mexico City from January 1, 1990 to January 1, 2007 were retroactively...
reviewed. Inclusion criteria were both sexes, any age, superficial urothelial cancer of the bladder diagnosis confirmed by histopathology study and complete case record. Exclusion criterion was incomplete case record. Recurrence and progression scores were calculated by analyzing tumor number, tumor diameter, previous recurrence, T grade, associated in situ carcinoma and tumor grade. One and five year recurrence and progression risk groups were formed with the above-mentioned variables using EORTC bladder cancer nomograms. Measures of central tendency and dispersion including range, mean, median, mode, standard deviation, proportion and percentage were employed for statistical analysis.

RESULTS

Seventy patients diagnosed with superficial bladder cancer were analyzed, sixty of whom met the required inclusion criteria. There were 44 men (73%) and 16 women (26.6%) with an age range from 19-91 years and mean age of 59.2 years. In the one year recurrence risk group, 6 patients (10%) were low risk, 46 (76.6%) were intermediate risk and 8 (13.3%) were high risk. Six patients registered scores of 0 points, 16 patients scores of 1-4 points, 30 patients scores of 5-9 points and 8 patients scores of 10-17 points. At one year there were 18 recurrence cases (28.3%). In relation to risk group 1 case was low risk (5.5%), 14 were intermediate risk (77.7%) and 3 were high risk (16.6%). At five years there were 8 recurrence cases (13.3%). In score analysis there were no cases of 0 points, one case of 1-4 points (12.5%), six cases of 5-9 points (75%) and one case of 10-17 points (12.5%). In relation to tumor progression there were 6 cases (10%) between 2 and 14 months. There were no cases of progression after 14 months.

DISCUSSION

According to our results the most important recurrence data were tumor size and number, which is consistent with that reported in the international literature. The present study differed from published reports in relation to recurrence in patients having presented with previous recurrence. In our study there was no difference in this category.

Progression was influenced by tumor number and there were no differences in the other variables analyzed. In relation to risk groups the largest number of recurrences presented in intermediate risk group patients, probably due to the fact that this group had the largest number of individuals. This was also the case in patients with a score of 5-9 points. The same phenomenon was observed in 5 year recurrence in up to 75% of intermediate risk patients with a 5-9 point score.

Progression presented between 2 and 14 months especially in high risk patients and a 14-23 point score, which was also probably due to the number of patients in those groups. These results are also consistent with those reported in the international literature (2,3).

These same findings have also been reported in different studies and so are considered to be important recurrence and progression factors in urothelial cancer. By separating recurrence and risk factors it is possible to decide between intravesical treatment or early cystectomy, especially in both high risk progression and recurrence patients in whom disease would advance despite intravesical treatment. Prognosis for patients presenting with T1G3 tumors has been a theme written about in various publications and many authors suggest that management of these patients should be individualized since progression risk is dependent on patient characteristics. This is especially true in relation to in situ carcinoma which, though not an independent progression factor in our study, is reported to have a 29-74% probability at one year. Early cystectomy should be seriously considered for these patients (8-11).

In several publications prognosis has been differentiated according to the degree of superficial tumor invasion, especially in the presence or absence of invasion of the muscularis mucosa or beyond (12). This aspect was not analyzed in the present study but could be evaluated in future studies along with bladder neck or trigone invasion. Other useful tools are molecular markers such as NMP22 which when added to urinary cytology can predict recurrence up to 84% as well as establish tumor biological aggressiveness up to 86.9%. However, this option is expensive and so is not available in many of our institutions (2,9,13).

One of the principal applications of our study is in patients with low recurrence and progression scores in whom cystoscopic surveillance could be carried out in more prolonged intervals as long as the patient is well-informed about and in agreement with this approach (2).

Although these nomograms have their limitations, we consider them to be an important instrument for suggesting how the pathology will behave and we feel they should be used as a guide in follow-up of patients presenting with superficial bladder tumor. They also aid in deciding which patients would benefit from early cystectomy. The data obtained in the present study show nomograms to be a useful tool that should be used as a guide in individualized management and follow-up of urothelial cancer cases. We also believe studies involving a greater number of patients and longer follow-up period will show more solid results for its use.
CONCLUSIONS

Nomogram use for predicting disease recurrence and progression is a useful tool for evaluating patients presenting with superficial bladder cancer, acting as a functional therapeutic and follow-up guide. Nomograms should be used only as guides and not as absolute treatment indications. It is important to analyze each case individually in order to employ the most adequate adjuvant treatment and follow-up. As is reported in the international literature, the most important factors to be evaluated are tumor size and number. It is also necessary to evaluate the degree of invasion into the muscularis mucosa in superficial tumors as well as into the bladder neck and trigone.

Molecular markers are important elements that can play a vital role in future treatment of this disease but their high economic cost makes them virtually unavailable to patients in our environment. Further studies involving a larger number of cases and a longer follow-up period are necessary to adequately evaluate the application of nomograms and their usefulness in the Mexican population.

BIBLIOGRAPHY