Real-World Study of High-Risk Non-Muscle Invasive Bladder Cancer in Mexico: Clinical Profile and Staging Patterns

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Background and rationale

Every year, approximately 74,000 individuals are diagnosed with bladder cancer in the United States, while over 430,000 patients are diagnosed globally. It ranks as the fourth most frequently diagnosed cancer in men and is the eighth leading cause of cancer-related deaths within this demographic. Men are at a 3 to 4 times greater risk of developing urothelial bladder carcinoma over their lifetime compared to women. Although bladder cancer is more prevalent among men, women tend to have a worse prognosis.

Upon diagnosis, roughly 75% of patients present with NMIBC, while 25% have MIBC or metastatic disease.

Several well-established factors are known to contribute to the high recurrence rates of this disease. Adjuvant treatments, particularly with intravesical Mycobacterium Bovis Bacillus Calmette- Guérin (BCG), have demonstrated a reduction in recurrence rates.

In Mexico, there is a significant lack of local data regarding epidemiology, patient pathways, multidisciplinary treatment approaches, and the clinical progression of high-risk NMIBC. Given the ongoing shortage of BCG, it is presumed that numerous hospitals have had to adjust their treatment methods, though the repercussions of these changes remain uncertain. This study aims to enhance the understanding of the epidemiology of high-risk NMIBC in our country and the treatment patterns in real-world contexts.

Objectives

- To describe histopathological characteristics and clinical patterns of high risk NMIBC patients from 3 reference centers
- To describe the patient journey of high-risk NMIBC from initial symptoms to diagnosis and treatment (Time to diagnosis, Time to treatment
- To describe treatment patterns for high-risk NMIBC, including surgical approaches (TURBT, radical/partial cystectomy) and intravesical treatment.

Methodology

This was a descriptive study that analyzes data from a database retrospectively. The research was carried out exclusively utilizing structured secondary data in a retrospective manner. This study included all patients diagnosed with high-risk non-muscle invasive bladder cancer (NMIBC) from the electronic databases of three participating hospitals, covering the period from January 1, 2010, to December 31, 2020.

Inclusion Criteria included patients with a pathological diagnosis of high-risk NMIBC (defined as carcinoma in situ (CIS), Tis, T1, tumors greater than 3 cm, or multifocality) found in the database, tumors with predominant urothelial histology (>50%), and those diagnosed within the specified time frame.

Exclusion Criteria consisted of patients with less than six months of follow-up, concurrent diagnoses of other malignancies (except non-melanoma skin cancer and certain non-invasive carcinomas), those participating in clinical trials for NMIBC treatment, individuals previously treated for bladder cancer, and those with small cell or neuroendocrine histologies.

Results

A total of 221 patient records meeting the inclusion criteria were collected and included in the analysis. The 62.4% of the cases were provided by the National Cancer Institute (INCAN), 24% by the Military Hospital (HOMIL), and 13.6% by the National Institute of Medical Sciences and Nutrition "Salvador Zubirán" (INCMNSZ, by its acronym in Spanish, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán).

The overall male-to-female ratio was 3:1, with the highest proportion observed at INCAN (3:1), followed by HOMIL (2.4:1) and INCMNSZ (2:1). Regarding tobacco use, the overall ratio was 1.4:1 in favor of smokers.

The average age of the included patients was 65 years (±15.64, interquartile range Most able at INCAN (64.8 years) and HOMIL (65.6 years) but higher at INCMNSZ (70.1 years).

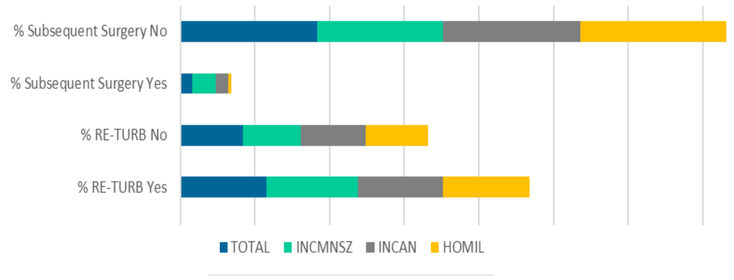
Most cases were low-grade carcinoma (84.62%), closely aligning with the proportion observed at INCMNSZ (86.6%). This predominance was nearly absolute among INCAN patients, with only 1 out of 137 cases (0.7%) classified as high-grade tumors. In contrast, at HOMIL, this relationship was reversed, with low-grade tumors slightly outnumbered by high-grade ones, showing a 1.2:1 ratio.

Table 1. Distribution of histological variants globally and by hospital center.

	INCMNSZ			INCAN			HOMIL			Total	
Histological variant	n	% center	% total	n	% center	% total	n	% center	% total	n	% total
Squamous	0	0%	0%	8	5.70 %	3.50 %	0	0%	0%	8	3.60 %
Glandular	0	0%	0%	5	3.60 %	2.20 %	0	0%	0%	5	2.20 %
Papillary	27	87.10 %	12%	4	2.80 %	1.80 %	46	86.70 %	20.60 %	77	34.80 %
Ring cell	0	0%	0%	4	2.80 %	1.80 %	0	0%	0%	4	1.80 %
Sarcomatoid	0	0%	0%	1	0.70 %	0.40 %	0	0%	0%	1	0.40 %
Epidermoid	0	0%	0%	1	0.70 %	0.40 %	0	0%	0%	1	0.40 %
Plasmacytoid	0	0%	0%	2	1.40 %	0.90 %	0	0%	0%	2	0.90 %
Giant-cell	0	0%	0%	1	0.70 %	0.40 %	0	0%	0%	1	0.40 %
Not specified	4	12.90 %	1.80 %	116	83.50 %	52.20 %	7	13.20 %	3.10 %	125	56%
Simultaneous	0	0%	0%	4	2.80 %	1.70 %	0	0%	0%	4	1.80 %

Time-to-diagnosis, defined as the number of days between the onset of symptoms and the histopathological result, had an average of 314 days (+/- 490.5, IQR 255 days, CV 1.6). The shortest time was recorded at INCMNSZ (zero days), while the longest delay was observed at INCAN, with an average of 389.3 days (+/- 588.2, IQR 276 days, CV 1.5), and a maximum of 4041 days (11 years). The average time to diagnosis at HOMIL deviated the most from the global mean, showing a 150-day advantage with less delay (165.6 days, IQR 109 days, CV 0.9), and a minimum value of 31 days.

According to Graph 1, slightly more than half of the population (58%) required a second transurethral intervention, with all the institutions showing a similar pattern (57%, 58% and 61% for INCAN, HOMIL and INCMNSZ, respectively). Only 8% underwent an additional surgical procedure, a figure in line with the average for patients under similar conditions at INCAN. By comparison, INCMNSZ performed the highest number of subsequent surgeries (16%) whereas HOMIL the lowest (2%).



Graph 1. Distribution of patients undergoing second look and subsequent surgical procedure, globally and by hospital center.

Of the 126 patients without a specified histological type, 60% received some form of adjuvant treatment. Among them, only three underwent mitomycin induction, with just one completing the full regimen. The remaining patients received BCG, achieving an 88% completion rate. Additionally, two patients received both therapies. Maintenance treatment was administered to 59 patients in this group (47%), all of whom received BCG. Of these, 78% completed the full course. Among patients with papillary carcinoma, 85% received adjuvant therapy.

Conclusions

This study examined 221 patient records from various hospital centers, uncovering a greater occurrence of T1 stage diagnoses and a majority of low-grade carcinomas. Notable differences were noted in patient demographics, smoking history, and timelines for treatment, with the majority of interventions consisting of transurethral resection of the bladder (TURB) and adjuvant therapies such as BCG. The results emphasize inconsistencies in clinical and treatment practices, indicating potential areas for enhancing the standardization of patient care.

References

1. (Barragán-Carrillo R, 2021; Deng S, 2022
2. (Kamat AM, 2016; Beijert IJ, 2022; Sun JX, 2022; Pan S, 2022)

Disclosure

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