



Asociación Urológica de  
Centroamérica y el Caribe

## Manejo del Cáncer de Vejiga sin Invasión Muscular de Alto Riesgo.

### *Management of High Risk Non-Muscle Invasive Bladder Cancer.*

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#### RESUMEN

El cáncer de vejiga no músculo invasivo es una neoplasia maligna común. Entre todos los pacientes diagnosticados con cáncer de vejiga, el 75 % se presenta como no invasivo y el 70 % recurre después de la resección transuretral del tumor vesical (TURBT), generalmente dentro de los 3 años.<sup>1</sup> Desafortunadamente, el 15-20 % progresa a enfermedad muscular invasiva. La progresión es más probable entre los pacientes con factores de riesgo significativos: mayor estadio, grado, mayor tamaño, antecedentes de recurrencia previa y multiplicidad y presencia de carcinoma in situ. Estos factores de riesgo forman la base de las categorías de riesgo de las guías de la American Urological Association, por las cuales se recomienda toda la vigilancia, el diagnóstico y el tratamiento.<sup>2</sup>

#### PALABRAS CLAVE

Importancia de la re-resección; *Uso juicioso de biomarcadores*; BCG es la primera línea.

#### ABSTRACT

Non-muscle invasive bladder cancer is a common malignancy. Among all patients diagnosed with bladder cancer, 75% present as non-invasive and 70% recur after transurethral resection of bladder tumor (TURBT), usually within 3 years.<sup>1</sup> Unfortunately, 15-20% progress to muscle invasive disease. Progression is more likely among patients with significant risk factors: higher stage, grade, increased size, history of prior recurrence and multiplicity and presence of carcinoma in situ. These risk factors form the basis for the American Urological Association guidelines risk categories, by which all surveillance, diagnosis and treatment are recommended.<sup>2</sup>

#### KEYWORDS

Importancia de la re-resección; *Uso juicioso de biomarcadores*; BCG es la primera línea.

Non-muscle invasive bladder cancer is a common malignancy. Among all patients diagnosed with bladder cancer, 75% present as non-invasive and 70% recur after transurethral resection of bladder tumor (TURBT), usually within 3 years.<sup>1</sup> Unfortunately, 15-20% progress to muscle invasive disease. Progression is more likely among patients

with significant risk factors: higher stage, grade, increased size, history of prior recurrence and multiplicity and presence of carcinoma in situ. These risk factors form the basis for the American Urological Association guidelines risk categories, by which all surveillance, diagnosis and treatment are recommended.<sup>2</sup>

Diagnosis of NMIBC begins with a high quality TURBT. TURBT should include a bimanual examination to rule out locally advanced disease. Additionally, directed biopsies may be warranted to detect carcinoma in situ of bladder neck or urethra. Directed biopsies are particularly useful when cytology is positive but the urologist cannot identify a lesion within the bladder. Once tissue is obtained, the pathologist should determine stage and grade, the latter of which should stratify between low or high grade according to the updated 1998 WHO/ISUP grading system. An additional consideration beyond stage and grade is histology. The majority (>90%) of tumors will be urothelial, but variant histology is possible. Non-invasive bladder cancer with variant histology should be considered high risk, and many are treated with upfront cystectomy or systemic therapy.<sup>3</sup>

In this article, I present 6 key points to consider when managing high risk non-muscle invasive bladder cancer.

1. *Importance of re-resection.* Among patients with HGT1 disease, re-resection should be performed within 6 weeks of initial resection. Re-resection is important to appropriately stage these patients, since upstaging can occur in up to 30%.<sup>4</sup> Re-resection can also further risk stratify patients. For example, if repeat resection confirms HGT1, the risk of progression is quite high, and the patient might be offered early cystectomy. Among patients with HGTa, re-resection can also be considered and is particularly useful for larger tumors for which a complete resection may not have been performed.

2. *Judicious use of biomarkers.* Unfortunately, biomarkers cannot yet replace cystoscopy. However, they can help in specific cases. For example, UroVysion® FISH might be useful to assess response to BCG, as the presence of a persistently positive UroVysion® FISH following completion of induction BCG predicts a higher likelihood of recurrence and progression. Another use of UroVision® FISH is to adjudicate equivocal cytology,<sup>5</sup> which can occur in up to 21% patients evaluated for hematuria.<sup>6</sup>

3. *BCG is first line.* Among patients with high risk NMIBC, a BCG induction course represents gold standard treatment.<sup>7</sup> Reasons for which BCG cannot be given are few, and could include intolerance. BCG intolerance is fortunately not common anymore due to advances in treatment of BCG-related side effects. Treatment of BCG intolerance may include dose reduction, use of anticholinergics, bladder emptying, and antibiotic prophylaxis.

4. *BCG maintenance for 3 years.* Two studies have confirmed the efficacy of BCG maintenance in preventing recurrence and progression. The SWOG 8507 study showed that maintenance BCG given as a weekly instillation for 3 weeks at months 3, 6, 12, 18, 24, 30, and 36 as compared to induction BCG alone increased the 5-year recurrence free survival from 41% to 60%.<sup>8</sup> EORTC 30962 showed that high risk patients benefited from full dose maintenance regimen for 3 years over maintenance for a single year.<sup>9</sup>

5. *Consider cystectomy for BCG refractory disease.* BCG refractory disease must be defined carefully. For patients with T1 disease, refractory disease is defined as persistent disease within 6 months after BCG. For patients with HGTA or CIS, refractory disease is defined as those who have failed two prior BCG courses or progression to T1. Patients with BCG refractory disease are at high risk for progression and subsequent metastasis, and therefore benefit from salvage cystectomy.<sup>10</sup>

6. *Risk-adjusted surveillance.* Surveillance for bladder cancer is dependent on risk classification. For patients with high risk NMIBC, surveillance must be careful and thorough. Patients should undergo cystoscopy with cytology every 3 months for 2 years, then every 6 months for the following 2 years and annually thereafter.<sup>11</sup> Upper tract surveillance imaging should be considered every 1-2 years to rule out urothelial involvement..

By understanding and adhering to risk-based classification, management of high risk NMIBC can result in excellent outcomes. Patients should be appropriately staged and treated with BCG induction with maintenance to provide the best recurrence free survival rates possible. Patients should be surveilled at pre-defined intervals, with judicious use of salvage cystectomy reserved for those patients for whom BCG fails.

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