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Original article

# Development of a predictive model for optimizing the selection of patients for second transurethral resection bladder

# Desarrollo de un modelo predictivo para optimizar la selección de pacientes para segunda resección transuretral vesical

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## Abstract

**Background:** Transurethral resection of bladder (TURB) is considered the gold standard treatment of non-muscle invasive bladder tumor (NMIBT). The urological clinical practice guidelines recommend second-TURB (re-TURB), in certain situations, to achieve a complete resection and appropriately stratify the tumor.

**Objective:** To design a predictive model of residual tumor in re-TURB, to optimize patient selection and avoid unnecessary surgeries.

**Methods:** Retrospective analysis of 413 NMIBT with a macroscopically complete TURB and identification of the muscle layer, with subsequent re-TURB (2-6 weeks), according to EAU Clinical Guidelines criteria, from January 2010 to December 2021.

We have identified predictive variables of residual tumor through univariate and multivariate analysis using logistic regression. The evaluation of the exactitude of the predictive model has been made using AUC (area under curve-ROC curve).

**Results:** Median age in the seçcond-TURB were mostly primary (64.6%), stage T1 (84.5%), high grade (82.6%), multifocal (54.8%) and with a size less than 3 cm (73.1%). Residual tumor was found in 28.1% of re-TURB. The independent predictors factors of residual tumor identified were: *recurrence tumor* (OR 1.87; IQ 1.14-3.06, p=0.01) and *multifocality tumors* (OR 2.11; IQ 1.31-3.4; p=0.002). *High-grade* shows a trend to statistical signification as risk factor (p=0.07) and *early administration of mitomycin-C* behaved as an independent protector factor (OR 0.40; IQ 0.3-0.81; p=0.006). The predictive model shows an AUC=0.7 (IQ 0.62-0.73; p=0.0001).

**Conclusion:** Our predictive model evaluates the probability of finding residual tumor in second-TURB with a 70% accuracy. This way, we could optimize the selection of patients in low risk of residual tumor, thus avoiding unnecessary surgeries.

**Keywords:**
Urinary bladder neoplasms, neoplasm recurrence, residual neoplasm, reoperation

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## Resumen

**Antecedentes:** La resección transuretral de vejiga (TURB) se considera el tratamiento estándar de oro del tumor vesical no músculo invasivo (TVNMI). Las guías de práctica clínica urológica recomiendan una segunda resección transuretral de vejiga (re-TURB) en determinadas situaciones para conseguir una resección completa y estratificar adecuadamente el tumor.
**Objetivo:** Diseñar un modelo predictivo de tumor residual en segunda resección transuretral de vejiga (re-TURB) para optimizar la selección de pacientes y evitar cirugías innecesarias.
**Métodos:** Análisis retrospectivo de 413 TVNMI con RTU macroscópicamente completa e identificación de la capa muscular, con posterior re-RTU (2-6 semanas), según criterios de las Guías Clínicas de la EAU, desde enero de 2010 hasta diciembre de 2021. Hemos identificado variables predictoras de tumor residual mediante análisis univariante y multivariante mediante regresión logística. La evaluación de la exactitud del modelo predictivo se ha realizado mediante AUC (area under curve-ROC curve).
**Resultados:** La mediana de edad de la serie fue de 74 años (38-91), siendo el 86.7% del sexo masculino. Los tumores que requirieron segunda RTU fueron en su mayoría primarios (64.6%), estadio T1 (84.5%), de alto grado (82.6%), multifocales (54.8%) y con un tamaño menor de 3 cm (73.1%). Se encontró tumor residual en el 28.1% de las resecciones transuretrales de vejiga (re-TURB). Los factores predictores independientes de tumor residual identificados fueron: recurrencia tumoral (OR 1.87; CI 1.14-3.06, p=0.01) y tumores multifocales (OR 2.11; CI 1.31-3.4; p=0.002). El grado alto muestra tendencia a la significación estadística como factor de riesgo (p=0.07) y la administración precoz de mitomicina-C se comporta como factor protector independiente (OR 0.40; CI 0.3-0.81; p=0.006). El modelo predictivo muestra un AUC=0.7 (IQ 0.62-0.73; p=0.0001).
**Conclusión:** Nuestro modelo predictivo evalúa la probabilidad de encontrar tumor residual en la segunda RTU con un 70% de precisión. De esta forma, podríamos optimizar la selección de pacientes con bajo riesgo de tumor residual, evitando así cirugías innecesarias.


**Palabras clave:**
Neoplasias de vejiga urinaria, recurrencia de neoplasia, neoplasia residual, reintervención

## Abbreviations

**TURB:** Transurethral resection of bladder
**NMIBT:** Non-muscle invasive bladder tumor (NMIBT)
**Re-TURB:** re-Transurethral resection of bladder / second TURB
**BC:** Bladder Cancer
**MMC:** mitomicyn-C
**AUC:** area under curve

## Introduction

Bladder cancer (BC) is the 10th most commonly diagnosed cancer worldwide, and the 7th if only male population is considered; with an incidence rate in Europe of 20 per 100,000 person/years for men and 2.6 for women.[1]

Approximately 80% of BC presents as non-muscle-invasive bladder tumors (NMIBT), tumors confined to the mucosa (Ta o CiS) or submucosa (T1). Transurethral resection of bladder (TURB) is considered the gold standard treatment of NMIBT, which can be followed by adjuvant intravesical treatment depending on the risk stratification.[1]

According to the literature, residual tumor is found in almost 60% of Ta and T1 stage, so the re-TURB is nowadays a fundamental step to achieve a complete resection and appropriately stratify the tumor.[2,3] Up to 2016, the European Association of Urology (EAU) Guidelines recommended to carry out a second TURB in patients with: first incomplete TURB, absence of muscular layer in the specimen after initial resection, and in cases of high grade or T1 NMIBT. However, since 2017, high grade indication has been removed from the EAU Guidelines.[1] The American Urological Association guidelines, on the other hand, do recommend considering performing a second resection in high-grade Ta tumors.[4]

The re-TURB implies and additional expense for the health system, and as an invasive procedure it is not free of complications: from pain, retention or hematuria to bladder perforation or urinary sepsis; and other long-term complications, such as urethral strictures.[5]

The objective of this study is to design a predictive model of residual tumor in re-TURB, to optimize patient selection and avoid unnecessary surgeries.

## Material and methods

We performed a retrospective analysis of 413 patients with NMIBT, diagnosed in our center between January 2010 and December 2021, and treated with a macroscopically complete initial TURB and identification of muscular layer in the pathological specimen. Treatment was completed by a second TURB performed at 2 to 6 weeks, according to current criteria of the EAU Guidelines. All surgeries were performed using a bipolar resector.

The pathological analysis was carried out by two reference pathologists from our center. Tumor staging was carried out following the 7th edition of the TNM classification, and histological grade was classified according to the 2004/2016 WHO classification system.[1,6]

A single intravesical instillation of mitomycin-C (MMC) was administered in the first 24 hours after the first TURB in some patients following the EAU and EORCT recommendations: in primary tumors or intermediate-risk recurrent tumors with a prior recurrence rate of less than or equal to one recurrence per year

and those with a 2006 EORTC recurrence score <5.[1,7]

Early complications (in the first 30 days) were classified according to the Clavien-Dindo classification.[5]

We have identified predictive variables of residual tumor by means of univariant and multivariant analysis using logistic regression. Statistical significance has been considered with p value <0.05. The evaluation of the exactitude of the predictive model has been made using AUC (area under curve). All statistical analysis have been made using statistical program IBM® SPSS® statistics v-25.

## Results

The baseline characteristics of the patients at the initial and the second TURB are detailed in Table 1.

**Table 1: Baseline characteristics of the patients**

| *Variable* | *n=413* |
|---|---|
| **Gender** | |
| Male | 358 (86.7%) |
| Female | 55 (13.3%) |
| **Stage** | |
| Ta | 64 (15.5%) |
| T1 | 349 (84.5%) |
| **Histological grade** | |
| Low grade | 72 (17.4%) |
| High grade | 341 (82.6%) |
| **Recurrence** | |
| Primary | 267 (64.6%) |
| Recurrent | 146 (35.3%) |
| **Number of lesions** | |
| Single | 187 (45.3%) |
| 2-7 | 189 (45.8%) |
| 8 or more | 37 (9%) |
| **Size** | |
| < 3cm | 302 (73%) |
| >/= 3cm | 111 (26.9%) |
| **Early instillation MMC** | |
| Yes | 161 (39%) |
| No | 252 (413%) |
| **Complications** | |
| Anemizing hematuria | 17 (4.1%) |
| ITU | 7 (1.7%) |
| Bladder perforation | 3 (0.7%) |

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| | |
|---|---|
| **Tumor detection rate after second TURB (initial Ta+T1)** | |
| No residual tumor | 297 (71.9%) |
| Ta | 51 (12.3%) |
| T1 | 42 (10.2%) |
| CiS | 14 (4.3%) |
| T2 | 9 (2.2%) |
| **Tumor detection rate after second TURB in inital Ta Stage** | |
| No residual tumor | 48 (75%) |
| Ta | 9 (14.1%) |
| T1 | 2 (3.1%) |
| CiS | 5 (7.8%) |
| **Tumor detection after second TURB in intial T1 stage** | |
| No residual tumor | 249 (71.3%) |
| Ta | 42 (12%) |
| T1 | 40 (11.5%) |
| CiS | 9 (2.6%) |
| T2 | 9 (2.6%) |
| **Histological grade after second TURB** | |
| Low grade | 46 (39.7%) |
| High grade | 70 (60.3%) |

The median age in the series was 74 (38-91) years old, and 86.7% (n=358) patients were male.

Tumors that required second TURB were mostly primary (64.6%), stage T1 (84.5%), high grade (82.6%), multifocal (54.8%) and with a size less than 3 cm (73.1%).

37 patients (6.5%) had early complications: 17(4.1%) hematuria, 7(1.7%) urinary tract infections, and 3 (0.7%) bladder perforation. All complications were managed conservatively (Clavien-Dindo <IIIb).

After analyzing pathological results, residual tumor was found in 28.1% of second TURB (n=116) and T2 tumor was re-stratified in 2.2% (n=9) cases (none of them with initial pathological anatomy T1). Considering the initial T stage, residual tumor was found in 25% (n=16) of the Ta patients: 56.25% (n=9) residual Ta tumor, 31.25% (n=5) residual Cis and 12.5% (n=2) residual T1. On the other hand, residual tumor was found in 28.7% (n=100) of the initial T1 patients: 42% (n=42) residual Ta, 40% (n=40) residual T1, 9% (n=9) Cis and other 9% (n=9) T2.

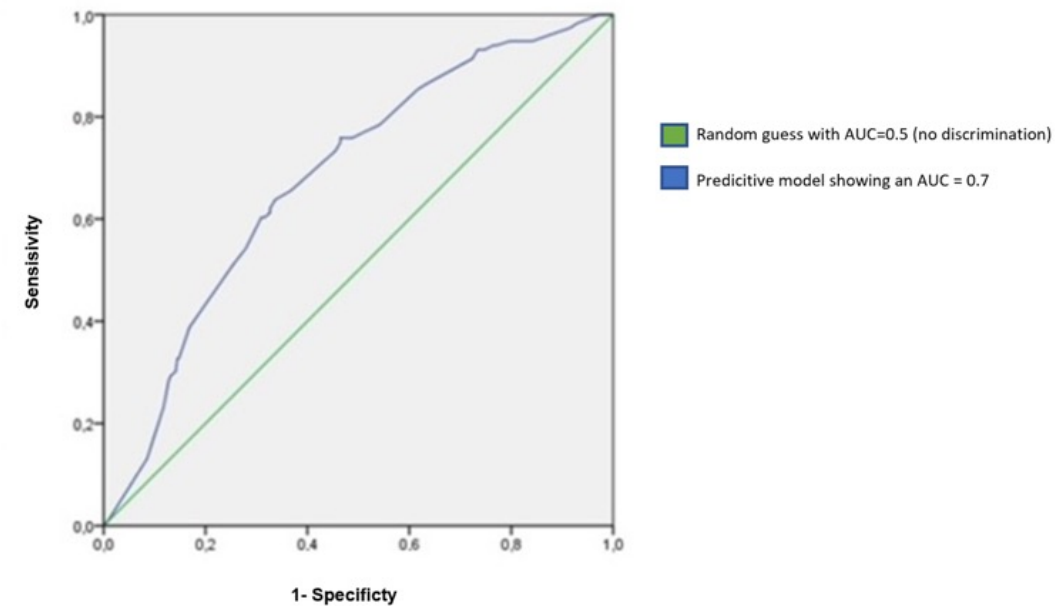
After final multivariant analysis we identified independent predictive factors of residual tumors (Table 2): recurrence tumor (OR 1.87; IQ 1.14-3.06, p=0.01) and multifocality tumors (OR 2.11; IQ 1.31-3.4; p=0.002), thus doubling the risk of residual tumor in re-TURB. High-grade shows a trend to statistical signification as risk factor (p=0.07) and early administration of mitomycin-C behaved as an independent protector factor (OR 0.40; IQ 0.3-0.81; p=0.006).

**Table 2: Multivariate risk factors for residual disease at the time of second TURB**

| *Variable* | *OR* | *IC95%* | *P* |
|---|---|---|---|
| **Primary tumor<br>Ta<br>T1** | 1.26 | 0.65-2.46 | 0.49 |
| **Grade<br>Low<br>High** | 1.84 | 0.95-3.56 | 0.07 |
| **Recurrence<br>Primary<br>Recurrent** | 1.87 | 1.14-3.06 | 0.01 |
| **Multifocality** | 2.11 | 1.31-3.40 | 0.02 |
| **Size<br><3cm<br>>3cm** | 1.49 | 0.88-2.52 | 0.13 |
| **Early MMC instillation<br>Yes<br>No** | 0.49 | 0.30-0.81 | 0.006 |

The predictive model shows an AUC=0.7 (IQ 0.62-0.73; p=0.0001) (Figure 1).

**Figure 1. Predictive model shows an AUC=0.7(IQ 0.62-0.73; p=0.0001) Curve ROC**



The formula that has generated our logistic regression model is:

$$P(Y=1)=\frac{1}{1+\exp(-\alpha-\beta 1X1-\beta 2X2-\beta 3X3-\cdots-\beta kXk)}$$

- **Y** is the dependent variable (tumor in second TURB= yes).
- **X1, X2, X3, ...,Xk** are the independent variables identified.
- $\alpha, \beta 1, \beta 2, \beta 3, \ldots, \beta k$ are the parameters of the model (Coefficient B in the logistic regression).
- **exp** is the simplified exponential function. It corresponds to raising the number e to the power contained within the parentheses. The number e is Euler's constant base of natural logarithms whose value in thousandths is 2.718.
- In our case the variables of the equation are in column B of the logistic regression (Table 3).

**Table 3. Variables in the equation**

| | B | E.T. | Wald | gl | Sig | OR | CI (95%) |
|---|---|---|---|---|---|---|---|
| Primary tumor Stage (T1) | **0.235** | 0.339 | 0.480 | 1 | 0.488 | **0.126** | **0.65-2.46** |
| Primary tumor grade (HG) | **0.610** | 0.337 | 3.226 | 1 | 0.071 | **1.84** | **0.95-3.56** |
| Recurrence (yes) | **0.625** | 0.251 | 6.176 | 1 | 0.013 | **1.87** | **1.14-3.06** |
| Multifocality (yes) | **0.748** | 0.243 | 9.459 | 1 | 0.002 | **2.11** | **1.31-3.4** |
| Size (>3cm) | **0.402** | 0.267 | 2.266 | 1 | 0.132 | **1.49** | **0.88-2.52** |
| Early MMC instillation (yes) | **0.706** | 0.255 | 7.657 | 1 | 0.006 | **0.49** | **0.03-0.81** |

Logit (p) = -4.825 + 0.235x (primary=T1a) + 0.610x (high grader=yes) + 0.625x(recurrence=si) + -0.748x(multifocality=si) + 0,402x (size> 3,4) + -0.706(MMC=yes)
Probability of the tumor in the second TURB = Yes= 1/1 + e- logit(p)

## Discussion

The objective of our study was the design of a predictive model of residual tumor, for optimizing the selection of patients who will receive a second TURB.

Residual tumor detection rates in the re-TURB was 28.6%, consistent with data described in the literature (ranging between 20%-60% of Ta and T1 tumors).[2,3] The largest reviews on this topic were carried out by Cumberbatch *et al.* and Naselli *et al.* In the first one, Cumberbatch *et al.*[2] carried out a systematic review including 31 publications analyzing re-TURBs in Ta and T1 tumors, but contrary to our study, including patients without presence of muscular tissue in the first surgery sample. They found residual tumor between 20-65% of cases, with detection rates four

times higher in T1 tumors than in Ta. Our low residual tumor rate may be because incomplete resections were not included in the analysis. In the meta-analysis carried out by Naselli *et al.*[3] they only analyzed T1 tumors and found that in the subgroup of patients with presence of muscle in the first TURB, residual tumor was detected in 47%, slightly higher than in our subgroup of similar characteristics (29.7%).

In addition, several studies have shown that there is a significant risk of upstaging after the first TURB in T1 disease, with upstaging to T2 on second TURB of up to 10%.[8,9] In our study, upstaging to T2 was detected in 9 patients from the initial T1 subgroup (2.6% from the 349 T1 patients), so re-TURB was essential for the correct stratification and posterior treatment of these patients.

Similar results have been obtained in studies carried out in Latin America. In the study carried out by Chamlati-Cuello *et al*., analyzing the results of re-TURB in a population that included patients in stages Ta and T1, they obtained a residual tumor rate of 39% of the cases, and restaging to muscle-invasive in 2.3% of cases.[10]

Despite the high rates of recurrence, the findings during re-TURB on few occasions are clearly suspicious of tumor persistence or recurrence the most frequent finding is to objectify the scar of the previous resection or sfascellus, and in less than 5% a clear tumor lesion.[11]

Residual tumor detection rates and staging are associated with the quality of the initial TURB and the characteristics of the tumor.[12] A TURB is considered of good quality when the resection is complete and including detrusor muscle, and the risk of detecting residual tumor can reach up to 75% if the resection was not optimal.[12,13] Although in our study only patients with apparent complete resection and muscular detected in the sample of the first TURB were included, the resection was considered complete at the discretion of the surgeon, so this is another subjective factor depending of the staff performing the surgery.

Regarding tumour characteristics, in our series there was a higher rate of residual tumor detection in recurrent and multifocal tumors. High-grade tumors showed a trend towards statistical significance (p=0.07), although probably with a larger sample the result would be statistically significant. Both multifocal and high-grade are factors widely described in the literature as predictors of residual tumor detection.[3,13] However, contrary to our results, recurrence does not seem to correlate as clearly with the rate of residual tumor detection in these and other similar studies.[3,14]

We also differ from similar studies in size tumor, which is a which stablished predicting factor.[13,15] In our analysis residual tumor rates were higher in ≥3cm tumors (OR 1.49), but it was not significant (p=0.13). This could be due to the size of our serie, but it could also be because the size of the tumor is subjectively indicated by the surgeon during surgery.

There is little evidence on the effect of MMC on the results of the second TURB. In our study, patients who received early and single instillation with mitomycin had a lower detection rate in the re-TURB (OR 0.40; p=0.006). It has been shown that early instillations with mitomycin reduce the risk of early recurrence in intermediate-risk tumors, so by acting on residual tumor cells, it could reduce this rate. Divrik *et al.*[16] compared the progression rates in two groups: one in which re-TURB and adjuvant mitomycin therapy was performed, and another in which only mitomycin was admi-

nistered: progression rates were significantly lower in the first subgroup, suggesting that intravesical chemotherapy with mitomycin does not compensate for inadequate resection.

It is important to consider that MMC was administered according to the EORCT recommendations, according to the intrinsic characteristics of the tumor, in lesions with a lower risk of, so the lower residual tumor detection rate in our series may be due to tumor characteristics rather than mitomycin itself.

The second TURB therefore allows for further staging, thus helping to reduce recurrences and progression rates.[2,9] However, some studies doubt the usefulness of re-TURB, affirming there is no the long-term benefits in terms of recurrence-free survival and progression-free survival, as they have not found differences in survival between high-grade T1 tumors treated with re-TURB plus BCG and those treated directly with BCG if muscle was present in the first intervention.[17] Similar results were reported by Gontero *et a.l*, which only found advantages if muscle was not present in the original sample.[14] In addition, it must considered that it is an invasive procedure, which requires general anesthesia, and is not free of complications, which entails a significant expense for the health system.[5]

In conclusion, it is necessary to adequately select the patients who can benefit the most from a second intervention based on the main predictive factors of residual tumor detection. Our predictive model shows a significant area under the curve of 0.7, thus showing an acceptable discrimination capacity, and could help select these patients.

Regarding to the limitations, this study is based on a retrospective design, which obviously makes it less reliable than randomized clinical trial (RCT). This is a single-institutional study, the surgeries were carried out over a prolonged period of time by multiple surgeons and the indication for early instillation of MMC was based on current scientific recommendations, but perhaps there is an added subjective criterion in your indication. Furthermore, the surgeon experience level can affect outcomes, and this was not documented in all cases. In addition, some prognostic pathological features are not uniformly reported, as for linfovascular invasion, sarcomatoid differentiation, nested tumors, etc. It is necessary to carry out multicentre, prospective, randomized studies assessing all factors to achieve strong conclusions.

## Conclusion

In our study, recurrence and multifocality tumors are independent predictive factors for residual tumor in a second TURB, while high-grade shows a trend to statistical signification as risk factor and early administration of mitomycin-C behaved as an independent protector factor (probably be due to tumor characteristics rather than mitomycin itself).

Our predictive model evaluates the probability of finding residual tumor in re-TURB with a 70% accuracy. This way, we could optimize the selection of patients in low risk of residual tumor, thus avoiding unnecessary second surgery

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The authors declare no conflicts of interest.

## References

1. **Rouprêt M, Babjuk M, Böhle A, Burger M, Compérat E, Cowan N, et al.** Upper Urinary Tract Urothelial Carcinoma. Non-muscle-invasive Bladder Cancer (TaT1 and CIS). Guidelines. 2021 Apr 1. [accessed 21 Feb 2023] Available from: https://bladder.uroonco.uroweb.org/guideline/upper-urinary-tract-urothelial-cell-carcinoma/
2. **Cumberbatch MGK, Foerster B, Catto JWF, Kamat AM, Kassouf W, Jubber I, et al.** Repeat Transurethral Resection in Non-muscle-invasive Bladder Cancer: A Systematic Review. Eur Urol. 2018 Jun;73(6):925–33. doi: 10.1016/j.eururo.2018.02.014
3. **Naselli A, Hurle R, Paparella S, Buffi NM, Lughezzani G, Lista G, et al.** Role of Restaging Transurethral Resection for T1 Non-muscle invasive Bladder Cancer: A Systematic Review and Meta-analysis. Eur Urol Focus. 2018 Jul;4(4):558–67. doi: 10.1016/j.euf.2016.12.011
4. **Chang SS, Boorjian SA, Chou R, Clark PE, Daneshmand S, Konety BR, et al.** Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline. J Urol. 2016 Oct;196(4):1021–9. doi: 10.1016/j.juro.2016.06.049
5. **Bansal A, Sankhwar S, Goel A, Kumar M, Purkait B, Aeron R.** Grading of complications of transurethral resection of bladder tumor using Clavien-Dindo classification system. Indian J Urol. 2016;32(3):232–7. doi: 10.4103/0970-1591.185104
6. **Brierley JD, Gospodarowicz MK, Wittekind C, editors.** TNM Classification of Malignant Tumours, 8th edition | UICC. 8th ed. Ginebra: Union for International Cancer Control/ Wiley Publications; 2016. [accessed 21 Feb 2023] Available from: https://www.uicc.org/resources/tnm-classification-malignant-tumours-8th-edition
7. **Sylvester RJ, van der Meijden APM, Oosterlinck W, Witjes JA, Bouffioux C, Denis L, et al.** Predicting recurrence and progression in individual patients with stage Ta T1 bladder cancer using EORTC risk tables: a combined analysis of 2596 patients from seven EORTC trials. Eur Urol. 2006 Mar;49(3):466–465; discussion 475-477. doi: 10.1016/j.eururo.2005.12.031
8. **Gendy R, Delprado W, Brenner P, Brooks A, Coombes G, Cozzi P, et al.** Repeat transurethral resection for non-muscle-invasive bladder cancer: a contemporary series. BJU Int. 2016 Apr;117 Suppl 4:54–9. doi: 10.1111/bju.13265
9. **Dobruch J, Borówka A, Herr HW.** Clinical value of transurethral second resection of bladder tumor: systematic review. Urology. 2014 Oct;84(4):881–5. doi: 10.1016/j.urology.2014.06.005
10. **Chamlati-Cuello JM, Garza-Gangemi AM, Gonzaga-Carlos N, Iturriaga-Goyón E, Castillejos-Molina RA.** Second-look histopathologic results in non-muscle-invasive urothelial carcinoma of the bladder: Is repeat resection necessary? Rev Mex Urol. 2017 Jul 17;77(3):183–90.
11. **Rosales Fajardo L, Santana Sarrhy LS, Cinta Alejo y Dreyde R.** Resultados de la re-RTU en el tumor de vejiga no musculo- invasivo de alto

grado. Revista Cubana de Urología. 2014 Jan 28;2(2). [accessed 21 Feb 2023] Available from: https://revurologia.sld.cu/index.php/rcu/article/view/189

12. **Akand M, Muilwijk T, Raskin Y, De Vrieze M, Joniau S, Van Der Aa F.** Quality Control Indicators for Transurethral Resection of Non–Muscle-Invasive Bladder Cancer. Clinical Genitourinary Cancer. 2019 Aug 1;17(4):e784–92. doi: 10.1016/j.clgc.2019.04.014
13. **Pisano F, Gontero P, Sylvester R, Joniau S, Serretta V, Larré S, et al.** Factores de riesgo de enfermedad residual en la re-RTU en una gran cohorte de pacientes con enfermedad T1G3. Actas Urológicas Españolas. 2021 Jul 1;45(6):473–8. doi: 10.1016/j.acuro.2020.08.016
14. **Gontero P, Sylvester R, Pisano F, Joniau S, Oderda M, Serretta V, et al.** The impact of re-transurethral resection on clinical outcomes in a large multicentre cohort of patients with T1 high-grade/Grade 3 bladder cancer treated with bacille Calmette-Guérin. BJU Int. 2016 Jul;118(1):44–52. doi: 10.1111/bju.13354
15. **Akitake M, Yamaguchi A, Shiota M, Imada K, Tatsugami K, Yokomizo A, et al.** Predictive Factors for Residual Cancer in Second Transurethral Resection for Non-muscle-invasive Bladder Cancer. Anticancer Res. 2019 Aug;39(8):4325–8. doi: 10.21873/anticanres.13598
16. **Divrik RT, Yildirim U, Zorlu F, Ozen H.** The effect of repeat transurethral resection on recurrence and progression rates in patients with T1 tumors of the bladder who received intravesical mitomycin: a prospective, randomized clinical trial. J Urol. 2006 May;175(5):1641–4. doi: 10.1016/S0022-5347(05)01002-5
17. **Ferro M, Di Lorenzo G, Buonerba C, Lucarelli G, Russo GI, Cantiello F, et al.** Predictors of Residual T1 High Grade on Re-Transurethral Resection in a Large Multi-Institutional Cohort of Patients with Primary T1 High-Grade/Grade 3 Bladder Cancer. J Cancer. 2018;9(22):4250–4. doi: 10.7150/jca.26129