Holmium Laser En-Bloc Resection versus Conventional Transurethral Resection of Bladder Tumors for Treatment of Non-muscle- Invasive Bladder Cancer

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Introduction

Non-muscle-invasive bladder cancer (NMIBC) is a prevalent malignancy that poses significant management challenges, primarily due to the potential for recurrence and progression. The cornerstone of initial treatment for NMIBC is transurethral resection of the bladder (TURB), which plays a critical role in diagnosis, staging, and therapeutic intervention. However, conventional TURB (cTURB) often results in tumor fragmentation, complicating histopathological assessment and potentially impairing patient outcomes due to incomplete resection and subsequent disease recurrence **(Matulewicz and Steinberg, 2020)**.

In response to these challenges, the concept of en bloc TURB (eTURB) has emerged, aimed at enhancing the quality of resection by allowing for the excision of tumors in a single piece. This method facilitates a more accurate pathological evaluation, improving the assessment of tumor characteristics such as detrusor muscle presence—a key indicator of resection quality associated with better oncological outcomes. Despite these theoretical advantages, robust evidence supporting the superiority of eTURB over cTURB remains limited **(D'Andrea et al., 2023)**.

Laser en-bloc resection of the bladder tumor (LERBT) is a complete tumor resection technique. LERBT improves the quality of resection, reduces perioperative complications, and has the potential to improve recurrence rates **(Hashem et al., 2021)**.

Conventional transurethral resection of the bladder tumor (CTURBT) with a monopolar or bipolar resectoscope obtains an inferior quality of specimen than laser en-bloc resection of the bladder tumor (LERBT) based on a previous meta-analysis study **(Zhang et al., 2020)**.

Recent advancements in laser technology, particularly the holmium laser, have introduced new treatment modalities for NMIBC. Holmium laser resection of bladder tumors (HoLRBT) has demonstrated promise in treating benign urological conditions, but its application in primary NMIBC is less understood. Existing studies primarily focus on recurrent cases with limited patient populations and follow-up durations, highlighting a significant gap in the literature regarding the long-term safety, feasibility, and efficacy of holmium laser in this context **(Maheshwari et al., 2020)**.

Therefore, this study aims to conduct prospective randomized trial comparing holmium laser en bloc resection (HoLRBT) with conventional transurethral resection (cTURB) for the treatment of NMIBC. The primary focus will be on the quality of the pathological specimen, specifically evaluating the presence of detrusor muscle, which will provide valuable insights into the quality of the resection and its implications for oncological outcomes **(Basile et al., 2024)**.

Aim of the work

Primary objective

To compare the quality of resection between holmium laser en bloc resection of bladder tumor (HoLERBT) and conventional transurethral resection of bladder tumor (cTURBT) in patients with suspected non-muscle-invasive bladder cancer, as assessed by the presence of detrusor muscle in the resected specimen.

Secondary objectives

To compare perioperative and short-term oncological outcomes between both techniques, including:

obturator nerve reflex

intraoperative bleeding

bladder perforation

operative time

conversion to conventional resection

positive lateral/deep margins

persistent disease at second-look TURBT

recurrence at 3 and 12 months

recurrence-free survival.

Patients and Methods

study setting:

at Beni-Suef university hospital from 1/2025 to 1/2026

Type of study:

Prospective interventional study.

study population:

Study design

A prospective, randomized, open-label, parallel-group controlled trial conducted at Beni-Suef University Hospital. A total of 100 eligible patients will be randomized in a 1:1 ratio to undergo either HoLERBT or cTURBT.

Inclusion criteria

- Adults aged 30 years or older.
- Patients with cystoscopically suspected primary NMIBC planned for endoscopic resection.
- Fit for surgery and anesthesia.
- Able and willing to provide written informed consent and comply with follow-up.

Exclusion criteria

- Muscle-invasive disease suspected preoperatively or evidence of metastatic disease.
- Prior bladder radiotherapy.
- Severe comorbidity precluding surgery.
- Pregnancy.
- Inability to provide informed consent.
- Upper urinary tract urothelial carcinoma or life expectancy less than 1 year

Randomization

Randomization and allocation concealment

Eligible patients will be randomized using a computer-generated random sequence in a 1:1 allocation ratio. Allocation concealment will be ensured using sequentially numbered, sealed, opaque envelopes prepared by an independent party not involved in patient recruitment or outcome assessment.

Due to the nature of the interventions, surgeons cannot be blinded. However, pathological assessment may be performed by pathologists blinded to treatment allocation whenever feasible.

Methods

All patients will be subjected to:

- **Complete history taking:**

➢ Demographic information: Age, sex, occupation, marital status, family history

➢ Presenting symptoms: Hematuria (frequency, duration, severity), urinary urgency, frequency, nocturia, dysuria, pain, retention, incontinence, pelvic or back pain

➢ Past medical history: Previous surgeries (especially urological), bladder cancer, other malignancies, chronic conditions, medications, allergies

➢ Risk factors: Smoking, occupational/environmental carcinogens, family history of bladder cancer, chronic infections, stones.

- **Complete physical examination:**

➢ **General examination:**

o Vital signs (blood pressure, temperature, heart rate, respiratory rate)

o General appearance and nutritional status.

➢ **Abdominal examination:** o Inspection for masses or distension o Palpation for tenderness or masses o Percussion for dullness or tympany o Auscultation for bowel sounds.

➢ **Digital rectal examination:** Assess for prostate enlargement or masses

➢ **Genital examination:** Inspect for any abnormalities

• **Laboratory investigations:**

➢ Complete blood count (CBC).

➢ Kidney function test (serum urea and creatinine).

➢ Liver function tests (AST and ALT).

➢ Fasting blood sugar.

➢ Coagulation profile (PT, PTT and INR).

➢ Urinary cytology to evaluate malignant cells.

➢ Cystoscopy to visual inspection of the bladder

• **Imaging**

➢ Ultrasound or (Contrast enhanced) CT scan of the abdomen and pelvis to assess tumor extent and metastases

➢ MRI of the pelvis may be used for further evaluation in certain cases

Surgical procedure

• **HoLRBT Group**

For the HoLRBT group, a holmium laser (VersaPulse PowerSuite 100 W; Coherent Inc.) will be utilized under continuous epidural anesthesia. A 550-μm end-firing fiber, sheathed in a 5F ureteral catheter, will be delivered through a 27F continuous holmium resectoscope (Olympus). The laser settings will be adjusted to an energy

of 1.5-2.2 J, a pulse rate of 15-20 Hz, and a power output of 20-40 W, with the possibility of modifications during the procedure.

En bloc resection will be prioritized. First, a circular coagulation mark will be made approximately 1.0 cm from the tumor edge. Any obvious vessels to and from the tumor will be coagulated to minimize bleeding. A fan-shaped incision will then be made into the bladder wall until the muscle layer becomes visible. The lesion will be uplifted using irrigation surge, allowing for easy exposure and subsequent resection. Tumors ≤3.0 cm will be retrieved using a syringe, while larger tumors will be removed with Elik's evacuator. After resection, careful coagulation of the tumor base and surrounding mucosa will be performed, and the specimen will be submitted for pathological evaluation as a single piece. For tumors located on the anterior bladder wall or dome, a combined resection and vaporization technique will be employed.

- **TURBT group**

In the TURBT group, a traditional piece-by-piece resection will be performed down to the muscle layer, with the bladder mucosa 2.0 cm away from the tumor base being electrocauterized.

Follow-up and endpoints

The primary outcome of the study will be the quality of the pathological specimen, measured in terms of detrusor muscle presence.

Secondary endpoints will include the bladder perforation rate, persistent disease at second-look TURB, positive lateral resection margins, positive deep resection margins, operation time, the occurrence of obturator reflex, conversion from eTURB to cTURB, recurrence-free survival (RFS), and disease recurrence at 3 and 12 months.

Obturator reflex will be defined as an adductor spasm of the leg occurring during TURB. Bladder perforation will be visually assessed during the intervention. The

severity of complications will be assessed using the Common Terminology Criteria for Adverse Events (CTCAE). Grade 2 will be defined as extraperitoneal perforation, while Grade 3 will be defined as intraperitoneal perforation. RFS will be defined as the time from surgery to histologically proven intravesical tumor relapse, last follow-up, or death.

Sample size calculation:

The sample size was calculated for comparison of two proportions, assuming a detrusor muscle presence rate of 85% in the en-bloc resection group and 60% in the conventional TURBT group. With a two-sided alpha error of 0.05 and a study power of 80%, the minimum required sample size was 49 patients per group. This was rounded up to 50 patients per group, resulting in a total sample size of 100 patients.

Statistical design

The statistical analysis will be conducted using the Software, Statistical Package for Social Science, (SPSS Inc. Released 2009- PASW Statistics for Windows Armonk: SPSS Inc. The collected data will be summarized in terms of mean ± Standard Deviation (SD and range (minimum - maximum) for quantitative data and frequency and percentage for qualitative data. The collected data will be analyzed using suitable statistical methods. Statistical significance will be accepted at P value <0.05. A P value <0.001 will be considered highly significant while a P value >0.05 will be considered nonsignificant.

Ethical consideration

- An approval from the Research Ethics Committee of the faculty of medicine will be obtained.
- An informed written consent from all patients before participation will be obtained; it will include data about aim of the work, study design, site, time, subject and methods, confidentiality.

- An official permission from the administrators of the defined Hospitals to conduct this study will be obtained.

References

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