RESEARCH ARTICLE

Comparison of holmium laser, bipolar and conventional monopolar transurethral resection of bladder tumour in primary non-muscle invasive bladder cancer

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Abstract

Objective: To compare the efficiency and safety profile of conventional monopolar, bipolar plasmakinetic and holmium laser techniques for transurethral resection of bladder tumour.

Method: The prospective comparative study was conducted from July 2019 to May 2021 after approval from the ethics review committee of Kafrelsheikh University, Egypt, and comprised patients of either gender with primary non-muscle invasive bladder cancer who qualified for transurethral resection of bladder tumour. The patients were stratified into low-risk group A, intermediate risk group B and high-risk group C in accordance with the guidelines of the European Association of Urology. Comprehensive cystoscopy and panendoscopy were done in all cases. Once panendoscopy was done, tumour resection was performed with monopolar resectoscope in group A, plasmakinetic resectoscope in group B and holmium laser in group C). Data was collected at preoperative, peroperative, postoperative and follow-up stages. Data was analysed using SPSS 21.

Results: Of the 84 patients, 67(79.76%) were males and 17(20.23%) were females. There were 27(32.14%) patients in group A; 21(77.8%) males and 6(22.2%) females withy mean age 60.63±11.76 years. Group B had 32(38%) patients; 26(81.2%) males and 6(18.8%) females with mean age 65.34±7.55 years. Group C had 25(29.76%) patients; 20(80%) males and 5(20%) females with mean age 59.48±12.6 years. The mean follow-up period was 12.97±2.70 months in group A, 12.81±2.75 months in group B and 13.48±3.3 months in group C. Visualised complete resection was done in 23(85.8%) group A patients, 29(90.6%) group B patients and 24(96%) group C patients (p=0.018). Visualised complete resection, tumour multiplicity, tumour size, catheter duration, and hospital stay were significant predictors ($p<0.05$). Survival analysis showed 26(96.3%), 30(93.75%) and 25(100%) cases in groups A, B and C, respectively.

Conclusion: Bipolar plasmakinetic and holmium laser techniques were found to be more effective and safer than the conventional monopolar technique for transurethral resection of bladder tumour in patients with primary non-muscle invasive bladder cancer.

Keywords: Bladder neoplasms, Lasers, Prognosis, Urology, Catheters. **DOI: 10.47391/JPMA.EGY-S4-50**

Introduction

Bladder cancer accounts for 6.6% of all cancer cases, being the fourth most frequent cancer in males after prostate, lung and colorectal cancers, while it is the 11th most frequent cancer in females.[1,2] The global incidence rate of bladder cancer is 10.1 and 2.5 per 100,000 in men and women, respectively.[2] Overall, bladder cancer is the 5th most prevalent cancer, accounting for 7,800 cases per year based on the Canadian Cancer Society Guidelines.[3]

Globally, age-standardized mortality rate was 3.2 per 100,000 person per year for men and 0.9 for women in 2012.[4]

Transurethral resection of bladder tumour (TURBT) has been regarded as the gold standard treatment for primary non-muscle invasive bladder cancer (NMIBC). Nevertheless, surgeons have noted a number of disadvantages associated with TURBT, like obturator nerve reflex (ONR), bladder detrusor muscle (BDM) deficiency, heat injury to adjacent tissues, clinical and subclinical perforation, prolongation of postoperative catheterisation and hospital stay, and the incising and scatter technique. These drawbacks make it a challenge to do a precise analysis of the specimens pathologically, and may increase the likelihood of recurrence.[5]

The current study was planned to evaluate the effectiveness and safety of conventional monopolar (CM-TURBT), bipolar plasmakinetic (PK-TURBT) and holmium laser (HOL-TURBT) techniques in the treatment of primary NMIBCs.

Patients and Methods

The prospective comparative study was conducted from July 2019 to May 2021 after approval from the ethics review committee of Kafrelsheikh University, Egypt, and comprised patients of either gender with primary NMIBC who qualified for TURBT. Patients aged >85 years, cases with negative biopsy or cytology results, pregnant or

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lactating women, patient's incapable of follow-up visits, those with concurrent severe diseases, such as tuberculosis, active urinary tract infection, upper tract urothelial tumour, and patients with impaired immune response regardless of cause were excluded.

After taking written informed consent from the patients, they were assessed and stratified into low-risk group A, intermediate risk group B and high-risk group C in accordance with the guidelines of the European Association of Urology (EAU)[6]. Patients with low risk were those with primary, solitary tumour, Ta tumour, G1 tumour, size <3cm, and no carcinoma in situ (CIS). Those with high risk included patients with T1 tumour, G3 tumour, CIS, multiple, recurrent and large >3cm Ta G1/2 tumours. Patients with tumours between the low and high groups were defined as carrying intermediate risk.[6]

After detailed medical history, all the patients were subjected to physical examination and laboratory investigations, including complete blood count (CBC), prothrombin time (PT), partial thromboplastin time (PTT), international normalized ratio (INR), random blood glucose (RBG), liver function tests (LFTs), C-reactive protein (CRP) and renal function tests (RFTs). Office cystoscopy was used as the initial diagnostic tool for NMIBC. Upper tract assessment was done for all cases, using ultrasonography and/ or contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI), whenever indicated, according to EAU guidelines.[6]

Before the procedure, the right period was decided in each case to discontinue the use of anticoagulants and antiplatelet medications, usually 5-7 days before TURBT. For patients on warfarin, INR was checked before the surgery. The morning before the surgery, instructions were given to patients to follow the directions regarding all regular medications. Intravenous (IV) antibiotics were given about 1 hour before instrumentation. The selection of antibiotic was up to the operating surgeon, but a broad-spectrum cephalosporin generally provided adequate protection against common genitourinary pathogens. After spinal anaesthesia was induced, the patient was prepared in the dorsal lithotomy position for transurethral resection. Comprehensive cystoscopy and panendoscopy were done using 17ch rigid cystoscopy, identifying the presence, size, site and morphology of all the present tumours.

Once panendoscopy was done, the patients were one to one randomized to receive tumour resection which was performed with CM-TURBT in group A, PK-TURBT in group B and HOL-TURBT in group C.

CM-TURBT was done using Storz 26 Fr continuous flow resectoscope with hot loop electrode. Power was maintained at default settings, with coagulation setting at 70W and the cutting current at 90W generated from irrigation using instilled water solution at room temperature.

PK-TURBT was performed with a bipolar resectoscope having a thin resection loop to decrease the thermal effect on the biopsy. It was done to ensure adequate tumour pathological information (grade). Power was maintained at the default settings, with both coagulation and cutting settings at 70W generated from irrigation using isotonic sodium chloride solution 0.9% at room temperature.

In the Hol-TURBT group, continuous-wave laser was used to perform en-bloc resection of bladder tumour (ERBT), with a power of 30W, a pulse of 20HZ and energy of 1.5. After the bladder mass was identified, laser was used 0.5cm from the edge of the tumour base. Incision was done vertically layer by layer from the mucosa up to the deep muscle layer. On reaching the deep muscular layer of the bladder, the cutting direction was changed to horizontal. Laser vaporesection was combined with the blunt dissection to remove the tumour. The resectoscope sheath was pushed to remove the tumour base from the deep muscle layer without harming the muscle layer specimen.

Intraoperative difficulties, such as bleeding, as well as complications, like obturator jerk and perforation, were noted. The bladder was then drained using a 20F three-way Foleys catheter that was usually kept for 48 hours. Single immediate postoperative intra-vesical chemotherapy comprising 50mg epirubicin for 1 hour was given in all cases within the first 6 hours of surgery unless bladder perforation was suspected after the TURBT or if significant haematuria was present[6]. The tumours were staged according to the 2009 Tumour-Node-Metastasis (TNM) classification of bladder cancer, and graded in line with the World Health Organisation (WHO) cell differentiation grade classification criteria.[7]

After discharge, the patients were followed up according to a predefined programme depending on the risk stratification group. The minimum follow-up period was 6 months. Six weekly dose-induction intra-vesical therapy was used followed by a monthly maintenance dose for 9 months. Intra-vesical therapy (50mg epirubicin or 120mg Bacillus Calmette-Guerin [BCG]) was used according to the risk stratification group.[8]

Data was analysed using SPSS 21. Data was expressed as mean ± standard deviation, or median with interquartile range (IQR) and frequencies and percentages, as appropriate. Univariate analysis to assess risk factors related

to perforation was done using Chi-square, Fisher exact, or independent t-test, as appropriate. Logistic regression analysis was used for multivariate analysis. Time intervals for survival were computed from the day of TUR to the first recurrence, disease-free survival (DFS), till death, overall survival (OS), and till cancer-specific mortality (CSM). Kaplan-Meier curve was used to present the cumulative recurrence over time. P<0.05 was considered statistically significant.

Results

Of the 84 patients, 67(79.76%) were males and 17(20.23%) were females. There were 27(32.14%) patients in group A; 21(77.8%) males and 6(22.2%) females with mean age 60.63±11.76 years. Group B had 32(38%) patients; 26(81.2%) males and 6(18.8%) females with mean age 65.34±7.55 years. Group C had 25(29.76%) patients; 20(80%) males and 5(20%) females with mean age 59.48±12.6 years. Age, gender body mass index (BMI) and comorbidities were not significantly different among the groups (p>0.05). Duration of catheterisation and duration of hospital stay were significantly different (Table 1).

The mean follow-up period was 12.97±2.70 months in group A, 12.81±2.75 months in group B and 13.48±3.3 months in group C (p=0.684). Visualised complete resection was done in 23(85.8%) group A patients, 29(90.6%) group B patients and 24(96%) group C patients (*p*=0.423). In terms of tumour profile, tumour grade was significantly different among the groups (*p*=0.005).

Mortality was reported in 3(3.57%) cases; 1(33.3%) in group A, and 2(66.6%) in group B. The cause of death was unknown. There was no significant difference in the incidence of recurrence and progression among the groups (Table 2).

On univariate analysis, visualised complete resection, tumour multiplicity, tumour size, catheter duration, and hospital stay were significant predictors (p<0.05). Survival analysis showed 26(96.3%), 30(93.75%) and 25(100%) cases in groups A, B and C, respectively (Figure).

Table-1: Demographic data.

		Monopolar (n=27)	Bipolar (n= 32)	Laser (n =25)	*p-value*
Age		60.63 ±11.76	65.34 ± 7.55	59.48± 12.6	0.089
BMI		27.66±2.52	27.46±3.78	27.02±2.01	0.908
Comorbidities	HTN	7(25.9%)	7(21.9%)	5(20%)	0.938
	DM	4(14.8%)	9(28.1%)	5(20%)	0.463
	Hepatic	3(11.1%)	1(3.1%)	5(20%)	0.126
Gender	Male	21 (77.8%)	26 (81.2%)	20 (80%)	0.948
	Female	6 (22.2%)	6 (18.8%)	5 (0%)	
Duration of catheterisation(days)		3 (1-5)	2 (1-4)	1 (1-3)	0.001*
Duration of hospital stay (in days)		3 (1-5)	2 (1-4)	1 (1-3)	0.001*

BMI: Body mass index, HTN: Hypertension, DM: Diabetes mellitus.

Table-2: Tumour characteristics.

		Monopolar (n=27)	Bipolar (n= 32)	Laser (n =25)	*p-value*
Tumour number	single	21 (77.8%)	23 (71.9%)	24 (96%)	0.063
	multiple	6 (22.2%)	9 (28.1%)	1 (4%)	
Tumour size	< 3cm	16 (59.3%)	12 (37.5%)	16 (64%)	0.09
	≥ 3cm	11 (40.7%)	20 (62.5%)	9 (36%)	
Tumour location	Posterior	11(40.7%)	1 (3.1%)	5(20.0%)	
	Lateral (Left)	3(11.1%)	9(28.1%)	9(36.0%)	
	Lateral (Right)	8(29.6%)	7(21.9%)	7(28.0%)	
	Anterior	0 (0.0%)	1 (3.1%)	0 (0.0%)	
	Domal	0 (0.0%)	2 (6.2%)	0 (0.0%)	
	Bladder neck/ Trigone	1 (3.7%)	0 (0.0%)	3 (12.0%)	
	Multicentric	4(14.8%)	12(37.5%)	1 (4.0%)	
Tumour stage	Ta	6 (22.22%)	8 (25%)	3 (12%)	0.522
	T1	20 (74%)	24 (75%)	22 (88%)	
	Primary CIS	1 (3.7%)	0 (0%)	0 (0%)	

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Table-2: *continued from previous page*

		Monopolar (n=27)	Bipolar (n= 32)	Laser (n =25)	*p-value*
Tumour Grade	Grade 1	14 (51.85%)	16 (50%)	22(88%)	0.005
	Grade 2	4 (14.8%)	7 (21.87%)	3 (12%)	
	Grade 3	9 (33.33%)	9 (28.12%)	0 (0%)	
Time of resection (minutes)		39.18 ± 5.67	38.34 ± 4.67	38.60 ± 8.3	0.874
Obturator jerk		2 (7.4%)	1 (3.1%)	0 (0%)	0.359
Perforation		2 (7.40%)	1 (3.12%)	0 (0%)	0.359
Visualised complete					
Resection		23 (85.19%)	29 (90.6%)	24 (96%)	0.423
Visualised detrusor					
Muscle		26 (96.3%)	31 (96.9%)	14 (70%)	0.984
Recurrence		4 (14.8%)	2 (6.25%)	0 (0%)	0.11
Progression		0 (0%)	0 (0%)	0 (0%)	0 (0%)
Second look		21 (77.7%)	22 (68.75%)	22 (88%)	0.232
The stage at Second look					
Free		20(95.23%)	21 (95.45%)	22 (88%)	0.609
T1		1 (4.7%)	1 (4.54%)	0 (0%)	
Grade at second-look					
Free		20 (95.23%)	21(95.45%)	22 (88%)	0.569
G2		0 (0%)	1 (4.54%)	0 (0%)	
G3		1 (4.7%)	0 (0%)	0 (0%)	

BMI: Body mass index, HTN: Hypertension, DM: Diabetes mellitus.

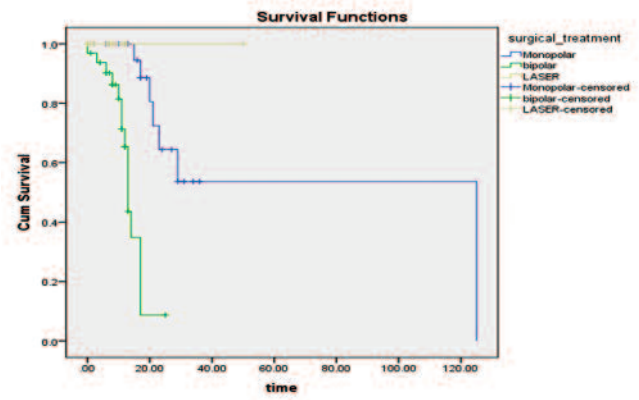

Figure: Survival analysis

Recurrence was reported in 4(14.8%) cases and 2(6.25%) cases in groups A and B, respectively (p=0.11).

Discussion

The use of laser as a less invasive technique for the management of urological diseases has been escalated in recent years, with TURBT still being the gold standard treatment for NMIBCs despite its obvious drawbacks. The use of laser as a new cutting energy has been proven as safe and minimally invasive for treating bladder cancer.[9-11]

Basically, insufficient specimen for pathological examination was the primary drawback of laser technique that had limited its use in the management of urinary bladder tumours. However, the modern holmium laser can maintain en-bloc excision of the tumour that leaves adequate tissue for histological examination.[12-14]

Non-invasive, small lesions are particularly receptive to laser energy that can achieve clearance rates comparable to those attained by the conventional electrocautery resection.[15-17] A randomised study reported a local recurrence rate of 7% for neodymium-doped yttrium aluminum garnet (Nd: YAG)-treated stage T1 tumours versus 43% for similar tumours treated with standard electrocautery.[18] Likewise, another study found a comparable local recurrence rate in a sample of 252 patients who underwent laser treatment for superficial lesions.[19]

In the current study, recurrence was reported in 4(14.8%), 2(6.25%) and 0 (0%) cases in monopolar, bipolar, and HoL-TURBT groups, respectively

In terms of tumour location, the current study found that the lateral bladder region was the most commonly affected site 40.7%, 50% and 64% in groups A, b and C, respectively. Others reported that the lateral bladder zone was the most commonly affected region in monopolar and HoL-TURBT groups, respectively.[20]

Regarding the duration of operation, there was no significant difference among the three groups in the current study, which is in line with an earlier study.[21]

However, one study reported prolonged operative time with laser.[22]

In the current study, gross complete resection achieved was not significantly different among the groups. A recent study agreed with the finding.[23]

In the present study, there was no significant difference among the groups regarding the incidence of perforation, which has been reported earlier as well[21]. In the current study, obturator jerk was not significantly different. The low incidence of obturator jerk may have been because the study followed a precautionary approach, like avoiding full bladder and deep resection as well as using a low current during resection. CM-TURBT carries a number of common hazards, such as the possibility of obturator nerve jerk during surgery, particularly for lesions in the lateral bladder wall, which may result in perforation of the bladder.[24]

The current findings related to duration of urinary catheterisation, duration of hospitalisation and tumour recurrence rate were in line with earlier findings.[20]

In the current study, mortality was reported only 3 cases; 1 in the CM-TURBT group, and 2 in the PK-TURBT group. The deaths were sudden and of unknown causes. In an earlier study, 2 patients died due to cardiovascular disease 26 and 23 months after the surgery, and 5 were lost to follow-up at various intervals during the 3-year follow-up, and till the time of the last follow-up, there was no evidence of tumour recurrence in any case.[20]

The current study has its limitations as it was done at a single centre, and the sample size was not calculated, which could have influenced the power of the study. This limitation should be addressed in the upcoming studies. Moreover, longer-term follow-up is needed.

Conclusion

Compared to CM-TURBT excision of primary NMIBCs, PK-TURBT and HoL-TURBT showed better results. However, the tumour recurrence rate of PK-TURBT and HoL-TURBT did not show a clear advantage over CM-TURBT.

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Conflict of Interest: None.

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