

RESEARCH ARTICLE

How Far We Should Go with Pelvic Lymph Node Dissection on the Controlateral Side in Unifocal Muscle Invasive Bladder Cancer

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Objectives. The purpose of this study was to determine the evolution of patients with unifocal lateral wall MIBC (muscle invasive bladder cancer) after cystectomy with PLND (pelvic lymph node dissection) at the Urology Clinic in Tirgu Mures, and to determine tumor stage and lymph node status before and after radical cystectomy with PLND. **Methods.** This is a prospective study, conducted between 1 August 2012 to 31 July 2014 at Urology Clinic, with a median follow-up of 14 months (range 7-25). Inclusion criteria were: patients undergone cystectomy with PLND, and unifocal MIBC on the lateral wall of the bladder; exclusion criteria were: multiple bladder tumor, other location and clinical T stage > 3. **Results.** Fourteen patients met the inclusion criteria, median age was 61 (range 55-72), 85.71 % were male. An increase in T3 patients was noticed from 1 to 5 cases, we noticed a decrease of N0 lymph nodes from 78.6% to 57.1% postoperatively and on the controlateral side the kappa coefficient between the preoperatively and postoperatively negative lymph nodes was 0.63. On the tumor side the most common location for positive lymph nodes was external iliac with 3 nodes (21.4 %) and obturator fossa with 4 nodes (28.6 %) and on the contralateral side 2 positive nodes (14.3 %, obturator fossa, external, internal and common iliac nodes). **Conclusions.** In unifocal bladder tumors, located on the lateral wall, PLND could be an alternative with comparable results with extended PLND especially in T1 and T2 patients associated with N0 before and after surgery.

Keywords: bladder cancer, muscle invasive, PLND, unifocal tumors

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Introduction

Radical cystectomy is the standard treatment in the management of localized or locally advanced bladder neoplasia. Pelvic lymph node dissection (PLND) represents an important component especially for postoperative histological analysis of lymph nodes to identify patients at risk and those who could actually benefit of adjuvant therapy [1]. A careful analysis of preoperative lymph nodes regarding: shape, size and location after contrast CT or MRI examination is recommended by European Urology guide [1]

One of the advantages of PLND is that the lymph dissection enhances loco-regional control of the disease, leading to a high survival rate. But even so, the exact number of lymph nodes or a sufficient number that should be removed in order to improve the oncological status has not yet been defined [2]. In a review published in 2009 the focus was on extended PLND, and its advantages which is the current standard, but unifocal lateral wall MIBC were not included and the opportunity for extended PLND to such patients, especially those with N0 at preoperative CT examination [3].

Whitmore and Smith reported since 1981 that the most common locations of lymphatic metastasis in bladder cancer are obturator fossa and iliac extern lymph nodes (74%

and 65%) [4]. The literature describes that approximately 25 % of negative lymph nodes at CT examination are histological positive [5-7].

Roth et al showed that crossed lymphatic drainage in case of unifocal tumor localized on the lateral bladder wall is a common phenomenon and a limitation of only unilateral pelvic lymph node dissection on the tumor side, may lead to retention of radioactive lymph positive on the controlateral side at approximately 40% of patients. They also observed that with the use of sentinel node procedure in these tumors located on the lateral wall, controlateral PLND may be limited to obturator fossa, external and common iliac regions, and this does not affect long-term prognosis and oncological radicality of surgery [8].

The purpose of this study was to determine the evolution of patients with unifocal lateral wall MIBC (muscle invasive bladder cancer) after cystectomy with PLND at the Urology Clinic in Tirgu Mures, and to determine tumor stage and lymph node status before and after radical cystectomy with PLND for unifocal lateral wall MIBC at CT scan and histology reports to see if standard PLND it is sufficient in this type of bladder tumors as was demonstrated before by Roth et al [7].

Methods

This is a prospective study, conducted between 1 August 2012 to 31 July 2014 at Urology Clinic in Tirgu Mures,

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with a median follow-up of 14 months. Durring this time 36 patients undergone radical cystectomy with PLND (external iliac, common iliac, internal iliac and obturator fossa lymph nodes) in our clinic. From those 14 (38.88%) patients met the inclusion criteria: patients with unifocal muscle invasive blader cancer on the lateral wall of the bladder. Exclusion criteria were multiple bladder tumor, location elsewhere than on the lateral wall and clinical T stage > 3.

Statistical analysis of data was performed with the Graphpad Prism 5 software. Categorical variables were summarized as percentages and compared with Fisher's exact test for two groups and chi-square tests for three or more groups. Agreement between the pre and post operatory, or ipsilateral side versus controlateral side for lymph node status overall, was assessed with the kappa method of interrater agreement. A kappa level over 0.7 was considered clinically significantly. The significance level was set at $p < 0.05$.

Results

From 36 cystectomy performed in our center 14 (38.88%) patients met study inclusion criteria (Fig. 1- CT scan preoperatory and intraopertory PLND), patient characteristics are described in (Table I), median age was 61 (range 55-72), 85.71 % were male and average follow-up was 14 months postoperatively (range 7-25).

The statistical analysis of preoperative and postoperative tumor stage showed an increase of T3 patients from 1 case 7.1 % to 5 cases up to 35.7% ($p = 0.16$) and a decrease of N0 from 78.6% to 57.1% postoperatively (Table II).

From all patients enrolled, 4 (28.57%) died during follow-up, diagnosed with systemic disease on average 7 months postoperatively, all with T3 and one T4 (micro-papillary carcinoma) stage. No other patient had local recurrence (limph nodes less than 2 cm on CT below the bifurcation of ilac vessels) or distant metastasis (higer than 2 cm, other than local recurrence) during the follow up period (Fig. 2).

At the analysis of pre and postoperative lymph nodes we observed that 85.7% of patients were N0 on controlateral side, only one patient with pre-operative N0 (7.1%) was

Table I. Patient characteristics unifocal MIBC of lateral wall

Pathologic tumour stage	No. (%) pre-op	Post-op
pT1	4 (28.5)	2 (14.3)
pT2	9 (64.3)	6 (42.8)
pT3	1 (7.2)	5 (35.7)
pT4	0 (0)	1 (7.2)
Pathologic lymph node status,	No. (%) pre-op	Post-op
pN0	11 (78.6)	8 (57.2)
pN+	3 (21.4)	6 (42.8)
Concomitant CIS		8 (57.2)
Number of TURB preoperatively		1 (11), 2 (2), 3 (1)
Pathologic lymph node status contralateral side	ipsilateral	controlateral
pN0	9 (64.3)	12 (85.7)
pN+	5 (35.7)	2 (14.3)

Table II. Stage, nodes and grade status pre and postoperative

		preoperator no (%)	postoperator no (%)	p value	Kappa coefficient
PT	PT1	4 (28.6)	2 (14.3)	0.64	0.167
	PT2	9 (64.3)	6 (42.9)	0.44	
	PT3	1 (7.1)	5 (35.7)	0.16	
	PT4	0 (0)	1 (7.1)	0.99	
PN	PN0	11 (78.6)	8 (57.1)	0.41	0.198
	PN1	2 (14.3)	1 (7.1)	0.99	
	PN2	1 (7.1)	3 (21.4)	0.57	
	PN3	0 (0)	2 (14.3)	0.46	
G	G2	1 (7.1)	1 (7.1)	0.46	1.0
	G3	13 (92.9)	13 (92.9)		

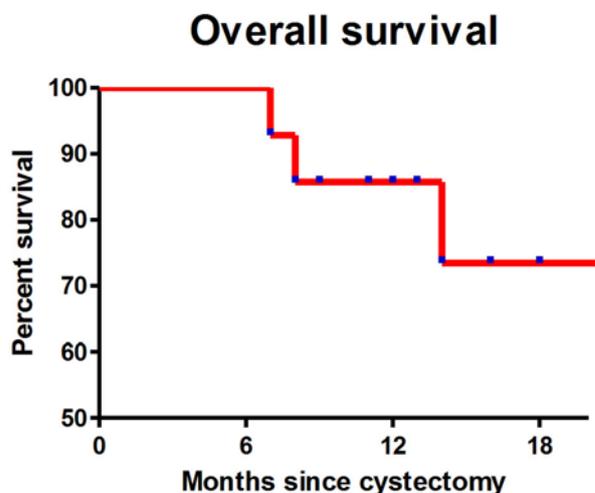


Fig. 2. Kaplan Mayer Survival curve

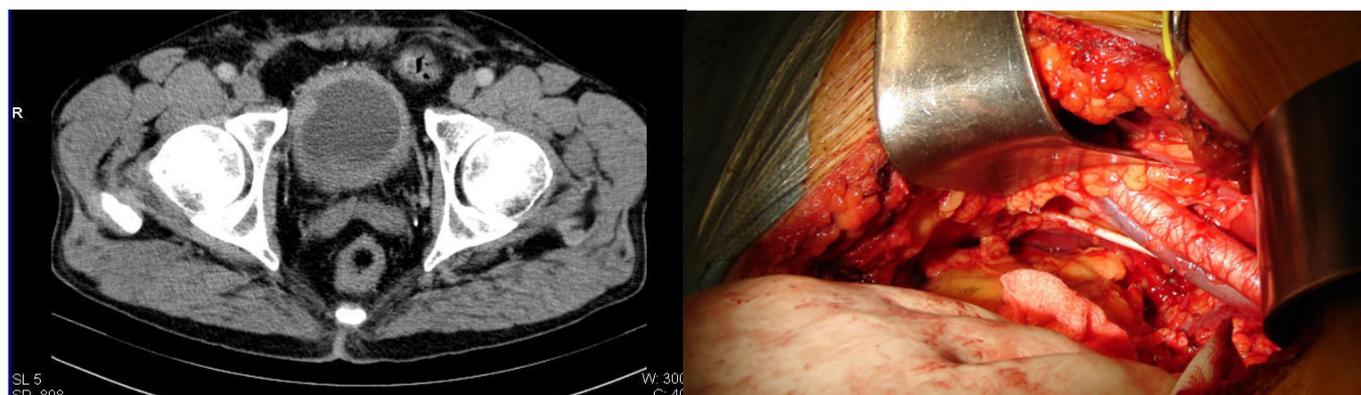


Fig. 1. A. CT unifocal MIBC on right wall without pathological lymph nodes. B. Intraoperatory PLND on the right side

diagnosed histologically N+ controlateral. Kappa coefficient calculated between controlateral N0 preoperative and N0 postoperative was 0.63. (Table III and IV).

Table III. Lymph node status overall

Lymph node	Status	ipsilateral side no (%)	controlateral side no (%)	p value	Kappa coefficient
external iliac	NEGATIVE	11 (78.6)	12 (85.7)	0.99	0.276
	POSITIVE	3 (21.4)	2 (14.3)		
internal iliac	NEGATIVE	12 (85.7)	12 (85.7)	0.59	0.417
	POSITIVE	2 (14.3)	2 (14.3)		
obturator fossa	NEGATIVE	10 (71.4)	12 (85.7)	0.64	0.176
	POSITIVE	4 (28.6)	2 (14.3)		
common iliac	NEGATIVE	12 (85.7)	12 (85.7)	0.59	0.417
	POSITIVE	2 (14.3)	2 (14.3)		

Table IV. Correlation between preoperative and postoperative lymph node status on controlateral side

Postoperative node stage controlateral	Preoperative node stage		Kappa 0.63 Total
	NEGATIVE	POSITIVE	
NEGATIVE	12	1	13 (92.8%)
POSITIVE	0	1	1 (7.2%)
Total	12 (85.8%)	2 (14.3%)	14

Discussion

The need for extensive lymph node dissection remains a hot topic in the literature [9]. Many studies focus on the distribution of lymphatic metastasis. A multicenter study published in 2004 reveals that the most common metastasis are obturator fossa metastases and those near the iliac vessels [10]. Our results showed that in case of unifocal lateral wall MIBC, on the tumor side the most common location for positive lymph nodes are external iliac (21.4 %) and obturator fossa with (28.6 %) and on the contralateral side 14.3 % equal in all lymph nodes removed.

Skinner et al also showed close correlation between the number of lymph nodes retrieved as high and the outcome of patients since 1982, so despite the low percentage of only 7.1% of patients with positive lymph nodes on controlateral side after N0 at CT, we can not say that a reduction of lymph nodes removed on controlateral side would have the same oncological benefit as an extended PLND [11].

The recent studies argue even for extended PLND at least up to the bifurcation of the abdominal aorta with the inclusion of Marcille fossa [12] or super extended up to emergence of the upper and lower mesenteric artery, and presacral space included from the bifurcation of the aorta to the sacral fossa [13], but without establishing a statistically significant difference in terms of long-term life expectancy between the two groups of patients with and without super extended PLND. Reported to literature our good results regarding unifocal lateral wall MIBC with negative controlateral lymph nodes (92.9 %) pleades for standard PLND (external iliac, common iliac, internal iliac and obturator

fossa) in these patients. Further studies could bring updates regarding comparison with extended PLND.

Fang et al conducted a study with a duration of 8 years in which analyzed two groups of patients: the first 4 years they performed PLND that included external iliac, internal iliac, obturator fossa and Cloquet nodes, up to bifurcation of the iliac vessels, then the next four years they have established a minimum of 16 lymph nodes extracted, so the average number of lymph nodes increased from 15 to 20, and survival from 42% to 72% with p <0.01 [14], resampling results in terms of prognosis and survival in patients who received extended PLND were reported by Brunocilla et al [15], with a 71.5% survival at 18 months in our group of patients with unifocal lateral wall MIBC, we can also say that standard PLND provides comparable oncological outcome with extended PLND in these patients.

Using the technique of sentinel lymph node Roth et al. demonstrated a more extended drainage than previously thought, so that a limited PLND to external iliac and obturator fossa removed only 50% of possible affected lymph nodes, however an extended PLND manages to remove up to 90% of lymph nodes affected [16]. In the absence of the possibility of using this technique our results recommended standard PLND, regarding to the low rate of positive lymph nodes on the controlateral side in these patients 7.1%.

In a study published in 2010 by Wendel et al showed in a group of 50 patients with lymphatic metastasis that there is a close correlation between lateral tumor location and secondary nodes metastasis [17], however, in our study we analyzed patients N0 at preoperative CT examination, and only 1 patient had controlateral positive lymph node at histological examination.

In terms of overall survival at 18 months with a rate of 71.5% and no local recurrence, this series of patients with unifocal lateral wall MIBC are within the limits described in the literature, and 100% survival at 24 months for patients with T1 and T2 / N0 postoperative also [18]. Cancer specific deads were due to particular histological variants such as micropapillary variant which is asociated with aggressive behavior and poor prognosis [19]

The limits of this study are given by the low number of patients enrolled, low follow-up period for survival and recurrence rate, but because we actually watched tumor stage and lymph node status before and after cystectomy this study fulfill the objectives and the good results reported to literature pleades for a standard PLND in these patients with a survival rate in patients with N0 according to previously published studies.

Conclusions

In the absence of the sentinel node technique, unifocal bladder tumors, located on the lateral wall, PLND (external iliac, internal iliac, common iliac and obturator fossa) could be an alternative with comparable results with extended PLND especially in T1 and T2 patients associated

with N0 before and after surgery. The low rate of positive contralateral lymph nodes represent a guarantee of standard PLND radicality in these patients.

List of abbreviations

MIBC – muscle invasive bladder cancer

PLND – pelvic lymph node dissection

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