

# SURVIVAL OF PATIENTS WITH BLADDER CANCER WHO HAD PARTIAL CYSTECTOMY IS BETTER THAN THOSE WHO HAD RADIOTHERAPY

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## ABSTRACT

**Objective:** To evaluate the survival on patient who had muscle invasive bladder cancer that had been operated or radiotherapy at Sardjito Hospital Yogyakarta. **Material & method:** From the year 2004-2010, we were data the patients with muscle invasive bladder cancer that had been operated or radiotherapy at Sardjito Hospital. We studied the age when diagnosed, gender, TNM status, histopathologic finding, histopathologic grade, kinds of surgery and status when follow-up. We evaluated the survival of each patient until 5-years post-surgery. We did bivariate analyze to assess the correlation of patient survival and TNM status, histopathologic grade, clinical stadium and kinds of management. We use Kaplan Meier curve to assess the the survival of patient who had muscle invasive bladder cancer. **Results:** There were 37 patients with bladder cancer; 3 female patients (8.1%) and 34 male patients (91.9%). Five patients were performed radical cystectomy, 4 patients performed partial cystectomy and 28 patients performed TUR-BT and radiotherapy. There were no significant correlation on the patient survival who had muscle invasive bladder cancer with gender, age, stadium, TNM staging, histopathologic grade and kinds of management ( $p > 0.05$ ). From Kaplan Meier curve, we found that the patients survival was better on stadium I, staging T1, N0, M0 and histopathologic G1 grade. While based on kinds of management, patients were performed partial cystectomy had the survival rate better than the one who only performed TUR-BT and radiotherapy. **Conclusion:** The surgery of partial cystectomy had a better survival rate than TUR-BT and radiotherapy.

**Keywords:** Survival, bladder cancer, muscle invasive.

## ABSTRAK

**Tujuan:** Untuk mengevaluasi ketahanan hidup pasien kanker kandung kemih invasif ke otot yang dilakukan terapi operasi maupun radioterapi di Rumah Sakit Sardjito Yogyakarta. **Bahan & cara:** Dari tahun 2004-2010, dilakukan pendataan pasien dengan kanker kandung kemih invasif ke otot yang dilakukan tindakan sistektomi maupun radioterapi di RS Sardjito. Data yang dipelajari adalah usia saat diagnosis, jenis kelamin, status TNM, gambaran histopatologi, grading histopatologi, jenis tindakan operasi dan status pada saat follow-up. Dievaluasi ketahanan hidup dari masing-masing pasien hingga 5 tahun pasca tindakan. Dilakukan analisa bivariat untuk menilai hubungan ketahanan hidup dengan status T, N, M, grading histopatologi, stadium klinis dan jenis penatalaksanaan. Digunakan kurva Kaplan Meier untuk menilai gambaran ketahanan hidup pasien kanker kandung kemih invasi ke otot. **Hasil:** Ada 37 pasien dengan tumor buli yang terdiri dari perempuan 3 orang (8.1%) dan laki-laki 34 orang (91.9%). Lima orang dilakukan radikal sistektomi, empat orang dilakukan parsial sistektomi dan 28 pasien dilakukan TUR-BT dan radioterapi. Tidak dijumpai hubungan bermakna antara ketahanan hidup pasien kanker kandung kemih invasif ke otot dengan jenis kelamin, usia, stadium, staging T, N, M, grading histopatologi maupun jenis penatalaksanaan ( $p > 0.05$ ). Berdasarkan kurva Kaplan Meier diketahui ketahanan hidup lebih baik pada stadium I, Staging T1, N0, M0 dan grading histopatologi G1. Sedangkan berdasarkan jenis tindakan, pasien yang dilakukan parsial sistektomi memiliki angka ketahanan hidup lebih baik daripada hanya dilakukan TUR-BT dan Radioterapi. **Simpulan:** Tindakan operasi parsial sistektomi memiliki angka ketahanan hidup lebih baik daripada TUR-BT dan Radioterapi.

**Kata kunci:** Ketahanan hidup, kanker kandung kemih, invasif ke otot.

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## INTRODUCTION

Bladder urothelial cancer which consist of 90% of all primary bladder cancer is the fourth most cancer found on male.<sup>1</sup> About 60% of patient diagnosed with bladder cancer will develop into muscle invasive disease and 80% of superficial cancer will develop into muscle invasive bladder cancer.<sup>2</sup>

In Indonesia, the incidence of bladder cancer is known increased 15% annually on the last decade.<sup>3</sup> Even bladder cancer was the most prevalence cases for Urooncology cases at Hasan Sadikin hospital compared to other cancer (39.3%).<sup>4</sup> At Cipto Mangunkusumo Hospital, there was 254 cases with 62.6% among them were muscle invasive bladder cancer.<sup>5</sup>

Treatment of choices of muscle invasive bladder cancer is radical cystectomy with pelvic lymphadenectomy.<sup>1</sup> While for patient who refused radical cystectomy or unfit for such operation could be considered for radiotherapy.<sup>6</sup>

Partial cystectomy is preferred for patients who had solitary lesion, located on area that did not use ureteral re-implantation procedure, absence of carcinoma in situ or patient with poor functional status.<sup>7</sup>

The 5-year survival on patients after radical cystectomy are 48-66%, while their survival after radiotherapy only 28-39%.<sup>2</sup> For patient who had partial cystectomy, the 5-year survival was reached 70%.<sup>8</sup> In Indonesia, the 5-year survival on second stage was 30%, on third stage was reached 18.8% and on fourth stage only 9.1%.<sup>5</sup>

## OBJECTIVE

This study is to know the 5-years survival on patient who had muscle invasive bladder cancer at Sardjito Hospital that had been operated or radiotherapy and its related factor affected survival.

## MATERIAL & METHOD

This was a retrospective study on patient who had muscle invasive bladder cancer at Sardjito hospital from year 2004–2010. We collected clinical data such age, sex, clinical stage, the TNM stage, histopatology findings, histopathology grading, therapy and survival status. The survival was followed up to 5 year after the therapy by phone call or home visit.

We include only patient with TCC bladder cancer who had radical cystectomy, partial cystectomy or radiotherapy with clear the TNM stage. Other type of bladder cancer, unclear the TNM stage or incomplete address were not included in this study.

Bivariate analysis using Fisher test to analyze correlation between survival status with factors such as T, N, M stage, histopathology grading, clinical staging and therapy. Kaplan Meier were used to calculate survival on patient with muscle invasive bladder cancer.

## RESULTS

During 9 years, there were 37 cases of patient with muscle invasive bladder cancer at Sardjito Hospital that dominate by male (34 patients or 91.9%) with average age  $63.59 \pm 11.56$  years old.

**Table 1.** Descriptive of muscle invasive bladder cancer at Sardjito hospital.

		Frequency	Percentage
Sex	Male	34	91.9
	Female	3	8.1
Age	40 - 60 years old	11	29.7
	> 60 years old	26	70.3

Based on clinical evaluation, imaging studies and histopatology findings, the more prevalence cases were on T2 stage (22 patients or 59.5%), on Nx stage (30 patients or 81.1%), on Mx stage (22 patients or 59.5%) with on Gx stage (16 patients or 43.2%).

**Table 2.** Bladder cancer staging at Sardjito hospital.

		Frequency	Percentage
T	T1	1	2.7
	T2	22	59.5
	T3	6	16.2
	T4	8	21.6
N	Nx	30	81.1
	N0	6	16.2
	N1	1	2.7
M	Mx	22	59.5
	M0	15	40.5
	M1	0	0
G	Gx	16	43.2
	G1	6	16.2
	G2	6	16.2
	G3	9	24.3

Based on clinical staging, only one patient were at first stage (2.7%), 22 patients at second stage (59.5%), 6 patients at third stage (16.2%) and 8 patients at fourth stage of cancer (21.6%).

**Table 3.** Clinical staging of bladder cancer at Sardjito hospital.

		Frequency	Percentage
Stage	I	1	2.7
	II	22	59.5
	III	6	16.2
	IV	8	21.6

We had 5 patients underwent radical cystectomy (13.5%) with urinary diversion such ileal conduit (4 cases) and TUUC on 1 case. Partial cystectomy had been done on 4 patients (10.8%) with ureteroneocystostomi on 1 case (2.7%). An-

other 28 patients underwent TUR-BT followed by radiotherapy.

Based on analysis, the 5-year survival on muscle invasive bladder cancer were not related by sex, age, clinical stage, the TNM stage, histopathology grading or therapy ( $p > 0.05$ )

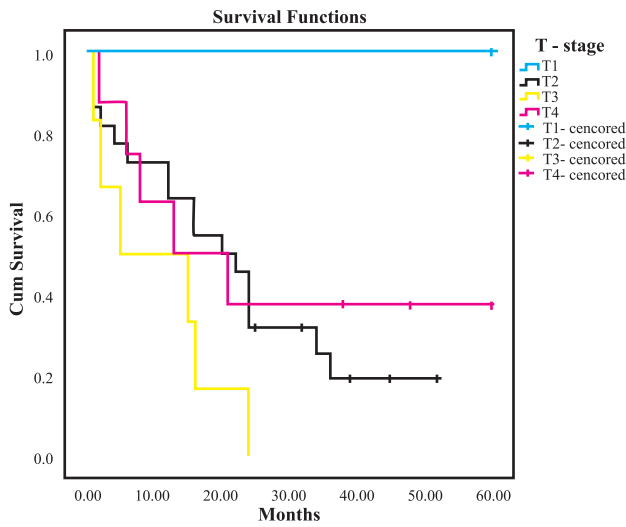
From Kaplan Meier analysis, the 5-year survival of muscle invasive bladder cancer patients were better at first stage, T1, N0, M0 stage and G2 histopathology grading. All patient who had radical cystectomy developed complication that they died within 1-22 months after surgery. On partial cystectomy group, only 2 patients who died at 5 and 24 months after surgery. While on Radiotherapy group there were 7 patient still alive and 22 patients died. Based on Kaplan Meier also showed that the survival of patient who had partial cystectomy were better than those who had TUR-BT and radiotherapy.

**Table 4.** Bladder cancer management at Sardjito hospital.

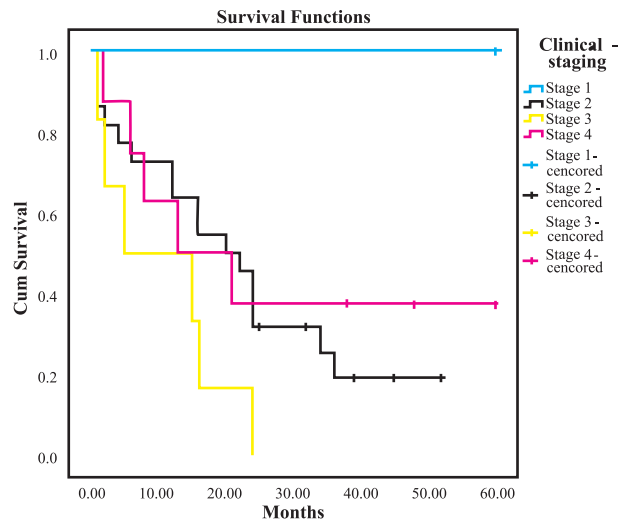
		Frequency	Percentage
Primary surgery	Radical Cystectomy	5	13.5
	Partial Cystectomy	4	10.8
	TUR-BT	28	75.7
Secondary surgery	Ileal Conduit	4	10.81
	TUUC	1	2.7
	Ureteroneocystostomy	1	2.7
Other therapy	Radiotherapy	28	75.7

**Table 5.** Correlation of survival analysis with sex, age, clinical stage, the TNM stage, histopathology grading and therapy.

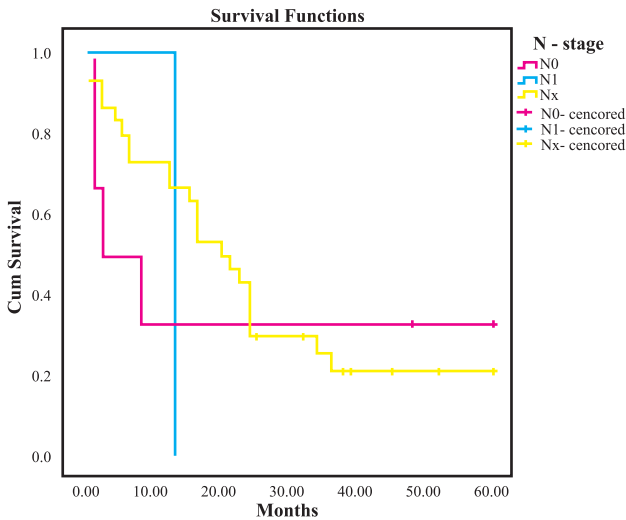
		Life	Died	p
Sex	Male	9	25	0.562
	Female	0	3	
Age	40-60 years old	2	9	0.695
	> 60 years old	7	19	
Clinical stage	Stage 1 + Stage 2	6	17	1.000
	Stage 3 + Stage 4	3	11	
T	T1 + T2	6	17	1.000
	T3 + T4	3	11	
N	N0 + Nx	9	27	1.000
	N1	0	1	
M	M0	6	9	0.118
	Mx	3	19	
G	G1 + Gx	6	16	0.711
	G2 + G3	3	12	
Therapy	Radical/Partial Cystectomy	2	7	1.000
	TUR-BT + Radiotherapy	7	21	



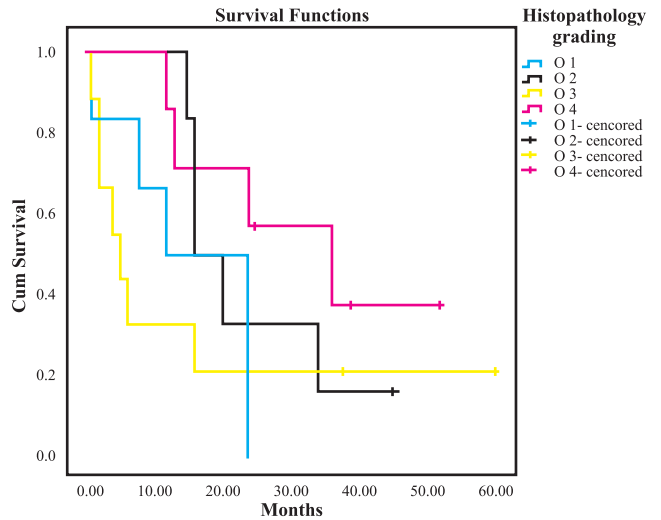
**Graphic 1.** Kaplan Meier curve based on T stage.



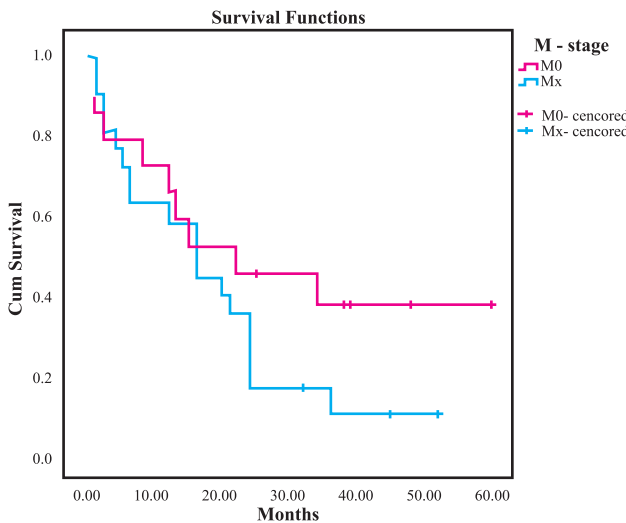
**Graphic 4.** Kaplan Meier curve based on clinical stage.



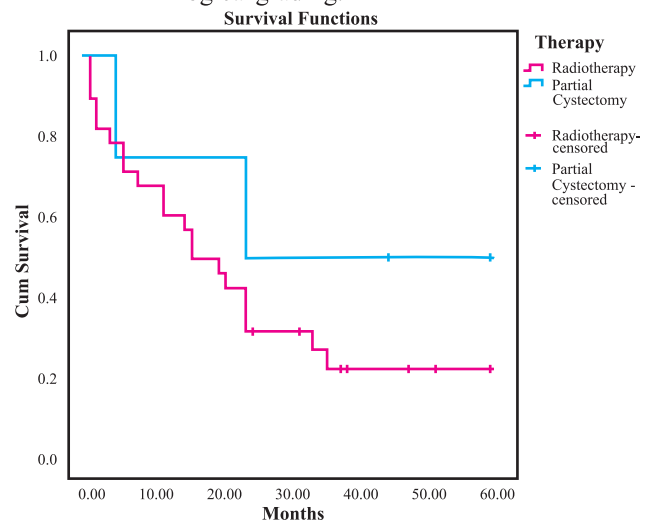
**Graphic 2.** Kaplan Meier curve based on N stage.



**Graphic 5.** Kaplan Meier curve based on histopathological grading.



**Graphic 3.** Kaplan Meier curve based on M stage.



**Graphic 6.** Kaplan Meier curve based on therapy.

## DISCUSSION

This study was the preliminary study which describe survival of muscle invasive bladder cancer at Sardjito hospital. Muscle invasive bladder cancer was an aggressive cancer. If left untreated its course is usually fatal with  $\geq 85\%$  of patients dying from their disease in 24 months.<sup>9</sup>

This study show the male to female ratio was 12 : 1 while study that conduct by Supit et al at Cipto Mangunkusumo hospital was 6 : 1. The difference may due to the number of patient at Sardjito hospital is less than Cipto Mangunkusumo.

Average age on this study was 63 years old or 9 year older than previous study at Cipto Mangunkusumo hospital. The difference of age may affect the lower of survival of muscle invasive bladder cancer's patient compare to Cipto Mangunkusumo's result. From study that conduct by Goessens et al showed older age, female, advanced stage, more comorbidity and not undergoing treatment with curative intent were associated with a lower survival.<sup>9</sup> However this study showed the survival was not related to age, sex, clinical stage, the TNM stage, histopathology grading or therapy ( $p>0.05$ ).

From study that conduct by Supit et al showed the patient's survival on second, third and fourth stage of cancer was reached 30%; 18.8%; 9.1%. However we have difference result by second stage was 5% and on the fourth stage even higher (30%). It was possible that difference demography, difference of number of patients and more advanced stage were affected the survival.

Radical cystectomy was gold standard therapy of T2-T4a, N0-Nx, M0 of muscle invasive bladder cancer. Other indication was high risk with recurrent of non muscle invasive bladder cancer, resistant of BCG therapy, incidence of Tis or high grade T1 (T1G3) and extensive papillary disease which uncontrollable with TUR-BT and intravesical chemotherapy treatment.<sup>10</sup>

Post radical cystectomy survival rate on one study was 36.5% after 5 years. More over 3-months mortality rate after radical cystectomy was 14.5%.<sup>7</sup> On our study, all patient who had radical cystectomy died on 1-22 months after surgery due to gastrointestinal complication such bowel leakage. This complication also mentioned by Chahal et al that gastrointestinal complication such bowel leakage, intestinal obstruction and prolonged ileus as common peri-operative complication. In the long term, upper tract urinary system may deteriorate by

overt renal failure.<sup>11</sup>

In properly selected patients, partial cystectomy had advantage compare to radical cystectomy include complete tumor excision with wide surgical margins, lower morbidity, adequate bladder and sexual function.<sup>7,8</sup> However its also had disadvantage such higher risk for tumor recurrence and need of secondary treatment.<sup>7</sup> Knoedler et al showed that post partial cystectomy intravesical recurrency rate was 38% that 19% of them need radical cystectomy.<sup>7</sup> Capitanio et al mentioned the 5-year survival rate on patient who had partial cystectomy was 57.2% compared to radical cystectomy which lower (50.2%).<sup>12</sup> On our study only two patient died on 5 and 22 months after partial cystectomy and the rest none develop any recurrence.

Radical radiotherapy that preserve the bladder may be just as effective as surgery in term of local control and patient's survival. On meta analysis by Shelley et al showed 3-years survival on radiotherapy group was 32% and surgery group gave 47% while the 5 years-survival rate down to 21% on radiotherapy group and 41% on surgery group.<sup>2</sup> Similar result was obtained by our study that 5-years survival rate was 18% on patient who had TUR-BT and radiotherapy group.

## CONCLUSION

There were no correlation between survival with clinical factors such as sex, age, clinical staging, the TNM stage, histopathological stage and therapy ( $p>0.05$ ). Based on Kaplan Meier analysis, patient's survival was better at first stage of cancer, T1, N0, M0 and G2 histopathological grading. Based on therapy, patient's survival on partial cystetomy was better than those who had radiotherapy.

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