

The Value of Restaging by Computed-Tomography (CT) in Monitoring Response Rates to Neoadjuvant Chemotherapy in Muscle Invasive Bladder Cancer: A Longitudinal Long-Term Single Centre Study

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#C92

OBJECTIVES

- There is currently **no consensus on restaging during and after administration of neoadjuvant chemotherapy (NAC)** in patients with **muscle invasive bladder cancer (MIBC)** prior to radical cystectomy.
- The aim of this study was to evaluate the **accuracy of radiological restaging after 2 and 4 cycles of NAC**, the **correlation between clinical and the final pathological tumour stage** at radical cystectomy (RC), and the **impact of restaging on further patient management**.

METHODS

Age at radical cystectomy (years); Median (IQR)	65 (59 – 73)
Sex	
Male	136 (76%)
Female	44 (24%)
Smoking status	
Never	70 (39%)
Past/Current	110 (61%)
Charlson Comorbidity Index	
≤2	135 (75%)
≥3	45 (25%)
BMI	
<25	87 (48%)
25-30	58 (32%)
>30	35 (19%)
Diabetes Mellitus Type 2	
Yes	17 (9.4%)
No	163 (91%)
Hydronephrosis	
None	127 (71%)
Left	40 (22%)
Right	9 (5.0%)
Bilateral	4 (2.2%)
Recurrent bladder cancer	
No (Primary)	141 (78%)
Yes	39 (22%)
Type of NAC	
Carboplatin-Gemcitabine	49 (27%)
Cisplatin-Gemcitabine	110 (61%)
Etoposide containing MVAC	5 (2.7%)
Cycles of NAC	
≤3	52 (29%)
4	112 (62%)
≥5	16 (8.9%)
Pre-NAC stage	
<T2N0M0	1 (0.6%)
T2N0M0	23 (13%)
T3N0M0	32 (18%)
T4aN0M0	12 (6.7%)
T4bN0M0	4 (2.2%)
TanyN+M0	63 (35%)
TanyNanyM1a	45 (25%)

- We conducted a **longitudinal, single-centre, cohort study** of prospectively collected data of **180 consecutive patients** who underwent **NAC for urothelial MIBC** between 07/2001 and 12/2017.
- Of those 180 patients, we identified 120 patients who had 4 cycles of NAC and in whom complete imaging (CT scans before, after 2 cycles and after completion of the NAC [before RC]) was available.
- All patients had **repeated CT scans** for restaging after **2 cycles of NAC** and **after completion of the NAC** before RC.
- All original findings of CT scans were re-reviewed by an **experienced urologist**.
- Primary endpoints were **overall survival, cancer specific survival and recurrence free survival**.
- Secondary endpoint was the **change in intended patient management and oncological therapy** according to the re-staging evaluation results.
- The data were prospectively recorded in the institutional database.

Supplementary table 1. Cross tables of patient's stage at different time points. Patients are N0M0 unless specified. (Green shading – down-staged, orange shading = up-staged).

		Prior to chemotherapy								After 2 nd cycle								After 4 th cycle							
		<T2	T2	T3	T4a	T4b	N+M0	M1a	<T2	T2	T3	T4a	T4b	N+M0	M1a	<T2	T2	T3	T4a	T4b	N+M0	M1a			
After 2 nd cycle	<T2	1	2	3	0	0	4	0	3	1	0	0	0	0	0	3	17	1	1	2	11	2			
	T2	0	19	3	0	0	8	4	1	17	1	1	2	3	0	0	0	18	0	0	3	2			
	T3	0	0	22	1	0	6	3	0	0	18	0	0	0	0	0	0	0	13	0	0	0			
	T4a	0	1	1	10	0	3	3	0	0	0	13	0	0	0	0	0	1	0	2	0	0			
	T4b	0	0	0	0	4	0	3	0	0	1	0	2	0	0	0	0	0	0	0	0	0			
	N+M0	0	0	1	0	0	35	12	0	0	1	0	0	20	0	0	0	0	1	0	20	0			
After 4 th cycle	<T2	0	2	2	0	0	1	0	0	0	0	0	0	1	9	0	0	0	0	0	1	9			
	T2	0	9	1	1	0	18	9	1	17	1	1	2	11	2	3	1	0	0	0	0	0			
	T3	0	0	15	0	0	6	4	0	0	18	0	0	0	3	2	0	0	18	0	0	3	2		
	T4a	0	1	0	9	0	0	3	0	0	0	13	0	0	0	0	0	0	13	0	0	0			
	T4b	0	0	0	0	2	1	0	0	0	1	0	2	0	0	0	0	1	0	2	0	0			
	N+M0	0	0	0	2	0	15	8	0	0	1	1	0	20	0	0	0	1	1	0	20	0			
After radical cystectomy	<T2	1	8	11	1	1	22	12	6	14	9	3	1	15	3	3	17	10	2	1	5	3			
	T2	0	7	7	1	0	8	4	3	7	7	2	2	3	0	2	10	3	2	0	0	0			
	T3	0	5	6	3	0	5	4	0	6	7	4	0	4	1	0	3	5	3	0	4	1			
	T4a	0	0	0	5	1	6	1	0	0	2	4	1	4	1	0	1	0	3	2	3	1			
	T4b	0	0	0	0	1	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0			
	N+	0	3	8	2	1	21	24	1	7	7	4	2	22	13	0	7	7	3	0	13	6			

Table 1: Pre-operative characteristics of the sample, N (%) unless otherwise specified.

RESULTS

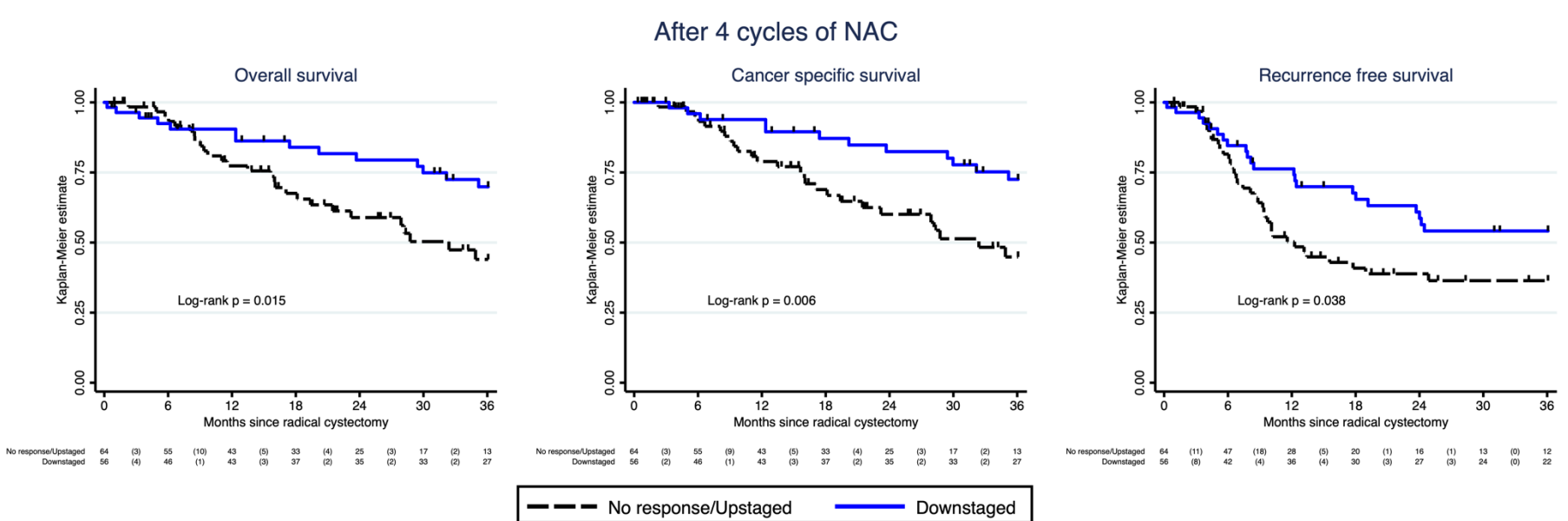
	N	Cancer specific survival	
		n (%) died of bladder cancer	HR (95% CI)
Change in stage after 2 cycles *			
No response/upstaged	73	28 (38%)	1.0
Downstaged	37	8 (22%)	0.48 (0.22 – 1.06)
Change in stage after 4 cycles **			
No response /upstaged	59	24 (41%)	1.0
Downstaged	51	12 (24%)	0.42 (0.21 – 0.85)
Change in stage after 4 cycles by status at 2 cycles ***			
No response /upstaged	59	24 (41%)	1.0
Downstaged by 2 cycles	36	8 (22%)	0.42 (0.19 – 0.94)
Downstaged by 4 cycles	15	4 (27%)	0.43 (0.15 – 1.25)
Clinical stage after 4 cycles			
≤T2N0M0	39	5 (13%)	1.0
T3N0M0	23	8 (35%)	3.66 (1.19 – 11.3)
T4aN0M0 or T4bN0M0	16	10 (63%)	6.38 (2.16 – 18.9)
TanyN+M0	22	10 (45%)	4.15 (1.41 – 12.2)
TanyNanyM1a	10	3 (30%)	3.16 (0.75 – 13.3)
Pathological stage			
<T2N0	37	2 (5.4%)	1.0
T2N0 or T3N0	31	11 (35%)	7.44 (1.65 – 33.6)
T4N0	9	4 (44%)	9.70 (1.77 – 53.1)
TanyN+	33	19 (58%)	15.1 (3.51 – 65.2)

Table 4. Patients followed up at 36 months with HR estimates. Patients included had stage imaging available before, after 2 cycles, and after 4 cycles of NAC and received at least 4 cycles of NAC (n=110).

Of all 180 patients, we identified **120 patients** who had **4 cycles of NAC** and in whom complete imaging was available. Clinical downstaging was achieved in **48/120 (40%) patients**, **69/120 (58%) patients** had no change in clinical stage and only 3/120 (2.5%) patients were clinically upstaged. Correlations between clinical stage and pathological stage was relatively strongest after **4 cycles of NAC** compared to findings after 2 cycles and prior to NAC (tau-b = 0.32, 0.28, 0.16 respectively).

With regards to the entire cohort, **further patient management was only changed in 2/180 (1%) patients** after 2 cycles of NAC based on radiological findings. Patients clinically down-staged after 4 cycles of NAC had a **statistically significant lower risk of cancer specific death** (HR = 0.46, 95%CI: 0.22 – 0.96, log-rank p=0.034) compared to those without downstaging after completion of NAC.

In the subset of patients with initial **cN+ disease** (before NAC) (n=76), 42/76 (55%) were staged cN0 on imaging after four cycles of NAC. 75% (100/133) of patients with ypN0 after completion of NAC remained ypN0 after PLND.



CONCLUSION

- Restaging of muscle invasive bladder cancer after completion of NAC by CT is a **strong predictor of CSS**. However; **re-staging after 2 cycles of NAC offers no additional information and does not change patient management** in the vast majority of (98%). Therefore, it may be omitted.