



PD60-05



Neoadjuvant chemotherapy plus radical cystectomy versus radical cystectomy alone in clinical T2 bladder cancer patients without hydronephrosis: results from a large multicenter cohort study

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Despite high-level evidence in favor of neoadjuvant chemotherapy (**NAC**) before radical cystectomy (RC), **compliance** with this recommendation remains **low**, **especially in cT2 disease** (probably as consequence of SWOG 8710 and BA06 30894 that showed a **greater survival for \geq T3 compared to T2**).

These results have led to a debate regarding which patients are most likely to benefit most from NAC, with the aim to find a balance between under and overtreatment.



The aim of the study was to **compare the efficacy of NAC + RC vs RC alone** in a large multicenter cohort of **cT2 patients without preoperative hydronephrosis**



Multicenter international retrospective collaboration
(**21 centers** across Europe, Canada and US)

Patients with cT2N0M0 without preoperative hydronephrosis were included

Primary endpoint: **pathologic response at RC**
Secondary endpoint: **overall survival**

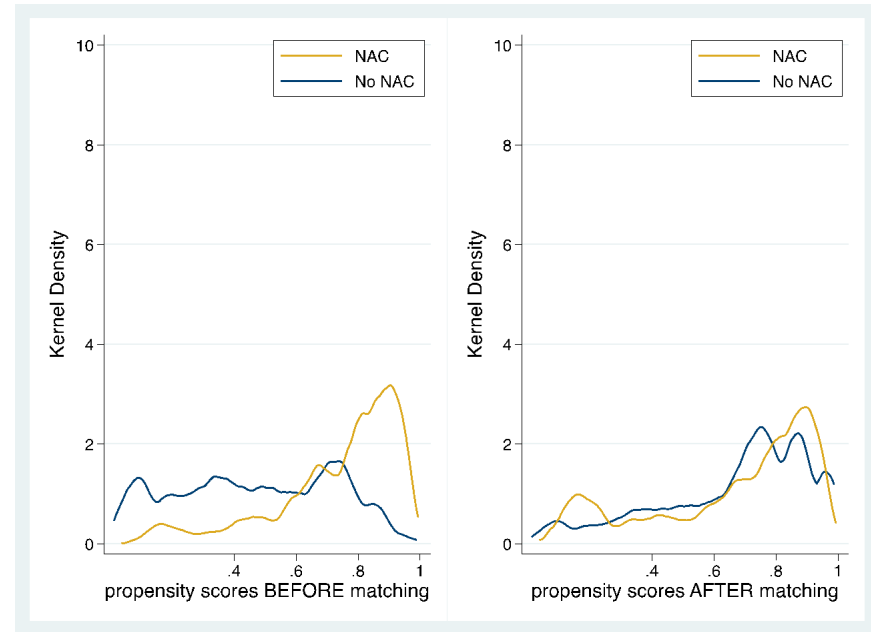
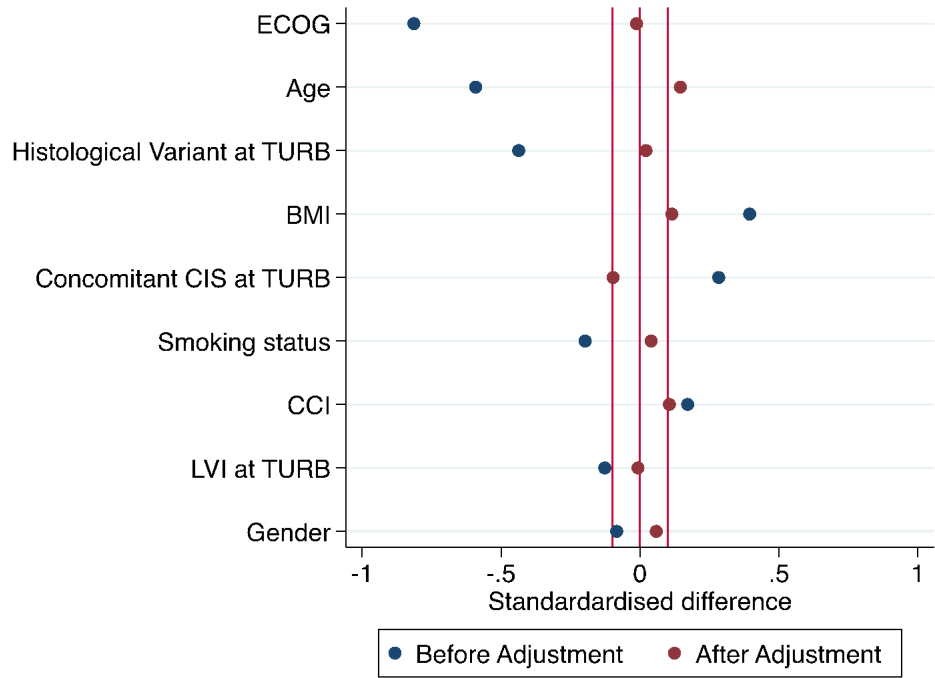


Multiple imputation to handle missing data for preoperative variables that were assumed to be missing at random for all covariates

Inverse probability of treatment weighting (**IPTW**) to account for potential selection bias



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Effect of inverse probability of treatment weighting adjustment on the baseline characteristics distribution among the study population.



RESULTS

619 patients (316 receiving NAC and RC and 303 treated only with RC) were included

Variables	Unweighted Study Population ^a				Weighted Study population ^b			
	Overall (n=619)	Receipt of neoadjuvant chemotherapy		Standardized difference, %	Overall	Receipt of neoadjuvant chemotherapy		Standardized difference, %
		No (n=303)	Yes (316)			No	Yes	
Median age (IQR), years	66 (59-73)	69 (63-76)	64 (57-70)	-53.5	67 (59-73)	67 (61-74)	67 (59-73)	14.5
Gender				4.3				5.8
Female	113 (19)	63 (21)	50 (16)		16	15	17	
Male	496 (81)	240 (79)	256 (84)		84	85	83	
Median BMI (IQR)	26.5 (23.7-30.0)	25.9 (23.1-28.6)	27.8 (23.7-31.0)	30.7	26.5 (24.1-30.0)	26.4 (24.1-29.3)	27 (24-30.6)	11.5
ECOG score				83.9				1.2
0	288 (74)	56 (50)	232 (84)		71	72	71	
1	74 (19)	34 (30)	40 (15)		22	20	23	
2	25 (6)	21 (19)	4 (1)		6	8	6	
3	1 (1)	1 (1)	0 (0)		0	0	1	
4	0 (0)	0 (0)	0 (0)		0	0	0	
Charlson Comorbidity Index				17				10.6
2-3	291 (57)	188 (64)	103 (47)		60	64	54	
4-5	156 (31)	80 (27)	76 (35)		26	22	30	
>6	64 (12)	24 (8)	40 (18)		14	13	15	
Smoking status				-25.2				4.0
Never smoker	113 (28)	23 (23)	90 (29)		27	29	24	
Former smoker	191 (46)	45 (45)	146 (47)		48	44	51	
Actual smoker	107 (26)	32 (32)	75 (24)		26	27	25	
Concomitant CIS at TURB	128 (21)	32 (11)	96 (30)	30.7	29	32	27	-9.7
LVI at TURB	113 (18)	41 (14)	72 (23)	-12.4	23	23	23	-0.7
Histological variants at TURB	91 (21)	44 (33)	47 (16)	-28.2	21	21	22	2.1

^a Data are presented as number (percentage) of patients unless otherwise indicated; ^b Data are presented as percentage of patients unless otherwise indicated

**RESULTS**

- **29% of NAC patients classified as complete responders vs 3% of RC only patients**
- Median follow up: 20 months (IQR9-41)
- Limitations: retrospective study, relatively short follow up

Pathologic outcomes after radical cystectomy among the study patients.

Variables	Overall (n=619)	Receipt of neoadjuvant chemotherapy		p value
		No (n=303)	Yes (316)	
Pathologic tumor stage, n (%)				<0.001
pT0	104 (16)	9 (3)	94 (30)	
pTa-Tis-T1	143 (23)	63 (21)	80 (25)	
pT2-T3-T4	373 (60)	231 (76)	142 (45)	
Lymph node metastases, n (%)	114 (20)	64 (24)	50 (16)	0.025
Pathologic LVI, n (%)	142 (33)	121 (41)	21 (16)	<0.001
Positive surgical margins, n (%)	48 (8)	26 (9)	22 (7)	0.5



Neoadjuvant chemotherapy showed to be associated with pathologic complete response and overall response at radical cystectomy even in patients with clinical T2 and absence of preoperative hydronephrosis

	OR	p value	[95% Conf. Interval]	
NAC	9.217004	<0.001	3.882896	21.87882
Age (cont.)	.9993815	0.974	.9626242	1.037542
Female gender	1.085481	0.863	.4278701	2.753801
Smoking	1.30361	0.305	.7858572	2.16248
CCI (re. 2-3)				
4-5	.5398769	0.155	.2310881	1.261281
≥6	.6649453	0.453	.2293004	1.928266
ECOG (cont.)	.7220173	0.351	.3643187	1.430915
BMI (cont.)	1.013032	0.702	.9479316	1.082603
Histological variant at TURB	.6323295	0.298	.2665489	1.500065
LVI at TURB	1.359339	0.452	.6109117	3.024663
CIS at TURB	.839383	0.664	.3814192	1.847216

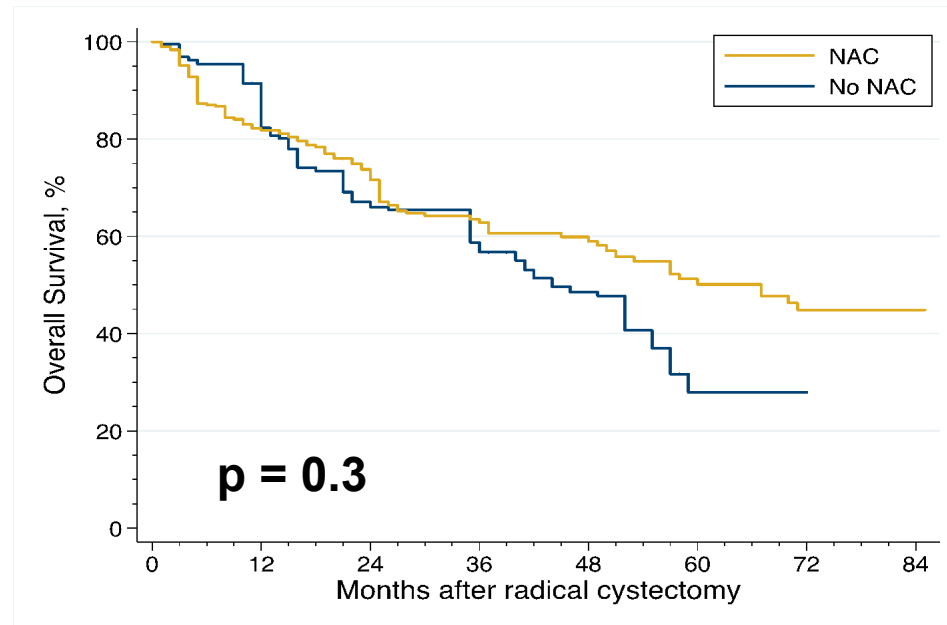
IPTW-adjusted multivariable logistic regression for the prediction of pTONOMO at radical cystectomy

	OR	p value	[95% Conf. Interval]	
NAC	3.680085	<0.001	2.188125	6.189328
Age (cont.)	1.004956	0.735	.9764405	1.034304
Female gender	.8457612	0.655	.4055378	1.76386
Smoking	1.645156	0.021	1.080066	2.505902
CCI (ref. 2-3)				
4-5	.7817034	0.421	.4290152	1.424332
≥6	.5689433	0.170	.2543146	1.272819
ECOG (cont.)	.6890991	0.124	.4288776	1.10721
BMI	1.013069	0.626	.9614529	1.067456
Histological variant at TURB	.6681212	0.197	.3619067	1.233428
LVI at TURB	.7446302	0.363	.3945533	1.405321
CIS at TURB	.9442428	0.849	.5231633	1.704237

IPTW-adjusted multivariable logistic regression for the prediction of <T2NOMO at radical cystectomy



However, we were not able to demonstrate a survival gain in favor of NAC, probably due to the relatively short follow up





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In **our multicenter retrospective propensity score-based analysis**, NAC showed to be associated with pathologic complete response at RC even in patients with clinical T2 and absence of preoperative hydronephrosis, thus **generating new evidences in favor of NAC also in low-risk patients**.

Thank you for your attention



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