CONCOMITANT CARCINOMA IN SITU AT RADICAL CYSTECTOMY: SURVIVAL, RECURRENCE AND FOLLOW-UP IMPLICATIONS

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Introduction & objectives:

- The presence of carcinoma in situ (CIS) at transurethral resection increases the risk of progression to invasive disease and recurrence.
- The evidence about the presence of concomitant CIS on survival outcomes after radical cystectomy (RC) due to bladder cancer (BC) is poor.
- **Aim of our study is to evaluate if the presence of concomitant CIS at RC impacts on recurrence and survival outcomes.**

Materials & methods:

- We evaluated **391 consecutive non metastatic patients diagnosed with BC and treated with RC** at a single tertiary referral centre between 2008 and 2015.
- Univariable and multivariable Cox proportional hazards regression analyses model was used to predict cancer specific mortality (CSM), overall mortality (OM) and recurrence.
- The Kaplan-Meier method was used to compare recurrence, CSM and OM in the overall population and in pT0-pT2 and pT3-pT4 patients stratified according to the presence of CIS.
- Covariates included age at surgery, gender, pathological T stage, pathological N stage, pathological grade, surgical margins and lymph vascular invasion.

Results:

Descriptive characteristics

Variables	OVERALL (n=391)
Age at surgery, years Median (IQR)	71 (40-90)
Gender, n (%) Male Female	322 (82) 69 (18)
ASA score, n (%) 1 2 3 4	36 (9) 183 (47) 145 (37) 27 (6)
Tumor stage, n (%) 2 3-4	217 (54,5) 174 (44,5)
Margins, n (%) Positive Negative	51 (13) 340 (87)
Pathologic nodal stage, n (%) pN0 pN +	274 (70.1) 117 (29.9)
Number of LN removed, n (%)	23 (10-73)
LVI, n (%) Yes No	35 (9) 356 (91)
Adjuvant chemotherapy, n (%) Yes No	57 (14.6) 334 (85,4)
Adjuvant radiotherapy, n (%) Yes No	25 (6.4) 366 (93.6)
Postoperative follow-up, months Median (IQR)	30 (5-130)

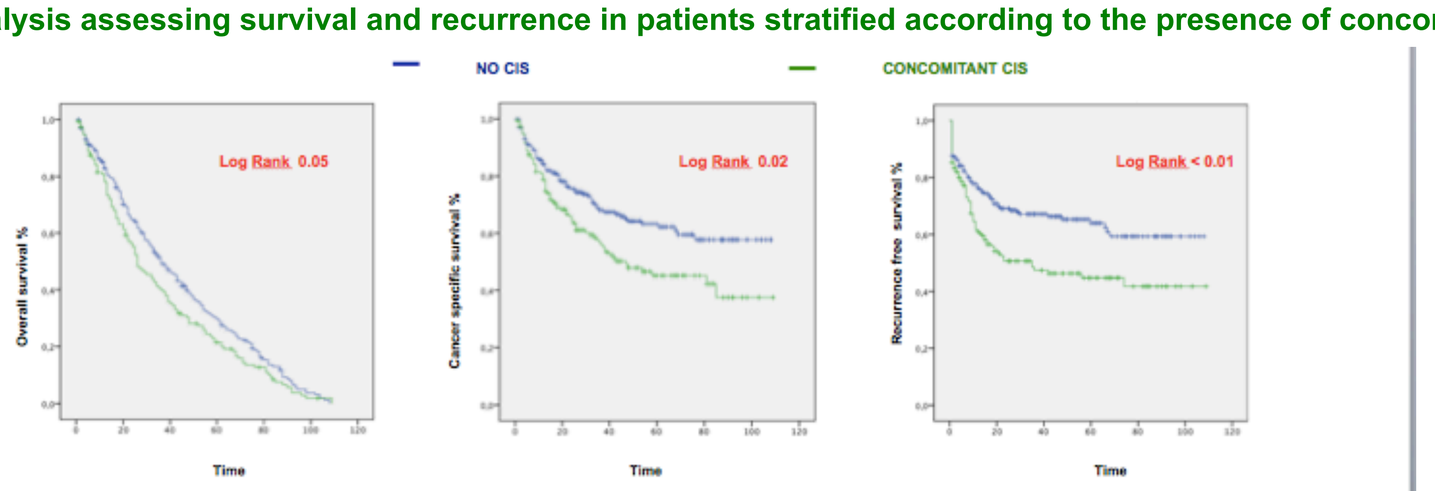
Univariable and Multivariable Cox Regression predicting CSM, OM and Recurrence

	CANCER SPECIFIC MORTALITY		OVERALL MORTALITY		RECURRENCE	
	Univariable		Univariable		Univariable	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age at surgery	1 (0.99-1.02)	0.7	1.09 (1.07-3.16)	<0.001	1 (0.99-1.02)	0.7
ASA	1.07 (0.91-1.25)	0.4	1.34 (1.22-1.47)	<0.001	1.07 (0.91-1.25)	0.4
Gender	2.5 (0.96-3.67)	0.6	1.22 (0.83-1.79)	0.3	1.5 (0.97-3.67)	0.3
Pathologic tumor stage T2 vs T3-T4	3.7 (2.39-5.73)	<0.001	0.93 (0.63-1.37)	0.7	3.7 (2.39-5.73)	<0.001
Pathologic nodal stage pN0 vs pN+	2.91 (1.79-4.73)	<0.001	1.38 (0.65-2.93)	0.4	2.91 (1.79-4.73)	<0.001
Surgical margins	1.5 (0.93-2.27)	0.1	1.22 (0.93-1.59)	0.3	1.5 (1.07-2.67)	<0.001
LVI	1.07 (1.91-2.25)	<0.001	1.11 (1.09-1.27)	0.3	1.07 (1.91-2.25)	<0.001
Adjuvant Radiotherapy	12.27 (5.90-22.32)	<0.001	1.17 (0.78-1.72)	0.3	11.4 (3.90-21.32)	<0.001
Adjuvant Chemotherapy	10.17 (4.88-21.34)	<0.001	1.14 (1.12-1.47)	0.4	10.6 (4.88-18.34)	<0.001
Concomitant Cis	1,55 (1.05-4.84)	<0.001	1.11 (1.09-1.27)	0.08	1.28 (1.02-3.92)	<0.001

	CANCER SPECIFIC MORTALITY		OVERALL MORTALITY		RECURRENCE	
	Multivariable		Multivariable		Multivariable	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age at surgery	1 (0.99-1.02)	0.7	1.09 (1.07-1.1)	0.02	1,6 (0.97-1.52)	0.5
ASA	1.07 (0.91-1.25)	0.4	1.34 (1.22-1.47)	<0.001	1.15 (0.61-1.15)	0.4
Gender	1.5 (0.82-3.67)	0.3	1.22 (0.83-1.79)	0.3	1.52 (0.7-1.67)	0.3
Pathologic tumor stage T2 vs T3-T4	3.7 (2.39-5.73)	<0.001	0.93 (0.63-1.37)	0.7	3.7 (2.39-5.73)	<0.001
Pathologic nodal stage pN0 vs pN+	2.91 (1.79-4.73)	<0.001	1.38 (0.65-2.93)	0.4	2.91 (1.79-4.73)	<0.001
Surgical margins	2.5 (0.96-3.67)	0.6	1.22 (0.83-1.79)	0.3	1.5 (0.97-3.67)	0.1
LVI	1.07 (0.91-1.25)	0.4	1.11 (1.09-1.27)	0.3	2.17 (1.41-4.25)	<0.001
Adjuvant Radiotherapy	1.27 (0.90-1.32)	0.07	1.17 (0.78-1.72)	0.3	11.27 (4.90-18.32)	<0.001
Adjuvant Chemotherapy	10.17 (4.88-22.34)	<0.001	1.14 (0.82-1.66)	0.4	14.17 (6.88-24.34)	<0.001
Concomitant Cis	1.27 (0.90-1.32)	0.5	1.17 (0.88-1.52)	0.3	1.37 (0.88-1.34)	0.5

	CANCER SPECIFIC MORTALITY		OVERALL MORTALITY		RECURRENCE	
	Multivariable		Multivariable		Multivariable	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Cis in pT0-2	1.8(1.09-5.02)	0.02	1.09 (0.67-1.1)	0.4	1,6 (0.97-1.52)	0.5
Cis in pT3-4	1.07 (0.91-1.25)	0.4	1.34 (0.62-1.47)	0.3	1.15 (0.61-1.15)	0.4

Kaplan meier analysis assessing survival and recurrence in patients stratified according to the presence of concomitant Carcinoma in Situ



Conclusions: **CIS is considered e negative prognostic factor at TURB that contributes to cystectomy indication. However concomitant presence of CIS at cystectomy does not increase the risk of recurrence and does not impact on survival outcomes. The most important features to consider in follow-up schedules are pathological stage, lymph node status and lymph vascular invasion.**