ROLE OF MIXED UROTHELIAL-SQUAMOUS HISTOLOGICAL VARIANT PERCENTAGE ON SURVIVAL OUTCOMES AFTER RADICAL CYSTECTOMY FOR BLADDER CANCER

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Introduction & objectives:

- About 20% of bladder cancer (BC) is represented by non-urothelial variants (pure or mixed). The different histologies are expression of different molecular alterations which are directly related to the disease aggressiveness.
- Identification of the histological variants is mandatory for the good quality treatments and disease management after radical cystectomy (RC).
- **Aim of our study was to evaluate the role of mixed urothelial-squamous histological variant percentage on survival outcomes after RC due to BC.**

Materials & methods:

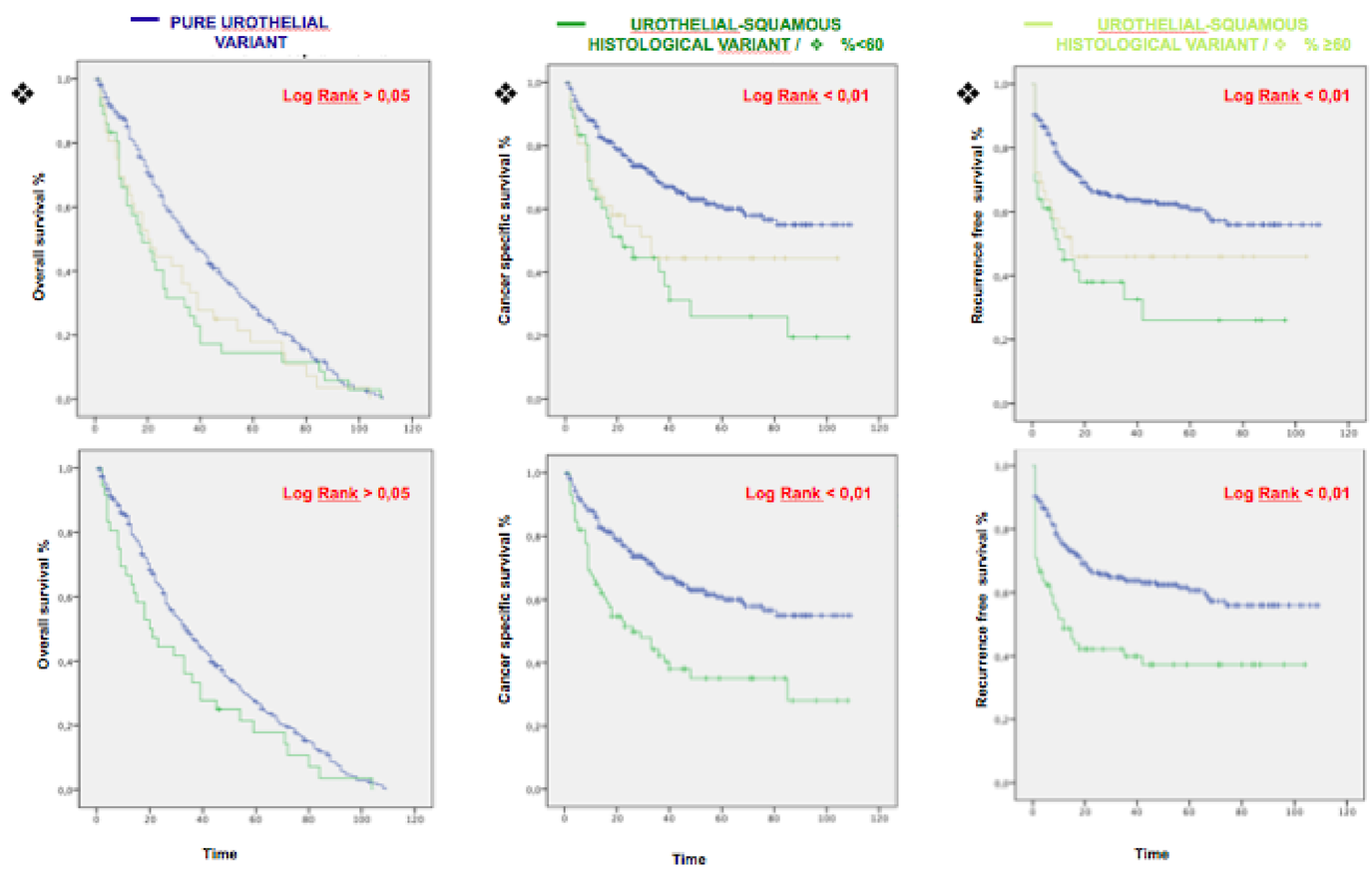
- We evaluated **34 consecutive non metastatic patients with BHV,** We evaluated **391 consecutive non-metastatic patients diagnosed with BC and treated with RC** at a single tertiary referral centre between 2008 and 2015.
- Specimens were evaluated by a dedicated uro-pathologist.
- Univariable and multivariable Cox proportional hazards regression analyses model was used to predict cancer specific mortality (CSM), overall mortality (OM) and recurrence rate. The Kaplan-Meier method was used to compare recurrence, CSM and OM in overall population considering patients with the mixed histological variants.
- 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)	MIXED UROTHELIAL (N= 72; 18%)	PURE UROTHELIAL (N= 319; 82%)	P-VALUE
Age at surgery, years Median (IQR)	71 (40-90)	71 (48-84)	70 (40-90)	0.5
Gender, n (%) Male Female	322 (82) 69 (18)	57 (79) 15 (21)	265 (82) 54 (18)	0.06
ASA score, n (%) 1 2 3 4	36 (9) 183 (47) 145 (37) 27 (6)	5 (7) 34 (47) 28 (39) 5 (7)	31 (9) 149 (47) 117 (37) 22 (7)	0.1
Tumor stage, n (%) 2 3-4	217 (54,5) 174 (44,5)	36 (50) 36 (50)	181 (56.7) 138 (43.3)	0.03
Margins, n (%) Positive Negative	51 (13) 340 (87)	14 (19.5) 58 (80.5)	37 (11,5) 282 (88,5)	0.01
Pathologic nodal stage, n (%) pN0 pN +	274 (70.1) 117 (29.9)	35 (48.6) 37 (51.4)	212 (66.5) 107 (43.5)	0.01
Number of LN removed, n (%)	23 (10-73)	25 (10-63)	22 (10-73)	0.05
LVI, n (%) Yes No	35 (9) 356 (91)	34 (47) 38 (53)	93 (29) 226 (71)	0.01
Adjuvant chemotherapy, n (%) Yes No	57 (14.6) 334 (85,4)	12 (16.6) 60 (84,4)	45 (14.1) 274(85,9)	0.06
Adjuvant radiotherapy, n (%) Yes No	25 (6.4) 366 (93.6)	5 (6.9) 67 (93.1)	20 (6.3) 299 (93.7)	0.2
Postoperative follow-up, months Median (IQR)	30 (5-130)	28 (5-110)	31 (5-109)	0.1

Kaplan meier analysis assessing survival and recurrence in patients stratified according to Histology and to Urothelial-Squamous Histological variant percentage (median 60%; IQR 5-95%)



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
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
Histological mixed variant	1,55 (1.05-4.84)	<0.001	1.11 (1.09-1.27)	0.08	1.28 (1.02-3.92)	<0.001
Histological mixed variant %	2,45 (1.35-5.64)	<0.001	1.17 (0.78-1.72)	0.3	1,88 (1.08-4.02)	<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
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
Histological mixed variant	1.27 (0.90-1.32)	0.5	1.17 (0.88-1.52)	0.3	1.27 (0.90-1.32)	0.5
Histological mixed variant %	1.17 (0.88-1.34)	0.4	1.18 (0.92-1.47)	0.4	1.17 (0.88-1.34)	0.4

Conclusions:

Our study confirms literature data about the frequency of histological variants at RC. Moreover, the mixed variants, although presenting more aggressive features, do not seem to impact negatively on survival outcomes compared with pure urothelial BC, even without considering the percentage of variant on the specimen

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