Urothelial Cancers

10:15am - 12:00pm Wednesday, 3rd November, 2021

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168 Practice Patterns for Non-Muscle Invasive Bladder Cancer in an Integrated Community Urology Practice: Where Do We Stand?

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Abstract

Objectives:

To determine the practice patterns for Non-Muscle Invasive Bladder Cancer (NMIBC) in an integrated community urology practice. We report the implementation of management guidelines for NMIBC. To ensure patients receive timely surveillance and intervention we sought to determine the incidence of patients who were lost-to-follow-up (LTFU).

Methods:

We evaluated the electronic medical records of all patients with diagnosis of BC between January 1, 2019 and December 30, 2019. One hundred patients who underwent transurethral resection of bladder cancer (TURBT) were randomly selected and manually reviewed by two urologists and two trained data analysts. Risk category was defined per European Association of Urology guidelines. High risk (HR) group includes high-grade (HG) tumors or recurrent and large low-grade (LG) tumors. Low risk (LR) group includes solitary small LG tumors. Intermediate risk (IR) includes all tumors not meeting the definition LR or HR tumors. We queried the use and indications for Intravesical BCG. The quality of TURBT was assessed by presence of muscularis propria for HG Ta and T1 tumors. LTF was defined as no follow-up in one year since first post-operative visit.

Results:

100 patients (19 female and 81 male) with NMIBC were identified. Fifty-six (56%), 14 (14%), and 30 (30%) patients were categorized in HR, IR, and LR groups, respectively. Staging was T1 in 29, Ta in 62, T1+CIS in 1, Ta+CIS in 5 patients, and CIS in 3 patients. Muscularis propria was present in 21 of 30 (70%) specimens for T1 tumors, 23 of 31 (74%) specimens for HG Ta tumors. BCG was administered in 59% (33 pts), 21% (3 pts), and 17% (5 pts) of patients with HR, IR, and LR tumors, respectively. Only 8 out of 100 patients were found to be LTFU. Of the 8 patients with LTFU, 3 had transferred care, 1 is deceased, 1 is 99 years old, and 3 were true LTFU.

Conclusions:

We identified a mixed practice pattern for NMIBC among community urologists, which includes overtreatment for LR and undertreatment for HR bladder tumors. This study highlights the importance of future quality improvement projects to promote adherence to NMIBC guidelines.

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None

196 Utility of Blue Light Cystoscopy for Post-BCG Bladder Cancer Recurrence Detection: Implications for Clinical Trial Recruitment and Study Comparisons

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Abstract

Purpose: The utility of blue light cystoscopy (BLC) in patients receiving Bacillus Calmette Guerin (BCG) during post-treatment cystoscopy is not well understood. Our objective was to determine if BLC improves recurrence detection in non-muscle invasive bladder cancer (NMIBC) patients undergoing BCG.

Materials and Methods: Using the prospective multi-institutional Cysview registry (2014-2019), NMIBC patients who received BCG within 1 year prior to BLC were identified. Primary outcomes were recurrences and whether lesions were detected on white light cystoscopy (WLC), BLC, or both. To demonstrate the utility of BLC, we calculated the percentage of cystoscopies with recurrence that would have been missed with WLC alone. The false positive rate was the proportion of cystoscopies with biopsies only due to BLC suspicious lesions with benign pathology.

Results: From 1703 BLC procedures, there were 283 cystoscopies in the analytic cohort. The overall recurrence rate was 44.9% (n=127). If only WLC had been used, 13% (n=16) of recurrences would have been missed because 9% (n=16) of cystoscopies with normal WLC had recurrences identified with BLC. Among the 16 patients with recurrence missed with WLC, 88% (n=14) had CIS. The false positive rate was 4% (n=11).

Conclusions: BLC helped identify patients with recurrences after recent BCG that would have been missed with WLC alone. Providers should consider using BLC for high-risk patients undergoing BCG. As clinical trials for novel therapies for BCG unresponsive disease increase and there are no clear guidelines on BLC use for post-BCG cystoscopies, it is important to consider how variable BLC use could affect comparisons of these studies.

Table 2. Highest Stage on WLC vs. BLC in Patients with Differences in Stage Noted

	Highest Stage Based on Blue Light Cystoscopy				
Highest Stage Based on White Light Cystoscopy	HGTa	HGTa + CIS	CIS	T1	T1 + CIS
T0	1	2	11	1	1
HGTa					
CIS					1

147 A Urine-Based DNA Methylation Marker Test to Detect Upper Tract Urothelial Carcinoma: A Pilot Study

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Abstract

Objectives: Diagnosis and preoperative risk stratification of the patients with upper tract urothelial carcinoma (UTUC) present distinct challenges given the limitations of currently available diagnostic tools. Herein, we explore the feasibility of a urine-based epigenetic assay to detect UTUC.

Materials and Methods: Under an IRB-approved protocol, urine samples were collected from UTUC patients before radical nephroureterectomy (RNU)/ureteroscopy (URS) between December 2019 and April 2021. Patients with concomitant bladder cancer and those who did not pass the quality control due to low DNA concentration were excluded. Samples were analyzed with Bladder CARE™, a urine-based assay that measures methylation levels of 3 cancer biomarkers (TRNA-Cys, SIM2, and NKX1-1) and two internal control loci using methylation-sensitive restriction enzymes coupled with qPCR. Results are reported as Bladder CARE Index (BCI) score and categorized as positive (BCI>5), high-risk (BCI 2.5-5), or negative (BCI<2.5), which correlate to the concentration of cancer DNA in the sample. The findings were compared to 64 sex/age-matched healthy individuals.

Results: A total of 29 patients (26 RNU, 3 URS) with a median age of 75 years were included in the study. Final pathology of patients who underwent nephroureterectomy revealed stage Ta (n=12), T1 (n=4), T2 (n=4), and T3 (n=6) UTUC. Among all samples, 28 showed positive and 1 high-risk BCI results. Urine cytology was available in 18 patients, in whom 6 had positive BCI results despite negative cytology. UTUC patients had significantly higher BCI values compared to the control cases (average BCI value of 214.04 vs. 1.7, respectively; $p < 0.0001$) (Figure 1-A). The Receiver Operating Characteristic (ROC) curve demonstrating the sensitivity, specificity, positive predictive value, and negative predictive value of 100%, 86%, 76%, and 100%, respectively (Fig. 1B).

Conclusions: In this pilot study, the proposed urine-based epigenetic assay showed high sensitivity and negative predictive value in the diagnosis of patients with UTUC. A larger sample size study to validate the accuracy of this test is the next step.

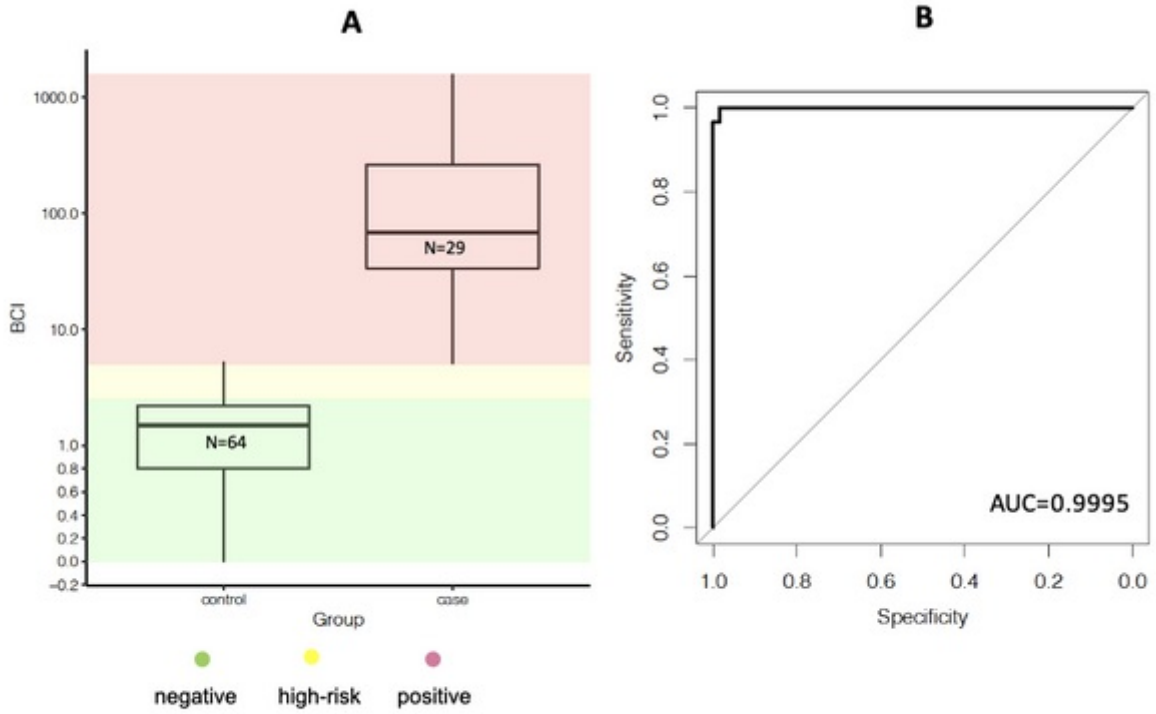

Figure-1. (A) Distribution of BCI in UTUC and control groups; (B) Receiver Operating Characteristic (ROC) curve using the BCI values

If funding provided, type in source company / entity name(s):

None

213 Single-cell transcriptional profiles of histologic variants in bladder cancer

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Abstract

Introduction and objectives: Histologic variants in bladder cancer are clinically aggressive tumors associated with poor prognosis. The rarity of these tumors has made transcriptomic characterization elusive. The aim of this study was to investigate the transcriptional profile of histologic variant bladder tumors at a single cell resolution.

Methods: Seven histologic variant and non-urothelial bladder tumors (plasmacytoid, micropapillary, lymphoepithelioma, squamous, nested, mixed, paraganglioma), 3 high-grade pure urothelial tumors, 3 normal mucosa specimens were collected from patients undergoing surgery at our institution. Pathologic diagnoses were independently confirmed. Cells from each specimen were isolated, captured, and sequenced using a bead-based single-cell RNA sequencing platform (SEQWELL) and analyzed using Seurat and cellxgene statistical and visualization software.

Results: After quality control, 20,689 cells, of which 6,626 were identified as tumor/epithelial cells, were available for analysis. Unsupervised clustering revealed that individual tumor cell populations to cluster separately by patient while stromal elements cluster by cell type. Histologic variant tumor cells showed varying degrees of urothelial differentiation and expression of common urothelial markers, with pure plasmacytoid demonstrating the highest degree of urothelial differentiation compared to pure squamous and paraganglioma, which were the lowest. A lack of CK20 was observed in all variants except plasmacytoid. Sub-clustering analysis of tumor cells from each patient demonstrated intratumoral heterogeneity in all tumors defined primarily by differential expression of transcription factors. Some heterogeneity could be explained by molecular subtyping at the single cell level. IGF2 and TM4SF1 expression were distinctive between pure urothelial tumors and histologic variants.

Conclusions: Histologic variants in bladder cancer have distinct transcriptional profiles compared with pure urothelial tumors. Transcriptional analysis at the single cell level can help identify genes that define histologic variants and may reveal novel targetable molecular interactions.

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California Urology Foundation

161 Impact of Variant Histology on Oncological Outcomes in Upper Tract Urothelial Carcinoma: Results from the ROBUUST Collaborative Group

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Abstract

Introduction:

Upper tract urothelial carcinoma (UTUC) is an aggressive tumor that is associated with high recurrence and mortality rates. While oncologic implications of variant histology (VH) have been extensively studied in bladder cancer, further investigation is needed in UTUC. Our study aims to evaluate the impact of VH on oncological outcomes in UTUC patients treated with minimally invasive radical nephroureterectomy (RNU).

Methods:

A retrospective analysis was performed on patients who underwent a robotic or laparoscopic RNU for UTUC using the ROBUUST database, a multi-institutional collaborative including 17 centers worldwide. Logistic regression was used to assess the effect of VH on urothelial (bladder, contralateral kidney/ureter) recurrence, metastasis, and survival following RNU.

Results:

A total of 687 patients were included in the study. Median (IQR) age of 71 (64-78) years and 470 (68%) had organ confined disease. VH was present in 70 (10.2%) patients. In a median follow-up of 15 months, the incidence of urothelial recurrence, metastasis, and overall mortality was 27%, 15%, and 12%, respectively. Oncologic outcomes and metastatic site details are shown in Table 1. VH was associated with increased risk of metastasis (HR 3.6, $p < 0.0001$) and death (HR 2.5, $p = 0.001$), but did not significantly influence urothelial recurrence (Figure 1). Multivariable analysis showed VH to be an independent risk factor for metastasis (HR 2.0, $p = 0.004$), but not for overall mortality or urothelial recurrence.

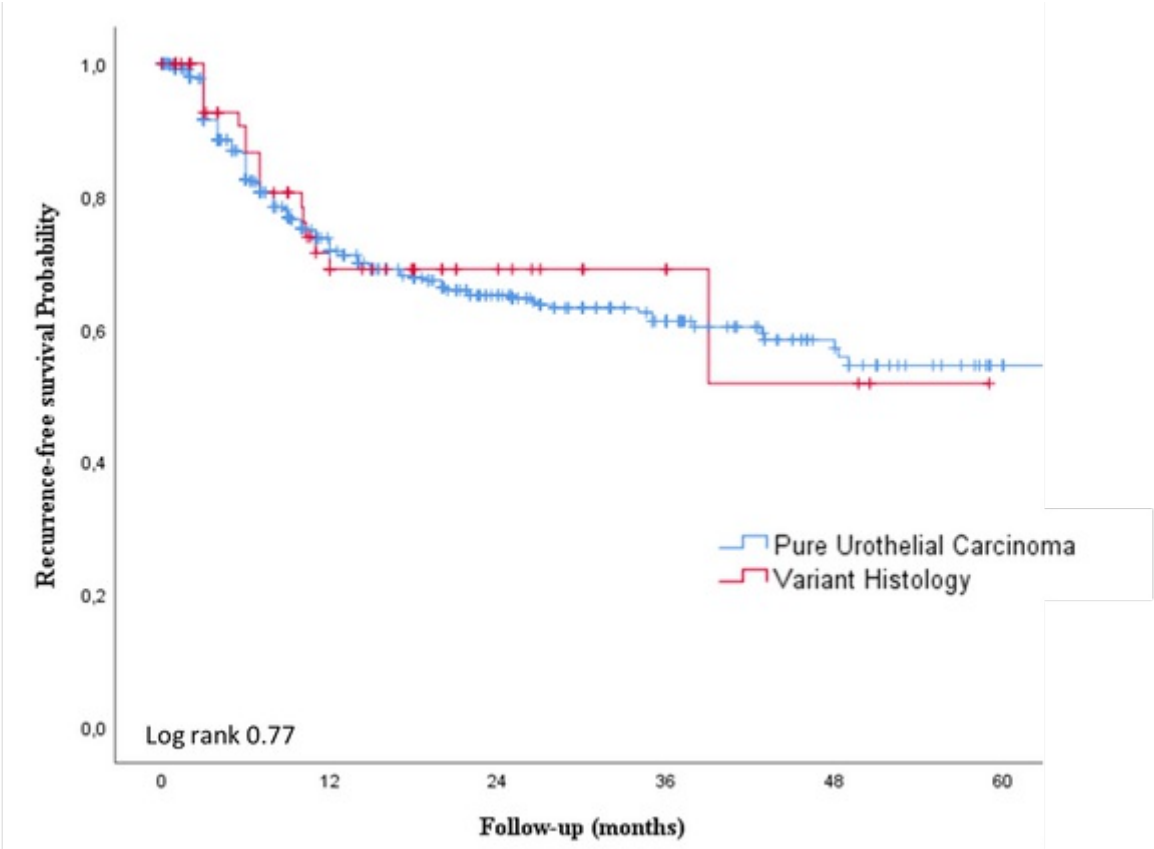
Conclusions:

Variant histology can be found in 10% of patients with UTUC. It was associated with higher rates of metastasis as well as overall mortality and was noted to be an independent risk factor for metastasis following RNU. There was no significant effect on urothelial recurrence in the bladder or contralateral kidney/ureter.

Table 1: Oncologic outcomes for 687 patients with UTUC who underwent RNU

		All patients	Pure Urothelial	Variant Histology	p-value
Recurrence N (%)	-	*184 (26.8)*	168 (27.2)	16 (22.9)	0.423
Site of Recurrence N (%)	**Bladder**	*169 (91.9)*	154 (91.7)	15 (93.75)	0.508
	Contralateral Kidney or ureter	*8 (4.5)*	8 (4.8)	0	
Time to Recurrence (months) Median (IQR)	-	*6 (3 – 11)*	6 (3 – 11)	6 (3 – 10.3)	0.79
Metastasis N (%)	-	*105 (15.3)*	78 (12.6)	27 (38.6)	**<0.001**
Site of Metastasis (Detail) N (%)	**Local Nodes**	21 (20)	19 (24.4)	2 (7.4)	**0.035**
	Distant Nodes	*7 (6.7)*	4 (5.1)	3 (11.1)	
	Lung	*19 (18.1)*	16 (20.5)	3 (11.1)	
	Bone	*7 (6.7)*	3 (3.8)	4 (14.8)	
	Liver	*11 (10.5)*	10 (12.8)	1 (3.7)	
	Multiple organs	*22 (21.0)*	13 (16.7)	9 (33.3)	
	Mesenteric	*4 (3.8)*	2 (2.6)	2 (7.4)	
	Local Soft Tissue	*4 (3.8)*	2 (2.6)	2 (7.4)	
	Other	*10 (9.5)*	9 (11.5)	1 (3.7)	
Time to Metastasis (months) Median (IQR)	-	*7 (3 - 14)*	7 (3 – 15)	6 (2 – 12)	0.181
Death N (%)	-	*81 (11.8)*	64 (10.4)	17 (24.3)	**0.001**
Cause of Death N (%)	**Tumor**	*71 (10.3)*	56 (9.1)	15 (21.4)	**0.001**
	Other	*46 (6.7)*	40 (6.5)	6 (8.6)	
Time to Death (months) Median (IQR)	-	*10.4 (4.1 – 18)*	9.5 (4 – 18.8)	11 (6 – 18)	0.647

1A



1B

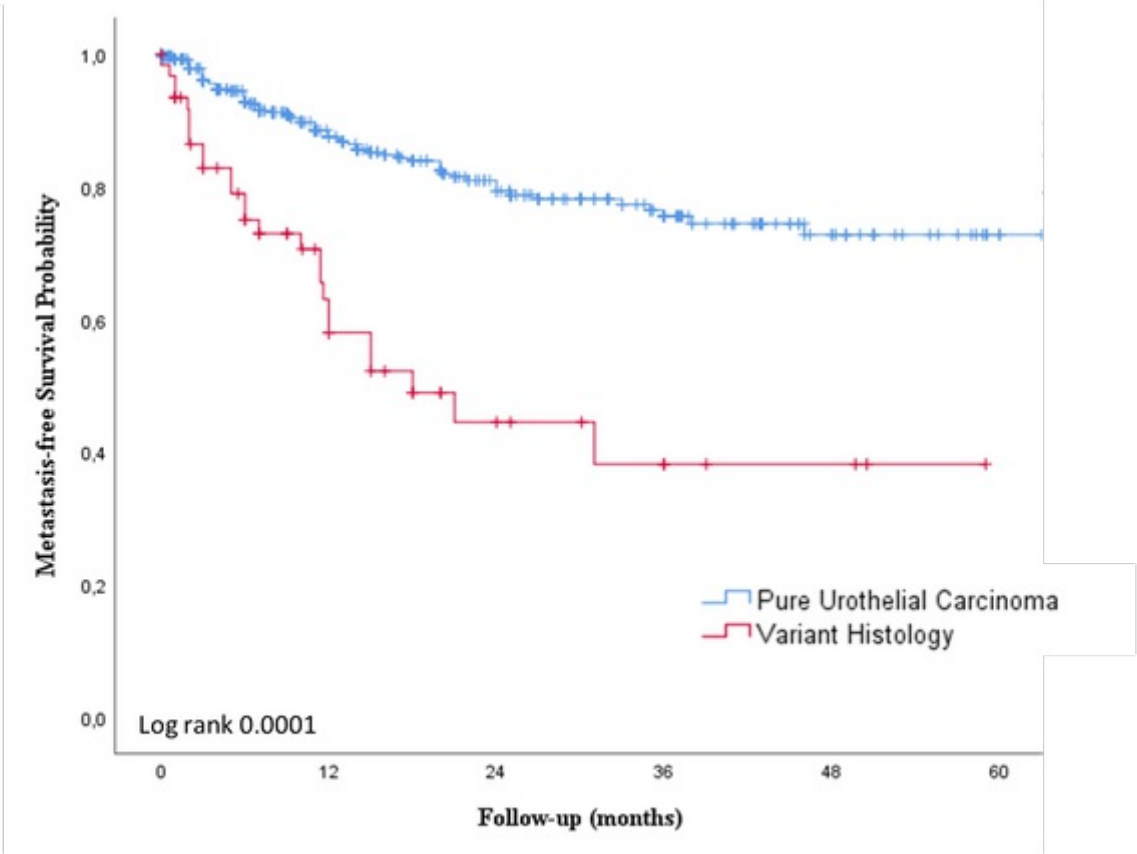


Figure 1: KM plot for Recurrence Free Survival (1A) and Metastasis Free Survival (1B) based on

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University of Southern California

226 The Care Assessment Need (CAN) score to estimate Life Expectancy in patients diagnosed with Bladder Cancer in the Veterans Health Administration

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Abstract

Objectives: Patients with muscle invasive bladder cancer are often older and present with comorbid conditions and tools that estimate life expectancy can guide clinical decision making for patients considering cystectomy. The Care Assessment Needs (CAN) score is an existing risk assessment tool that utilizes a variety of variables from electronic health records (EHR) and is automatically calculated for individual patients receiving care in the Veterans Health Administration (VHA). The CAN score produces a percentile score (0 to 99) that incorporates patient age, diagnoses, laboratory data, vital signs, medication use, and services utilization. We sought to investigate the utility of the CAN score to estimate 5-year life expectancy in patients with bladder cancer undergoing radical cystectomy.

Materials and Methods: We identified all patients diagnosed with bladder cancer who underwent radical cystectomy between 2013 and 2018 in the VHA. We utilized the CAN 1-year mortality model version 2.5, with score recorded within one month prior to surgery. We visualized unadjusted survival using Kaplan-Meier plots. We fit unadjusted and multivariable Cox proportional hazards models to determine the association between the CAN score and overall survival.

Results: We identified 1,192 patients with bladder cancer that were treated with radical cystectomy and had an available CAN score in the month prior to diagnosis. Median age at surgery was 68.2 (IQR 63.9, 72.6), 1,180 (99%) patients were male, 112 (9.4%) had neobladder urinary diversion, 680 (57%) had T2 or greater stage disease, 387 (32.5%) received neoadjuvant chemotherapy. Median Charlson comorbidity index (CCI) was 2.0 (IQR 0.0 ,4.0). Median CAN score was 60 (IQR 40, 75). In models adjusted for age, race, chemotherapy, and diversion type, the CAN score was independently associated with survival (HR per 5-unit change=1.08, 95%CI 1.06,1.10).

Conclusions: The CAN score is a readily available EHR score that is automatically calculated for individual patients receiving care in the VHA. The CAN score is strongly associated with survival following radical cystectomy for bladder cancer. Incorporating the CAN score into clinical practice can help clinicians efficiently risk-stratify patients to provide patient-centered bladder cancer care.

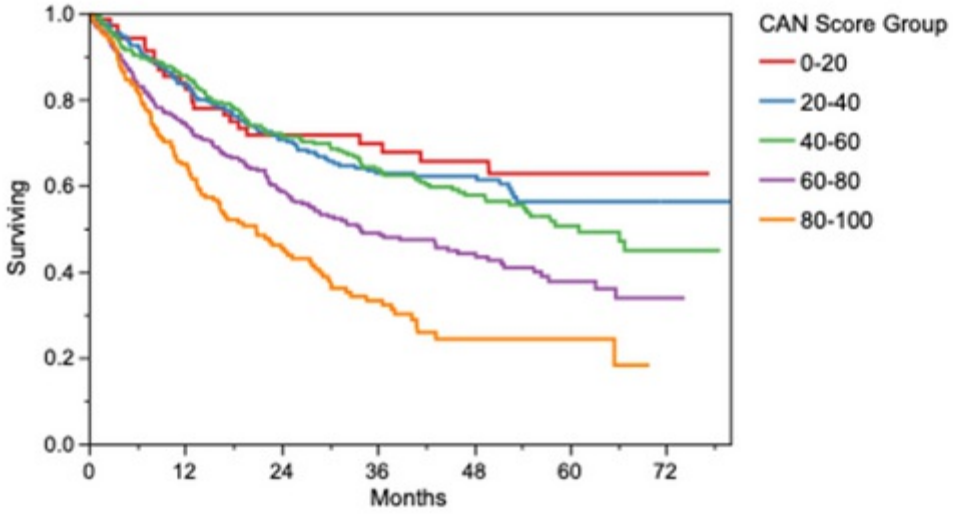

Figure 1: Unadjusted overall survival outcomes for patients stratified by Care Assessment Need (CAN) scores using Kaplan-Meier product-limit plots. An increased CAN score is associated with decreased overall survival in patients who underwent radical cystectomy for bladder cancer.

30 Neoadjuvant Platinum-Based Chemotherapy is Associated with Significant Reductions in Skeletal Muscle Mass and Visceral Fat Prior to Radical Cystectomy: Implications for Chemotherapy-Associated Adverse Events and Oncologic Outcomes

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Abstract

Objectives: Skeletal muscle index (SMI) is associated with oncologic outcomes and chemotherapy-related adverse events (CTACE) in muscle-invasive bladder cancer (MIBC) and numerous other malignancies. Prior small case series suggest neoadjuvant chemotherapy (NAC) is associated with reduced SMI with limited data for subcutaneous fat index (SFI) and visceral fat index (VFI). Herein, we examine changes in SMI, SFI, and VFI with NAC and describe associations with CTCAE and all-cause mortality (ACM) in patients with MIBC.

Methods: Retrospective review of patients with (≥pT2 N0/x M0) MIBC and those with computed tomography scans within 75 days prior to start (T1) and following completion (T2) of NAC (2006-19). SMI, SFI, and VFI (cm^2/m^2) were measured at the level of the mid-third lumbar vertebra. Associations with grade ≥3 CTCAE during NAC, and ACM were quantified using multivariable logistic regression and Cox proportional hazards models. Median follow-up was 18 months (IQR:10-33).

Results: The study cohort included 170 patients with median age of 63 years. NAC consisted of Gemcitabine/Cisplatin (52%), MVAC (28%), or other (20%), with a median of 4 cycles (IQR:3-5). Changes in SMI, SFI, and VFI during a median of 112 days (IQR:94-146) are presented in the Table. 117 (69%) patients experienced grade ≥3 CTCAE. Neither baseline nor change in body composition metrics during NAC were associated with grade ≥3 CTCAE. SMI at T1 (HR:0.98; 0.97-0.99, p=0.008), as well as SMI (HR:0.98; 0.96-0.99, p=0.003), SFI (HR:0.99; 0.98-1.0, P=0.03), and VFI (HR:0.99; 0.99-1.0, p=0.05) at T2 were associated with ACM after adjusting for age, T and N stage, and performance status.

Table: Change in skeletal muscle, visceral fat, and subcutaneous fat indices during neoadjuvant chemotherapy for bladder cancer.

Body Composition Variable	Pre-NAC (median, IQR)	Post-NAC (median, IQR)	Change	% change	P-value (Paired Wilcoxon Rank Sum)
SMI (cm^2/m^2)	49.3 (41.6, 55.3)	46.1 (41.1, 53.1)	-3.17	-6.4%	<0.0001
Muscle density (HU)	41 (34, 47)	42 (34, 47)	+1	+2.4%	0.81
VFI (cm^2/m^2)	54.8 (31, 86.6)	51.9 (27, 82.8)	-2.89	-5.2%	0.04
SFI (cm^2/m^2)	54 (33.7, 75.1)	54.4 (33.6, 75.3)	+0.47	+0.86%	0.45

Conclusions: Patients undergoing NAC prior to radical cystectomy experienced a 6.4% decrease in SMI and 5.2% decrease in VFI. CTCAE were not associated with change in SMI, SFI or VFI. Baseline SMI and post-

treatment SMI, SFI and VFI were associated with ACM on multivariable analysis. These data suggest that comprehensive body composition analysis of patients with MIBC before NAC warrants further study.

If funding provided, type in source company / entity name(s):

None

220 Early postoperative acute kidney injury following radical cystectomy and urinary diversion in patients on enhanced recovery protocol: Incidence, predictors and associated outcome

Sina Sobhani MS, Hamed Ahmadi MD, Wenhao Yu MS, Alireza Ghoreifinejad MD, Giovanni Cacciamani MD, Gus Miranda BS, Jie Cai PhD, Sumeet Bhanvadia MD, Anne Schuckman MD, Siamak Daneshmand MD, Hooman Djaladat MD
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Abstract

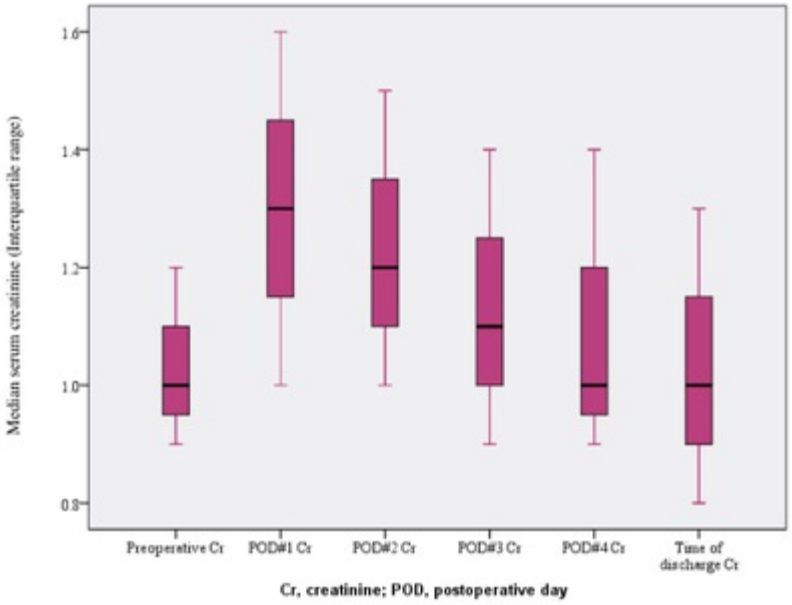
INTRODUCTION: Acute kidney injury (AKI) commonly occurs following radical cystectomy (RC), is associated with morbidity, and may affect the timely delivery of adjuvant systemic therapy, if indicated. Here we assess incidence and predictors of early postoperative AKI (EP-AKI) in RC patients.

METHODS: All patients with bladder cancer who underwent intent-to-cure open RC and urinary diversion from 2012-2020 at USC were enrolled. EP-AKI was defined per AKIN criteria: Increase in creatinine (Cr)>50% (stage 1), >100% (stage 2), or >150% (stage 3) compared to preoperative baseline Cr within 72 hours postoperatively. The association between EP-AKI and perioperative data including age, gender, preoperative Cr (Pre-Cr), neoadjuvant chemotherapy, Charlson comorbidity index, operative time (OT), blood loss, blood transfusion (BT), length of hospital stay (LOS), 30- and 90-day complication rate (CR), and readmission rate (RR) were examined. Predictors of EP-AKI were determined using multivariate analysis (MVA).

RESULTS: Out of 311 patients who underwent RC and urinary diversion on ERAS protocol with goal-directed fluid therapy, 259 were included, of whom 60 (23%) experienced EP-AKI during index hospitalization, of which 47 (18%), 10 (3%), and 3 (1%) were Stage 1, 2, and 3, respectively **(Figure 1)**. Patients with EP-AKI had significantly higher Pre-Cr (1vs.0.9;P=<0.001), rate of BT (32%vs.18%;P=0.009), and longer OT (5.9vs.5.3 hours;P=0.003). The rate of EP-AKI was significantly higher in continent diversion compared to ileal conduits (26%vs.12%;P=0.02). On MVA, baseline Cr and BT were independent predictors of EP-AKI **(Figure 2)**. EP-AKI was associated with higher 30-d CR (68%vs.51%;P=0.02) and RR (31%vs.14%;P=0.002) rates. There was no significant association between EP-AKI and LOS or 90-d CR and RR.

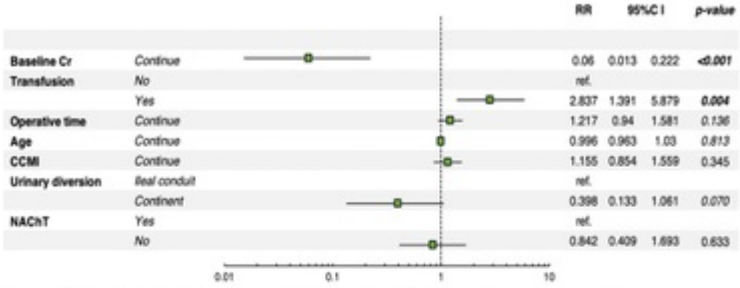
CONCLUSIONS: A quarter of RC patients experience EP-AKI, which is associated with higher early postoperative CR and RR. Baseline Cr and perioperative BT are independent predictors of EP-AKI.

Figure1. Postoperative trend of serum creatinine during the hospital stay following radical cystectomy and urinary diversion



Cr, creatinine; POD, postoperative day

Figure 2. Forest plot for independent predictors of early postoperative acute kidney injury in 259 patients who underwent open RC with enhanced recovery protocol



Cr, creatinine; CCMI, Charlson Comorbidity index, NAChT, neoadjuvant chemotherapy

119 A Comparison of Naloxegol vs Alvimopan at the time of Cystectomy and Urinary Diversion

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Abstract

Objective: The use of alvimopan, a mu-opoid antagonist, at the time of cystectomy with urinary diversion has been associated with expedited return of bowel function, reduced hospital length of stay (LOS) and reduced incidence of postoperative ileus. Naloxegol is a less costly mu-opoid antagonist that has been used in some centers as an alternative to alvimopan. Little is known regarding the comparison between these two agents in this population of patients.

Methods: This was a retrospective review that included all patients who underwent cystectomy with urinary diversion at our institution between 2007-2020. Comparisons were made between patients who received perioperative alvimopan, naloxegol and no mu-opioid antagonist (controls).

Results: In 715 patients who underwent cystectomy, 335 received a perioperative mu-opoid antagonist, of whom 57 received naloxegol. Control patients, compared to naloxegol and alvimopan patients, experienced a significantly ($p<0.05$) delayed return of bowel function (4.3 vs 2.5 vs 3.0 days), longer hospital LOS (7.9 vs 7.5 vs 6.5 days), delayed time until tolerating liquid diet (5.0 vs 1.5 vs 3.5 days) and delayed time until tolerating a regular diet (6.3 vs 4.9 vs 4.7 days), respectively. The incidence of nasogastric tube use (14.2% vs 12.5% vs 6.5%) and postoperative ileus (21.6% vs 21.1% vs 13.3%) was also most common in the control group compared to the naloxegol and alvimopan cohorts, respectively. A multivariable analysis revealed that when comparing naloxegol and alvimopan, there was no difference in return of bowel function (OR 0.88, $p=0.17$), incidence of postoperative ileus (OR 1.60, $p=0.44$), or hospital readmission (OR 1.22, $p=0.63$). Naloxegol remained associated with increased hospital LOS (OR 1.37, $p<0.001$).

Conclusions: Naloxegol expedites the return of bowel function to the same degree as alvimopan in cystectomy patients. Given the lower cost of naloxegol, this agent may be a preferable alternative to alvimopan.

If funding provided, type in source company / entity name(s):

This study was supported by Grant Number P30 CA015083 from the National Cancer Institute (NCI) from the Robert D. and Patricia E. Kern Center for Health Care Delivery Science (M.D.T.), the Christian Haub Family Career Development Award for Cancer Research Honoring Dr Richard Emslander (M.D.T.), and the Eric and Gail Blodgett Foundation (M.D.T.). Its contents are solely the responsibility of the authors and do not necessarily represent the official view of the NIH