Non-prostate Genitourinary Cancers Tuesday, June 29, 2021

Cite as: *Can Urol Assoc J* 2021;15(6S2):S58-62. http://dx.doi.org/10.5489/cuaj.7398

POD-4

Patient trajectories of a real-world cohort initiating neoadjuvant chemotherapy for localized muscle-invasive bladder cancer: A population-based study analyzed by a multi-state modelling framework

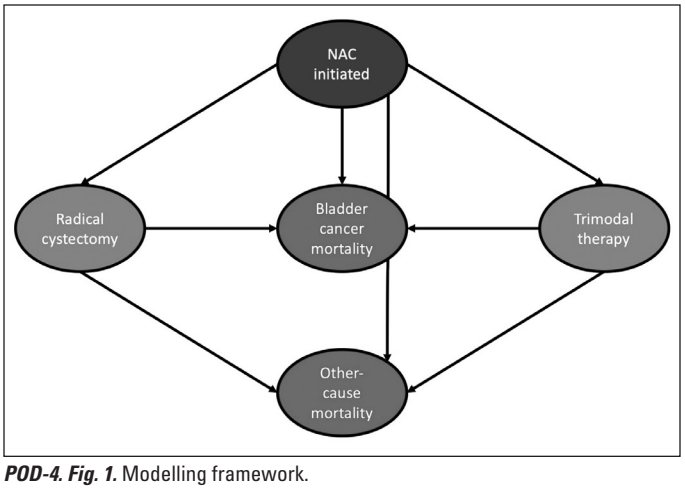
Marian S. Wettstein[1,2,3], Song Pham[2], Syed R. Qadri[1], Kathy Li[1], Ning Liu[2], Thomas Hermanns[3], Peter W. Chung[4], Srikala S. Sridhar[5], Girish S. Kulkarni[1,2]
[1]Division of Urology, Department of Surgery, Princess Margaret Cancer Centre, University Health Network, University of Toronto, Toronto, ON, Canada; [2]ICES, Toronto, ON, Canada; [3]Department of Urology, University Hospital of Zurich, University of Zurich, Zurich, Switzerland; [4]Radiation Medicine Program, Princess Margaret Cancer Centre, University Health Network, University of Toronto, Toronto, ON, Canada; [5]Division of Medical Oncology, Department of Medicine, Princess Margaret Cancer Centre, University Health Network, University of Toronto, Toronto, ON, Canada

Introduction: The use of neoadjuvant chemotherapy (NAC) for localized muscle-invasive bladder cancer (MIBC) is supported by level-1 evidence. Opponents of NAC suggest missing a window of opportunity to deliver definitive radical therapy due to NAC-related toxicity or NAC-unresponsive disease. The aim of the current study was to investigate the proportion of patients initiating NAC who go on to receive definitive radical therapy for localized MIBC.

Methods: Province-wide bladder cancer pathology reports (April 2004 to December 2015; Ontario, Canada) were linked to the Cancer Activity Level Reporting database to derive a cohort of patients diagnosed with localized MIBC who had at least one administration of systemic therapy with neoadjuvant intent. Patients were followed for the receipt of radical cystectomy, initiation of trimodal therapy, or the occurrence of death (cause-specific). A multi-state modelling framework was used to describe the trajectory of these patients (Fig. 1).

Results: We identified a cohort of 485 patients with a median age of 67 years (interquartile range 60–73). Most patients (n=422, 89.3%) received a NAC regimen containing at least one dose of cisplatin. Six months after NAC initiation, the probabilities to have received radical cystectomy, to have initiated trimodal therapy, to have died of bladder cancer, to have died of other causes, and to be alive without having received any definitive radical therapy were 36.6%, 3.5%, 4.2%, 3.9%, and 51.8%, respectively. Five years after the receipt of definitive radical therapy, the probabilities to have died of bladder cancer/other causes were 25.4%/29.6% (radical cystectomy) and 15.2%/45.5% (trimodal therapy).

Conclusions: In a real-world cohort that initiated NAC for MIBC, only about 40% of all patients will ultimately receive definitive radical therapy after six months. This study provides realistic estimates for patients being counselled about NAC in MIBC.



POD-4. Fig. 1. Modelling framework.

MP-16

Sexual dimorphism in outcomes of non-muscle-invasive bladder cancer: A role of CD163+ macrophages, B cells, and PD-L1 immune checkpoint

Stephen Chenard[1,2], Chelsea Jackson[1,3], Kashif Visram[4], Thiago Vidotto[5], Lina Chen[3], Celine Hardy[1,3], Tamara Jamaspishvilli[1,3], David Berman[1,2,3], D. Robert Siemens[1,2,4], Madhuri Koti[1,2,4]
[1]Queen's Cancer Research Institute, Queen's University, Kingston, ON, Canada; [2]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada; [3]Department of Pathology and Molecular Medicine, Queen's University, Kingston, ON, Canada; [4]Department of Urology, Queen's University, Kingston, ON, Canada [5]Department of Pathology, Johns Hopkins School of Medicine, Baltimore, MD, United States

Introduction: Non-muscle-invasive bladder cancer (NMIBC) is significantly more common in men than women. However, female patients with NMIBC often present with more aggressive disease and do not respond as well to immunotherapy treatments. We hypothesized that sexual dimorphism in the tumor immune microenvironment (TIME) may contribute to the inferior clinical outcomes observed in female patients.

Methods: To test this hypothesis, we interrogated the expression patterns of genes associated with specific immune cell types and immune checkpoint pathways using tumor whole transcriptome profiles from male (n=357) and female (n=103) patients with NMIBC. High-grade tumors from female patients exhibited significantly increased expression of CD40, CTLA4, PDCD1, LAG3, and ICOS immune checkpoint genes. Next, we evaluated the density and spatial distribution of CD8+Ki67+ activated T cytotoxic cells, FoxP3+ T regulatory cells, CD103+ tissue resident T cells, CD163+ (M2-like tumor-associated macrophages), CD79a+ (B-cells), PD-L1+ (programmed-death ligand-1), and PD-1+ cells using multiplexed immunofluorescence in an independent cohort of 332 patient tumors on a tissue microarray (n=259 males and n=73 females).

Results: Tumors from female patients showed significantly higher density of CD163+ macrophages and PD-L1+ cells compared to tumors from male patients. Notably, increased abundance of CD163+ macrophages and CD79a+ B cells are independently associated with decreased recurrence-free survival.

Conclusions: These findings are the first evidence of sex-associated differences in the TIME of NMIBC.

MP-17

Association between chronic urinary catheterization and bladder cancer incidence and mortality: A population-based study

Amanda Hird[1], Refik Saskin[2], Ying Liu[2], Yuna Lee[3], Khaled Ajib[1], Rano Matta[1], Ronald T. Kodama[1], Lesley Carr[1], Girish S. Kulkarni[1], Sender Herschorn[1], Steven Narod[4], Robert K. Nam[1]

[1]Urology, University of Toronto, Toronto, ON, Canada; [2]ICES, Toronto, ON, Canada; [3]Internal Medicine, University of Toronto, Toronto, ON, Canada; [4]Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada

Support: Ajmera Family Chair in Urologic Oncology.

Introduction: Chronic inflammation of the bladder is a known risk factor for bladder cancer. The risk of bladder cancer among patients requiring chronic bladder catheterization has been poorly characterized. No large-scale studies have explored the relationship between catheter duration and bladder cancer risk. Our objective was to compare bladder cancer incidence and mortality among patients with a chronic urinary catheter to general population controls.

Methods: This was a retrospective, population-based cohort study between 2003 and 2018 in Ontario, Canada. Adult patients with a chronic bladder catheter were hard matched to general population controls. The presence of a chronic catheter was defined as a minimum of two physician encounters for bladder catheterization, suprapubic tube insertion, or home care for catheter care separated by at least 28 days. Urinary tract infection (UTI) rates were collected. Our primary outcome was bladder cancer incidence after a one-year lag period. Secondary outcomes included bladder cancer-specific mortality and bladder cancer histology. We also examined the association between catheter duration and bladder cancer incidence.

Results: We identified 36 903 patients with a chronic catheter matched to 110 709 controls. The median age was 62 years (interquartile range [IQR] 50–71) and 52% were female. The median catheter duration was 2.0 years (IQR 0.6–5.0). Patients were followed for a median of 8.8 years (IQR 5.2–11.9). More patients in the catheter group developed bladder cancer compared to controls (393 [1.1%] vs. 304 [0.3%], p<0.001). There were 106 (0.3%) bladder cancer deaths in the catheter group and 59 (0.1%) in the control group (p<0.001). Chronic catheterization (adjusted sub-distribution hazards ratio [sdHR] 4.80, 95% confidence interval [CI] 4.26–5.42, p<0.001) and the number of UTIs (adjusted sdHR 1.04 per UTI, 95% CI 1.04–1.05, p<0.001) were independent predictors of bladder cancer. The relative rate of bladder cancer-specific death was more than eight-fold higher among patients with a chronic catheter compared to controls (adjusted sdHR 8.68, 95% CI 6.97–10.81, p<0.001). Bladder cancer risk was highest among patients in the two longest catheter duration quintiles (2.9–5.9 years and 5.9–15.5 years). Urothelial carcinoma was the most diagnosed cancer in both groups. Squamous cell carcinoma was more common in the catheter group.

Conclusions: This is the first study to quantify the increase in bladder cancer incidence and mortality in a large, diverse group of patients with chronic bladder catheterization. Patients with a chronic catheter beyond 2.9 years may benefit from regular screening, although future studies are needed to confirm these findings and explore the optimal frequency and nature of these screening interventions.

MP-18

Assessment of the alignment between research funding allocation and consensus research priority areas in kidney cancer

Steven Lu[1], Jeenan Kaiser[2], Michael A. Jewett[3], Daniel Y.C. Heng[4], Nimira Alimohamed[4], Bimal Bhindi[5]

[1]Cumming School of Medicine, University of Calgary, Calgary, AB, Canada; [2]Faculty of Medicine and Dentistry, University of Alberta, Edmonton, AB, Canada; [3]Department of Surgery (Urology) and Surgical Oncology, Princess Margaret Cancer Centre, University Health Network and University of Toronto, Toronto, ON, Canada; [4]Tom Baker Cancer Centre, University of Calgary Cumming School of Medicine, Calgary, AB, Canada; [5]Section of Urology, Department of Surgery, University of Calgary, Cumming School of Medicine, Calgary, AB, Canada

MP-18. Table 1. Top 10 research priorities as defined by patients, caregivers, and clinicians from the 2017 kidney cancer research priority-setting partnership

Priority #	Description	Funded projects, n (% of total)	Funding allocated, $CAD (% of total)
1a	Development and evaluation of new effective treatment for patients with advanced kidney cancer of the non-clear-cell varieties/subtypes	7 (6%)	$4 556 268 (4%)
1b	Identification and validation of biomarkers that may be used to predict the response to a treatment for kidney cancer	38 (31%)	$19 831 874 (18%)
1c	Identification and validation of biomarkers that may be used for the detection of kidney cancer	12 (10%)	$4 283 896 (4%)
4	Development and evaluation of new immunotherapies for the treatment of kidney cancer, including immune biomarkers of patient and tumor characteristics and response	50 (41%)	$25 443 644 (23%)
5	Identification and validation of novel indicators or biomarkers that can be used to predict the development and progression of metastatic kidney cancer	21 (17%)	$10 236 968 (9%)
6	Assessment of supportive care needs and appropriate supportive care interventions for patients with kidney cancer and their families	0 (0%)	$0 (0%)
7	Development of decision-making tools for patients and healthcare providers to help guide treatment decisions in all stages of kidney cancer	6 (5%)	$2 804 101 (3%)
8	Defining the role and criteria for using biopsy in the management of kidney cancer	0 (0%)	$0 (0%)
9	Evaluation of the impact of differences in regional funding and access to treatment on patient outcomes for kidney cancer	2 (2%)	$1 456 360 (1%)
10	Identification of risk factors and cause(s) of kidney cancer	78 (64%)	$39 942 170 (36%)
Biomarkers (1b, 1c, 5)	The role of biomarkers and other novel indicators in both the detection of kidney cancer and its progression	71 (59%)	$34 352 738 (31%)
Non-priority areas		3 (2%)	$1 006 650 (1%)

Introduction: Finite resources are available to fund research, and it is important to ensure stakeholder input is identified and prioritized. In this light, the Kidney Cancer Research Network of Canada (KCRNC) and Canadian Institutes of Health Research (CIHR) sponsored a consensus-based, priority-setting partnership that brought together a group of patients, caregivers, and clinicians to identify the top 10 research priorities in kidney cancer (Table 1), with a consensus document published in 2017.[1,2] We sought to determine how research funding allocation has aligned with these previously identified priority areas.
Methods: We queried publicly available Canadian and American research databases to identify all research funds allocated to kidney cancer from 2018–2020. Each funded project was assessed to determine which priority areas were addressed. We evaluated the percent of projects and percent of funding dollars (converted to CAD) allocated to priority areas. Descriptive statistics were used.
Results: A total of 121 kidney cancer research projects were funded from 2018–2020, with 15 Canadian projects (total $2 421 126 CAD) and 106 American projects (total $ 71 523 080 CAD). Half (50%) of the projects focused on localized cancer, while 26% of projects focused on metastatic kidney cancer. Overall, 49% of projects aligned to one priority area, 47% of projects aligned to multiple priority areas, and 4% of projects were not aligned to priority areas. The priority areas that received the most funding were causes of kidney cancer (priority #10: 64% of funds), biomarkers (priorities #1b, 1c, 5: 59%), and immunotherapies (priority #4: 41%) (Table 1). Unfunded priority areas were supportive care (priority #6) and the role of biopsy in kidney cancer management (priority #8).
Conclusions: Nearly all kidney cancer projects funded since 2018 were aligned with one or multiple stakeholder-identified research priority areas, although some priority areas remain underfunded. Mechanisms to improve distribution of funding to all priority areas may be warranted.
References

1. Jones J, Bhatt J, Avery J, et al. The kidney cancer research priority-setting partnership: Identifying the top 10 research priorities as defined by patients, caregivers, and expert clinicians. *Can Urol Assoc J* 2017;11:379-87. https://doi.org/10.5489/cuaj.4590
2. Jones JM, Bhatt J, Avery J, et al. Setting research priorities for kidney cancer. *Eur Urol* 2017;72:861-4. https://doi.org/10.1016/j.eururo.2017.04.011

MP-19

Role of the upfront cytoreductive nephrectomy in patients with metastatic renal cell carcinoma

Alice Dragomir[1], Simon Tanguay[2], Rodney H. Breau[3], Bimal Bhindi[4], Anil Kapoor[5], Sebastien Hotte[6], Naveen Basappa[7], Adrian Fairey[8], Ricardo A. Rendon[9], Alan I. So[10], Christian Kollmannsberger[11], Lori A. Wood[9]
[1]Department of Surgery, McGill University, Montreal, QC, Canada; [2]Division of Urology, McGill University, Montreal, QC, Canada; [3]Division of Urology, University of Ottawa, Ottawa, ON, Canada; [4]Department of Surgery, University of Calgary, Calgary, AB, Canada; [5]Division of Urology, McMaster University, Hamilton, ON, Canada; [6]Juravinski Cancer Centre, Hamilton, ON, Canada; [7]Department of Oncology, University of Alberta, Edmonton, AB, Canada; [8]Department of Surgery, University of Alberta, Edmonton, AB, Canada; [9]Department of Urology, Dalhousie University, Halifax, NS, Canada; [10]Department of Urologic Sciences, University of British Columbia, Vancouver, BC, Canada; [11]Division of Medical Oncology, University of British Columbia, Vancouver, BC, Canada
Introduction: The objective of this study was to evaluate the association between upfront cytoreductive nephrectomy (CN) and survival of these patients.
Methods: The Canadian Kidney Cancer information system (CKCis) database was used to identify patients diagnosed with histologically confirmed synchronous metastatic renal cell carcinoma (mRCC) between January 2011 and April 2020 who were treated within 12 months from initial diagnosis. Patients were classified in two groups according to whether the initial treatment received was CN or systemic therapy (ST). Inverse probability of treatment weighting (IPTW) using propensity scores was used. Kaplan-Meier analysis was used to estimate the overall survival from diagnosis of metastatic disease to death from any cause. A Cox proportional hazards model was used to assess the association of CN (vs. initial ST) in the weighted cohort, while adjusting the subsequent treatment received as time-dependent covariate (i.e., ST for patients receiving initial CN, and CN for patients receiving initial ST, respectively).
Results: A total of 1114 patients were included, 736 patients in the upfront CN group, and 378 patients in the upfront ST group. The median age at diagnosis was 63 years and 74.1% were men. The median survival was 38 months after diagnosis in the CN group, and 22 months in the ST group. In the weighted analysis, CN was associated with a reduction of mortality compared to ST (hazard ratio [HR] 0.76, 95% confidence interval [CI] 0.62–0.95). Among patients in the CN group, a subsequent treatment of ST was associated with a higher risk of death (HR 4.02, 95% CI 2.60–6.10), while among patients in the ST group, a subsequent treatment of CN was associated with a decreased risk of death (HR 0.63, 95% CI 0.45–1.03), yet not statistically significant.
Conclusions: This study evaluated the association between upfront CN vs. ST and survival in mRCC patients using real-world data. Our study demonstrated that the selected patients who receive initial CN have an associated improvement in survival.

MP-20

Minimizing followup intensity of active surveillance for clinical stage 1 non-seminoma germ cell tumors (CS1 NSGCT): A 40-year experience at Princess Margaret Cancer Centre

Peter Gariscsak[1], Lynn Anson-Cartwright[2], Di Maria Jiang[3], Peter Chung[4], Philippe Bedard[3], Aaron Hansen[3], Padraig Warde[4], Martin O'Malley[6], Joan Sweet[5], Robert J. Hamilton[2]
[1]School of Medicine, Queen's University, Kingston, ON, Canada; [2]Department of Surgery, Urology, Princess Margaret Cancer Centre, University Health Network and The University of Toronto, Toronto, ON, Canada; [3]Division of Medical Oncology and Hematology, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; [4]Department of Radiation Oncology, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; [5]Department of Pathology, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada; [6]Department of Medical Imaging, Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada
Introduction: The Princess Margaret Cancer Centre has recommended active surveillance as the preferred management option for clinical stage I (CSI) testicular non-seminoma germ cell tumors (NSGCT) since 1980. Over time, the recommended intensity of surveillance has decreased, however, the impact on relapse detection has not been thoroughly investigated.

MP-20. Table 1. NGSCT patient baseline characteristics

Patient characteristics	Number (%)
Age at orchiectomy, years, mean (SD)	29.71 (8.81)
Right-sided primary	341 (53.2)
pT stage	
T1	477 (74.4)
T2	158 (24.6)
T3	4 (0.6)
T4	2 (0.3)
Stage at presentation	
Stage 1A	477 (74.4)
Stage 1B	164 (25.6)
LVI	156 (24.3)
Pure embryonal carcinoma in orchiectomy pathology	95 (14.8)
Both LVI and pure embryonal in orchiectomy pathology	43 (6.7)

MP-20. Table 2. NSGCT patient characteristics at relapse

Schedule iteration	1980–1985 (n=52)	1986–1989 (n=62)	1990–2009 (n=334)	2010–2020 (n=193)	p
Number relapsed	24 (46.2)	20 (32.3)	80 (24.0)	41 (21.2)	0.0016*
Median (range) time from orchiectomy to relapse (months)	6.54 (2.67–21.13)	6.89 (3.10–331.90)	7.37 (1.90–76.63)	4.47 (2.10–64.50)	0.0248*
N at relapse, n (%)					0.3945
N0	7 (29.2)	5 (25.0)	16 (20.0)	9 (22.0)	
N1	7 (29.2)	6 (30.0)	39 (48.8)	21 (51.2)	
N2	9 (37.5)	7 (35.0)	23 (28.8)	11 (26.8)	
N3	1 (4.2)	3 (10.0)	2 (2.5)	0	
M at relapse, n (%)					0.3413
M0	20 (83.3)	15 (75.0)	61 (76.3)	26 (63.4	
M1a	4 (16.6)	5 (25.0)	16 (20.0)	15 (36.6)	
M1b	0	0	3 (3.8)	0	
S at relapse, n (%)					0.2590
S0	7 (29.2)	5 (25.0)	36 (0.45)	14 (34.1)	
S1	17 (70.8)	14 (70.0)	37 (46.3)	26 (63.4)	
S2	0	1 (5.0)	6 (7.5)	0	
S3	0	0	1 (1.3)	0	
Unknown	0	0	0	1 (2.4)	
IGCCCG class, n (%)					0.2923
Good	24 (100)	19 (95.0)	71 (88.8)	40 (97.5)	
Intermediate	0	1 (5.0)	5 (6.3)	0	
Poor	0	0	4 (0.5)	0	
Unknown	0	0	0	1 (2.5)	
Modes of therapy required, n (%)					0.1260
Multimodal	12 (50.0)	14 (70.0)	59 (75.6)	28 (70.0)	
Unimodal	12 (50.0)	6 (30.0)	19 (24.4)	12 (30.0)	
First therapy, n (%)					<0.0001*
Chemotherapy	12 (50.0)	13 (65.0)	44 (56.4)	28 (70.0)	0.3785
RPLND	6 (25.0)	7 (35.0)	33 (42.3)	9 (22.5)	0.1434
Other surgery	0	0	1 (1.3)	3 (7.5)	0.1266
Radiation	6 (25.0)	0	0	0	<0.0001*
Modality identifying relapse, n (%)					0.0031*
Imaging	6 (25.0)	6 (30.0)	44 (55.0)	23 (56.1)	0.0159*
Tumor markers	14 (58.3)	12 (60.0)	22 (27.5)	11 (26.8)	0.0026*
Imaging + tumor markers	2 (8.3)	0	12 (15.0)	7 (17.1)	0.2211
Patient complaint Investigation	0	1 (5.0)	2 (2.5)	0	0.4670
Physical exam	1 (4.2)	1 (5.0)	0	0	0.1310
Positive modality at relapse workup, n (%)					
Tumor markers	17 (70.8)	15 (75.0)	44 (55.0)	27 (65.6)	0.2450
CT A/P	17 (70.8)	15 (75.0)	65 (81.3)	31 (75.6)	0.7019
CXR	3 (12.5)	1 (5.0)	10 (12.5)	0	0.0990
CT T	1 (4.17)	3 (15.0)	14 (17.5)	14 (34.1)	0.0213*
Physical exam	5 (20.8)	6 (30.0)	7 (8.8)	1 (2.4)	0.0054*
History	1 (4.2)	1 (5.0)	2 (2.5)	1 (2.4)	0.9200
Number second relapse, n (%)	5 (20.8)	4 (20.0)	15 (18.8)	7 (17.1)	0.9832

*Significance, p<0.05.

Methods: CSI NSGCT patients under active surveillance from 1980–2020 were analyzed. To lower surveillance intensity, the surveillance schedule underwent four iterations during this time period, with the aim of decreasing healthcare resource use and patient radiation exposure without compromising cure rates. The primary endpoints analyzed were relapse rate, time to relapse, stage of disease at relapse, and number of treatment modalities at relapse across the differing surveillance schedules.
Results: In total, 641 patients were included, with an average age of 29.7 years at initial presentation and a median followup time of 5.20 years. Patient characteristics at baseline and relapse are listed in Tables 1 and 2, respectively. The number of surveillance computed tomography (CT) scans and chest x-rays used per patient decreased from 11 to 5 and 27 to 0, respectively. The relapse rate decreased significantly from 46.2% to 21.2% (p=0.002), while the time to relapse also shortened over time from 6.54 months to 4.47 months (p=0.025). There was no difference in disease burden at time of relapse, indicated by staging of N (p=0.395), M (p=0.341), S (p=0.259), or IGCCCG risk classification (p=0.293). There was no change to treatment burden at relapse, with most patients receiving unimodal therapy (p=0.126).
Conclusions: Over time, there has been considerable reductions in the intensity of active surveillance without a significant increase in rates of relapse, burden of disease at relapse, or burden of treatment at relapse. These results support that current lower intensity active surveillance schedules are safe for managing CSI NGSCT.