Impact of the COVID-19 pandemic on diagnosis of renal cell carcinoma and disease stage at presentation

W.C. Ian Janes[1], Mitchell G. Fagan[1], J. Matthew Andrews[2], David R. Harvey[2], Geoff M. Warden[3], Paul H. Johnston[2], Michael K. Organ[2]

[1]Faculty of Medicine, Memorial University, St. John's, NL, Canada; [2]Division of Urology, Memorial University, St. John's, NL, Canada; [3]Division of Anesthesia, Health Sciences Centre, St. John's, NL, Canada

Cite as: Janes WCI, Fagan MG, Andrews JM, et al. Impact of the COVID-19 pandemic on diagnosis of renal cell carcinoma and disease stage at presentation. *Can Urol Assoc J* 2024;18(4):E113-9. http://dx.doi.org/10.5489/cuaj.8519

Published online December 21, 2023

ABSTRACT

INTRODUCTION: Renal cell carcinoma (RCC) is often associated with significant morbidity and mortality, with overall survival contingent on multiple factors — most importantly, disease stage at diagnosis. Disruptions in healthcare delivery during the COVID-19 pandemic have resulted in various reported diagnostic and treatment delays, which have had detrimental impacts on malignancies such as RCC.

METHODS: Surgically managed cases of RCC at our center were identified using a retrospective chart review of all nephrectomies conducted from March 1, 2018, to February 28, 2023. Examination of disease characteristics in three time period cohorts (before, during, and following the COVID-19 pandemic) was undertaken. Timeframes were consistent with implementation and abolition of public health restrictions in the province of Newfoundland and Labrador.

RESULTS: A total of 483 surgically managed RCC cases were identified during the study period. The median age was 65 years (interquartile range [IQR] 56–71), and 62.3% of patients were male. Demographics did not vary across timeframes. Before and during the pandemic, pathologic stage 3 (pT3) disease was reported in 38.9% and 35.4% of cases, respectively, whereas the post-pandemic period saw this presentation in 50.0% of patients. Surgical wait times increased significantly across study timeframes (p=0.003).

CONCLUSIONS: The first year following the COVID-19 pandemic saw an 11.1% increase in patients presenting with pT3 RCC. These findings are suggestive of a clinically significant stage migration, which paired with prolonged wait times for surgery, provide critical consideration in the urgency of diagnostic and treatment decisions for RCC in the immediate future.

INTRODUCTION

Renal cancer involves a diverse variety of renal pathologies with variable patterns of aggressiveness and malignant potential.[1] Renal cell carcinoma (RCC) are insidious neoplasms frequently associated with high mortality rates despite only accounting for approximately 2% of all cancer diagnoses.[2] Current global age-standardized incidence of RCC has been reported at 4.4/100 000; however, incidence and mortality for these malignancies have been increasing over the past several years. The highest rates have been observed in North America, with an age-standardized incidence of approximately 12/100 000 compared with near negligible numbers in several Central African nations, representing discrepancies in risk factors between geographical locations.[2-5]

The pathogenesis of RCC has been linked to several risk factors, categorized relative to environmental and behavioral patterns, or inheritance of genetic mutation.[3-6] Smoking is a major predictor for development of RCC in multiple studies, with greater than half of diagnoses among current or former smokers.[7-9] Elevated risk is also associated with an increasing number of comorbidities, including obesity, hypertension, and type 2 diabetes mellitus.[5,10] Risk of RCC increases 25–35% for an approximate 5 kg gain in bodyweight, and hypertension is associated with a doubled risk for development.[5,11-16] Genetic mutations, including Birt-Hogg-Dube and Vonn Hippel Lindau syndrome, have established predisposition for development of renal malignancies.[17-19]

Most cases of RCC are discovered incidentally on imaging. Prognosis is contingent on multiple factors, including tumor grade, histology and, more importantly, disease stage at diagnosis.[20,21] Accordingly, patients presenting with localized disease amenable to surgical resection have a five-year overall survival (OS) of 93%.[22,23] OS decreases to 72.5% in those with regional spread, and further declines to 12% among those with distant metastases.[15,24,25] The decreased utility of surgical intervention in later-stage disease prompts need for improved public health initiatives to promote early diagnosis of RCC.

Disruptions in healthcare delivery during the COVID 19 pandemic have resulted in various diagnostic and treatment delays, and subsequently detrimental impacts on the management of malignancies, including RCC.[26-30] Pandemic-induced delays have consistently increased morbidity and mortality for oncology patients during this timeframe.[31-33] Urogenital malignancies have typically accounted for a small percentage of cancers and have seen significant advancement in management options over the past several decades. Such considerations have likely rendered these afflictions as low priority in access to resources throughout the COVID-19 pandemic.

To date, there has been limited research assessing pandemic-induced delays in diagnosis and treatment of urogenital malignancies. The province of Newfoundland and Labrador (NL) possesses the highest national rates of obesity, smoking, and hypertension, along with a propensity to act as a microcosm for rare genetic conditions that correlate with higher risk of renal malignancies.[34-36] The present study aimed to assess how the COVID-19 pandemic, and associated healthcare restrictions, affected the diagnosis, staging, and final surgical pathology of RCC at our institution. We hypothesized that a greater proportion of RCC diagnoses presented with late-stage disease during and following the pandemic compared to the pre-pandemic era. It was also predicted that individuals with a diagnosis of RCC during and following the pandemic would have experienced greater delays in treatment secondary to implemented healthcare restrictions.

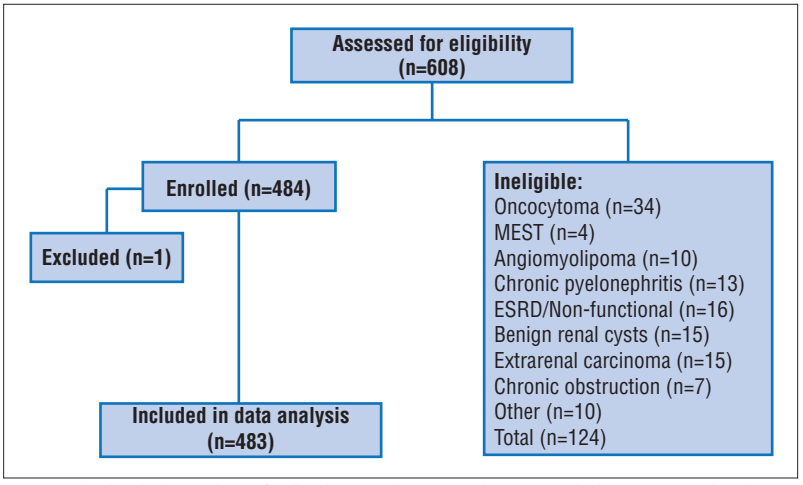

Figure 1. Flowchart displaying indication for all nephrectomies between March 1, 2018, and February 28, 2023, by inclusion and exclusion criteria. ESRD: end-stage renal disease; MEST: mixed epithelial stromal tumor.

METHODS

This study was approved by the provincial health research ethics board at Memorial University (St. Johns, NL, Canada). A retrospective chart analysis was conducted of all surgically managed cases of RCC from March 1, 2018, to February 28, 2023. Patients undergoing radical or partial nephrectomy during this timeframe were identified using operating room (OR) codes. Pathology reports for each identified case were examined to determine eligibility as RCC or separate pathology, with the latter being excluded. Tumor staging for all eligible charts was completed in accordance with American Joint Committee on Cancer guidelines. The assessed study timeframe was further subdivided into pre-pandemic, pandemic, and post-pandemic periods, consistent with the implementation and abolition of COVID-19 public health restrictions in the province of NL. Timeframes were defined as follows:

- Pre-pandemic: March 1, 2018, to March 31, 2020 (25 months)
- Pandemic: April 1, 2020, to February 28, 2022 (23 months)
- Post-pandemic: March 1, 2022, to February 28, 2023 (12 months)

Each case was assessed for time from surgical booking to operative intervention, along with further, relevant epidemiological and pathologic variables. Differences across timeframes were calculated using the Kruskal-Wallis test for non-parametric samples, with significance set at $p=0.05$. All demographic and comorbidity data were retrieved from preoperative anesthetic assessment reports. Statistical analyses were conducted using SPSS version 27.0 (IBM Corporation, Armonk, NY, U.S.). Continuous variables have been reported as means and standard deviations, while descriptive analyses are summarized as absolute counts and percentages.

RESULTS

There were 608 identified nephrectomies in the study timeframe, with 484 procedures in 477 individuals meeting the inclusion criteria. Given the goals of the

present study, each undertaken surgical procedure was included as a separate case. One case was accidentally documented twice and subsequently excluded, leaving a total of 483 analyzed cases. Breakdown of all identified nephrectomies is outlined in Figure 1.

Patient characteristics

Mean age across the study timeframe was 63.20±11.22 years, while 301 (62.3%) members of the cohort were male. Incidental discovery of RCC on imaging was noted for 336 (69.6%) cases. Hypertension and type 2 diabetes were reported for 327 (67.7%) and 123 (25.5%) individuals, respectively. There were 239 (47.5%) participants reported as either current or former smokers. Predisposing genetic mutations were noted for seven (1.8%) individuals and 277 (57.3%) patients were classified as obese. Demographics information and comorbidity status across pandemic timeframes is displayed in Table 1.

Tumor pathology

Stage pT3 disease accounted for 38.9% of cases in the pre-pandemic period and 35.4% of cases throughout the pandemic, before increasing to 50.0% of individuals during post-pandemic restrictions (p=0.07) (Figure 2).

The most used surgical procedure across all study time periods was laparoscopic radical nephrectomy, which was employed in 212 (43.9%) cases. Laparoscopic approaches further accounted for 278 (57.6%) of total cases. A full breakdown of the surgical procedures used by pandemic timeframe is outlined in Table 2.

Several histopathologic classifications of RCC were identified (Figure 3), with clear-cell RCC (ccRCC) observed in 367 (76.0%) cases. Papillary RCC, which accounted for 77 (16.0%) cases, was subclassified during the study period.

Tumor necrosis was found on 115 (23.8%) pathology specimens, while sarcomatoid and rhabdoid features were seen in 14 (2.9%) and 56 (11.6%) cases, respectively. Table 3 details tumor pathology across the stratified time periods.

Outcomes

Two patients had malignancy discovered incidentally on pathology and were excluded from analysis of surgical wait times, as these cases were not indicative of RCC-associated surgical delays. The average time from surgical booking to operative intervention prior to the pandemic was 44.5±35.1 days, increasing to 56.8±46.8 and 61.2±42.2 days during and following the abolition of public health restrictions, respectively. Surgical wait times increased significantly across the study period (p=0.003).

Table 1. Patient demographic and comorbidity status stratified by defined pandemic timeframes

Demographic variables	Pre-pandemic n=203	Pandemic n=178	Post-pandemic n=102	p
Sex, n (%)				0.615
Male	123 (60.6%)	116 (65.2%)	62 (60.8%)	
Female	80 (39.4%)	62 (34.8%)	40 (39.2%)	
Age, $\bar{x}$ ± SD	62.79±11.98	62.7±10.39	64.91±11.06	0.419
BMI, median (IQR)	31 (23–39)	30.5 (22.8–38.2)	31.9 (21.5–42.1)	0.830
BMI classification, n (%)				0.459
Non-obese	85 (41.9%)	81 (45.5%)	39 (38.2%)	
Obese (BMI≥30)	118 (58.1%)	96 (54.5%)	63 (61.8%)	
Smoking status, n (%)				0.474
Never	103 (50.7%)	93 (52.2%)	58 (56.8%)	
Current	48 (23.6%)	42 (23.6%)	26 (25.5%)	
Former	52 (25.6%)	43 (24.2%)	18 (17.6%)	
Hypertension, n (%)				0.543
Yes	132 (65.0%)	125 (70.2%)	70 (68.6%)	
No	71 (35.0%)	53 (29.8%)	32 (31.4%)	
Type 2 diabetes, n (%)				0.829
Yes	52 (25.6%)	43 (24.2%)	28 (27.5%)	
No	151 (74.4%)	135 (75.8%)	74 (72.5%)	
Genetic condition, n (%)				0.893
Yes	3 (1.5%)	3 (1.7%)	1 (1.0%)	
No	200 (98.5%)	175 (98.3%)	101 (99.0%)	
Vital status, n (%)				0.077
Alive	193 (95.1%)	172 (96.6)	102 (100.0%)	
Deceased	10 (4.9%)	6 (3.4%)	0 (0.0%)	

BMI: body mass index.

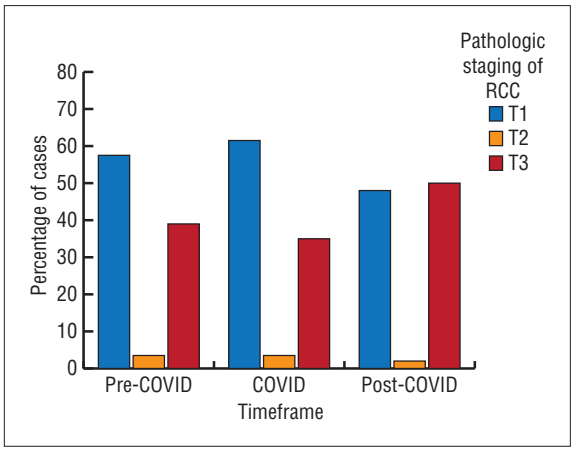

Figure 2. Stage of renal cell carcinoma (RCC) identified by relative to pandemic timeframes.

Following surgical intervention, metastatic disease was seen in 48 (9.9%) patients, with 39 undergoing additional treatments. Pulmonary metastases repre-

Table 2. Employed surgical procedures presented by pandemic timeframe

Surgical procedure	Pre-pandemic n (%)	Pandemic n (%)	Post-pandemic n (%)
Open radical nephrectomy	24 (11.8%)	32 (18.0%)	16 (15.7%)
Open partial nephrectomy	58 (28.6%)	43 (24.2%)	32 (31.4%)
Laparoscopic radical nephrectomy	95 (46.8%)	71 (39.8%)	46 (45.1%)
Laparoscopic partial nephrectomy	26 (12.8%)	32 (18.0%)	8 (7.8%)
Total	203 (100.0%)	178 (100.0%)	102 (100.0%)

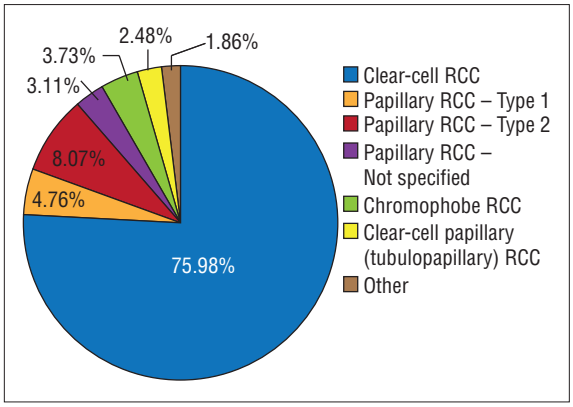

Figure 3. Renal pathology of all surgically managed cases of renal cell carcinoma (RCC) in Newfoundland and Labrador from March 1, 2018, to February 28, 2023.

sented the most common site of spread in 24 (51.0%) cases. Characteristics and treatment of patients with metastatic disease stratified by pandemic timeframe are displayed in Table 4.

DISCUSSION

Our study is one of the few to date that attempts to assess the impacts of the COVID-19 pandemic on RCC diagnoses and outcomes. The most pertinent finding of the present study was an 11.1% increase in the proportion of pT3 disease in the post-pandemic period, which, compared with the pre-pandemic era, is suggestive of a stage migration for RCC. Pathologic T3a RCC represents locally advanced disease with invasion of the vascular supply and/or perinephric fat and is associated with comparatively poorer oncologic outcomes.[37]

RCC often presents with a variable clinical course, which has led to the design of several prognostic models for this patient population dependent on multiple variables, including disease extent, tumor size, grade, and necrosis.[20,21,38] Unequivocally, these models depict

Table 3. Histopathologic characteristics of patients with surgically managed RCC in Newfoundland and Labrador during the COVID pandemic timeframes

Tumor characteristics	Pre-pandemic n=203	Pandemic n=178	Post-pandemic n=102
Tumor size (cm), median (IQR)	3.30 (0.20–6.40)	3.55 (0.09–7.01)	4.15 (1.55–6.75)
Pathologic staging, n (%)			
pT1a	102 (50.2%)	88 (49.4%)	35 (34.3%)
pT1b	14 (7.4%)	21 (11.8%)	14 (13.7%)
pT2a	4 (2.0%)	2 (1.1%)	2 (2.0%)
pT2b	3 (1.5%)	4 (2.2%)	0 (0.0%)
pT3a	77 (38.0%)	62 (34.8%)	51 (50.0%)
pT3b	2 (1.0%)	1 (0.6%)	0 (0.0%)
Nodal assessment, n (%)			
NX	187 (92.1%)	163 (91.6%)	94 (92.2%)
N0	14 (6.9%)	13 (7.3%)	8 (7.8%)
N1	2 (1.0%)	2 (1.1%)	0 (0.0%)
Grade, n (%)			
N/A	14 (6.9%)	10 (5.6%)	7 (6.9%)
G1	12 (5.9%)	5 (2.8%)	0 (0.0%)
G2	85 (41.9%)	66 (37.1%)	39 (38.2%)
G3	55 (27.1%)	65 (36.5%)	41 (40.2%)
G4	37 (18.2%)	32 (18.0%)	15 (14.7%)
Sarcomatoid features, n (%)			
Present	7 (3.4%)	5 (2.8%)	2 (2.0%)
Absent	196 (96.6%)	173 (97.2%)	100 (98.0%)
Rhabdoid features, n (%)			
Present	31 (15.3%)	16 (9.0%)	9 (8.8%)
Absent	172 (84.7%)	162 (91.0%)	93 (91.2%)
Tumor necrosis, n (%)			
Absent	158 (77.8%)	132 (74.2%)	78 (76.5%)
1–25%	31 (15.3%)	29 (16.3%)	17 (16.7%)
26–50%	2 (1.0%)	2 (1.1%)	0 (0.0%)
51–75%	3 (1.5%)	2 (1.1%)	0 (0.0%)
76–100%	5 (2.7%)	4 (2.2%)	3 (2.9%)
Unknown %	4 (2.0%)	9 (5.1%)	4 (3.9%)
LVI, n (%)			
Positive	6 (3.0%)	4 (2.2%)	1 (0.9%)
Negative	197 (97.0%)	174 (97.8%)	101 (99.1%)

IQR: interquartile range; LVI: lymphovascular invasion; RCC: renal cell carcinoma.

worsening survival outcomes with increasing disease stage, as previous reports have indicated five-year cancer-specific survival decreasing from 97% in those with T1a disease to 71% in individuals with T3a disease.[21,38,39] Further, likelihood of progression to metastatic disease increases for individuals with later-stage disease on pathology, with five-year OS in disseminated disease cited at 12%.[5,15]

There have been several studies that have attempted to assess the impact of the COVID-19 pandemic on cancer patients, with notable increases in the percentage

of patients presenting with inoperable or metastatic conditions compared with the pre-pandemic era.[40] Similarly, attempts to classify stage migration among various cancers during the pandemic have indicated increases in advanced-stage disease at presentation for otolaryngologic, breast, and colorectal malignancies; however, there are notable discrepancies across studies.[26-30]

A recent retrospective Canadian study documented similar findings, with a 7.6% increase in stage III disease staging of testicular germ cell tumors throughout the pandemic without assessment of the post-pandemic period.[41] There has been limited reporting regarding pandemic impacts on RCC staging, with one Italian study conducting an annual comparison of RCC from 2018–2020 and finding insignificant differences in staging across this timeframe.

Interestingly, the present study showed a 3.5% decrease in the proportion of pT3 RCC diagnosed during the pandemic compared with the pre-pandemic period. Arguably, pandemic-induced healthcare restrictions at our center may have limited assessment to urgent presentations of various conditions with incidentally detected RCC that had yet to progress to later-stage disease. Unlike the previous authors, our timeframes were established based on the implementation and abolition of public health restrictions in our province. While our results did not achieve statistical significance, we have documented a clinically significant stage migration for RCC in the year following the pandemic at our center that may have important implications in future management.

We further identified a statistically significant increase in surgical wait times between the pre- and post-pandemic timeframes. Previous attempts have been made to classify the consequences of prolonged surgical wait times in management of RCC, with conflicting results. Srivastava et al assessed the implications of delaying surgery for stage T1b–T2b RCC during the pandemic and found up to a three-month delay in surgery did not significantly increase risk of tumor progression.[42]

On the contrary, a recent meta-analysis found insufficient evidence to support delays in surgery for localized RCC, citing worsened cancer-specific survival in individuals with T1a disease over a mean observation period of approximately two years.[43] Important to note is that this review reported considerable heterogeneity among analyzed studies and found no significant differences in OS. These authors further reported assessment of delayed surgery in malignancies beyond T1b was limited, contradictory, and prone to selection bias.[43] Regardless of interpretation, our study demonstrated a clear stage migration, which was likely multifactorial during pandemic-induced restrictions in healthcare delivery and unlikely to be due wholly to observed increases in surgical wait times.

Table 4. Characterization of patients with metastatic RCC stratified by defined COVID timeframes

Metastatic characteristics	Pre-pandemic n=20	Pandemic N=22	Post-pandemic n=6	Total n=48
Site of metastases, n (%)				
Retroperitoneal LN	3 (15.0%)	1 (4.5%)	3 (50.0%)	7 (14.9%)
Lungs	9 (45.0%)	15 (68.3%)	2 (33.3%)	26 (54.2%)
Bone	5 (25.0%)	4 (18.2%)	0 (0.0%)	9 (18.8%)
Thyroid	1 (5.0%)	0 (0.0%)	0 (0.0%)	1 (92.0%)
Adrenals	1 (5.0%)	1 (4.5%)	1 (16.7%)	3 (6.3%)
Multiple	1 (5.0%)	1 (4.5%)	0 (0.0%)	2 (4.2%)
Additional treatment, n (%)				
Immunotherapy				
Monotherapy	10 (50.0%)	10 (45.5%)	0 (0.0%)	20 (41.7%)
+ TKI	0 (0.0%)	3 (13.6%)	1 (16.7%)	4 (8.3%)
TKI monotherapy	11 (55.0%)	7 (31.8%)	2 (33.3%)	20 (41.7%)
Radiation	5 (25.0%)	2 (9.1%)	0 (0.0%)	7 (14.6%)
Surgery	0 (0.0%)	1 (4.5%)	0 (0.0%)	1 (2.1%)
None	4 (20.0%)	2 (13.6%)	2 (33.3%)	9 (18.8%)
Vital status, n (%)				
Alive	11 (55.0%)	18 (81.9%)	6 (100.0%)	35 (72.9%)
Deceased	9 (45.0%)	4 (18.1%)	0 (0.0%)	13 (27.1%)

Multiple sites of metastases indicates combined osseous and pulmonary metastatic deposits. LN: lymph nodes; RCC: renal cell carcinoma; TKI: tyrosine kinase inhibitor.

The present study is the first, to our knowledge, that has assessed a timeframe beyond the peak pandemic period and presents with findings suggestive of delays in both diagnosis and management of RCC impact longitudinal outcomes for these patients. Those with surgically managed RCC had a greater occurrence of metastatic disease and cancer-specific mortality in the pandemic and pre-pandemic periods when compared to the post-pandemic era. These findings were inevitably the result of a length-time bias, however, given the pertinent findings of this study, it will be important to conduct longitudinal followup in patients diagnosed with pT3 disease following the pandemic. It is also important to note that our cohort consisted of surgically managed cases of RCC and did not account for individuals who presented with metastatic disease and received non-operative interventions. Examination of these patients may shed further light on the burden of pandemic-induced delays for those with RCC.

The risk profile seen in our study did not differ significantly across defined timeframes and was, again, comparable to extant literature, as RCC has consistently been causally associated with smoking, obesity, and hypertension.[3,5,44]

Our results indicated 47.5% of patients had used tobacco products, consistent with previous studies stating increased risk for RCC in current and former smokers, whom account for approximately 50% of all RCC diagnoses.[7,45] Smoking has direct correlations with hypertension, which has frequently been recorded as an independent risk factor for RCC in a dose-dependent fashion, therefore, it is unsurprising that this variable was present in greater than two-thirds of our sample.[44,46]

Alternatively, obesity, previously reported in 30–40% of RCC diagnosis, was seen in nearly 60% of our cohort, which may have contributed to an increased risk among our population and may warrant greater examination.[4,44,46] Despite lack of consistent evidence for type 2 diabetes as a risk factor, this condition was still seen in one-quarter of our patients, supporting the likelihood of a previously proposed interplay with other chronic comorbid conditions in the development of RCC.[5]

The province of NL has traditionally possessed the highest national incidence of various malignancies, paired with a unique risk factor profile for RCC. Considering the findings of the present study, additional research should aim to assess the epidemiology of these malignancies in this province. Evidently, the events of the pandemic have negatively impacted staging for several malignancies, including RCC, which may have real-world implications for survival during the continued recovery from this global catastrophe. Future research should aim to assess how these findings impact longitudinal outcomes and OS in this patient population in comparison to the pre-pandemic period and assess allocation of limited management resources.

Limitations

Several limitations must be considered when interpreting the findings of the present work.

First and foremost is the retrospective nature of the project, which presents a natural predisposition for inconsistent reporting or missing variables. Despite lack of omitted information in collected variables, the possibility for inaccuracies in the data recorded still exist. Regardless, we are confident that the results reported are indicative of a true stage migration, given the rigorous reporting procedures required in pathologic interpretation. Further, our focus on the proportion of cases rather than absolute counts provides further reassurance in the accuracy of study findings.

A second limitation exists in the interpretation of surgical wait times, as delayed timeframes may not be a true representation given the amenability of small renal masses to active surveillance, and do not represent emergent situations. In avoiding potential skews in data interpretation, surgical delay was calculated from time of surgical booking rather than first presentation.

Additionally, prolonged wait times may present if other necessitated and more immediate interventions are required; however, it is expected that the chance occurrence of these cases would have been equal across timeframes. We are confident that our results are indicative of increasing time from surgical booking to operative intervention resultant from the pandemic, given the backlog of urgent operative oncologic cases at our institution paired with the observed stage migration.

Further limitation exists in the unequal timeframes, given the shorter post-pandemic time-period, which have inevitably subjected these results to a length-time bias such that future research should focus on assessing longitudinal outcomes for these patients.

Finally, the island of Newfoundland has been documented as having significant potential to act as a microcosm for rare malignancies, including those with predisposition to RCC, which may limit applicability of these findings to other geographies; however, results of the present study demonstrated limited genetic influence paired with a risk factor profile consistent with extant literature on RCC such that we are confident the findings are applicable to other centers.

CONCLUSIONS

We identified a clinically significant stage migration for RCC paired with increasing wait times for surgical intervention during the immediate post-pandemic period. The impacts of the COVID-19 pandemic on diagnostic and therapeutic outcomes for patients with RCC cannot be ignored and warrant greater consideration in the prevention of detrimental outcomes.

COMPETING INTERESTS: The authors do not report any competing personal or financial interests related to this work.

This paper has been peer-reviewed.

REFERENCES

1. Athanazio DA, Amorim LS, da Cunha IW, et al. Classification of renal cell tumors - current concepts and use of ancillary tests: Recommendations of the Brazilian Society of Pathology. *Surg Exp Pathol* 2021;4:1-21. https://doi.org/10.1186/s42047-020-00084-x
2. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;71:209-49. https://doi.org/10.3322/caac.21660
3. Medina-Rico M, Ramos HL, Lobo M, et al. Epidemiology of renal cancer in developing countries: Review of the literature. *Can Urol Assoc J* 2018;12:E154-62. https://doi.org/10.5489/cuaj.4464
4. Chow W-H, Dong LM, Devesa SM. Epidemiology and risk factors for kidney cancer. *J Clin Oncol* 2010;7:245-57. https://doi.org/10.1200/JCO.2018.79.1905

5. Capitanio U, Bensalah K, Bex A, et al. Epidemiology of renal cell carcinoma. *Eur Urol* 2019;75:74-84. https://doi.org/10.1016/j.eururo.2018.08.036
6. Kabaria R, Klaassen Z, Terris MK. Renal cell carcinoma: Links and risks. *Int J Nephrol Renovasc Dis* 2016;9:45-52. https://doi.org/10.2147/IJNRD.S75916
7. Gansler T, Fedewa SA, Dana Flanders W, et al. Prevalence of cigarette smoking among patients with different histologic types of kidney cancer. *Cancer Epidemiol Biomarkers Prev* 2020;29:1406-12. https://doi.org/10.1158/1055-9965.EPI-20-0015
8. Yuan JM, Castelao JE, Gago-Dominguez M, et al. Tobacco use in relation to renal cell carcinoma. *Cancer Epidemiol Biomarkers Prev* 1998;7:429-33.
9. Theis RP, Dolwick Grieb SM, Burr D, et al. Smoking, environmental tobacco smoke, and risk of renal cell cancer: A population-based case-control study. *BMC Cancer* 2008;8:1-11. https://doi.org/10.1186/1471-2407-8-387
10. Joh HK, Willett WC, Cho E. Type 2 diabetes and the risk of renal cell cancer in women. *Diabetes Care* 2011;34:1552-6. https://doi.org/10.2337/dc11-0132
11. Kim CS, Han K Do, Choi HS, et al. Association of hypertension and blood pressure with kidney cancer risk: A nationwide population-based cohort study. *Hypertension* 2020;75:1439-46. https://doi.org/10.1161/HYPERTENSIONAHA.120.14820
12. Colt JS, Schwartz K, Graubard BI, et al. Hypertension and risk of renal cell carcinoma among white and black Americans. *Epidemiology* 2011;22:797-804. https://doi.org/10.1097/EDE.0b013e3182300720
13. Graff RE, Sanchez A, Tobias DK, et al. Type 2 diabetes in relation to the risk of renal cell carcinoma among men and women in two large prospective cohort studies. *Diabetes Care* 2018;41:1432-7. https://doi.org/10.2337/dc17-2518
14. Tseng CH. Type 2 diabetes mellitus and kidney cancer risk: A retrospective cohort analysis of the National Health Insurance. *PLoS One* 2015;10:1-14. https://doi.org/10.1371/journal.pone.0142480
15. Padala SA, Barsouk A, Thandra KC, et al. Epidemiology of renal cell carcinoma. *World J Oncol* 2020;11:79-87. https://doi.org/10.1007/s00761-019-0580-7
16. MacLeod LC, Hotaling JM, Wright JL, et al. Risk factors for renal cell carcinoma in the VITAL study. *J Urol* 2013;190:1657-61. https://doi.org/10.1016/j.juro.2013.04.130
17. Maher ER. Hereditary renal cell carcinoma syndromes: Diagnosis, surveillance and management. *World J Urol* 2018;36:1891-8. https://doi.org/10.1007/s00345-018-2288-5
18. Morrison PJ, Donnelly DE, Atkinson AB, et al. Advances in the genetics of familial renal cancer. *Oncologist* 2010;15:532-8. https://doi.org/10.1634/theoncologist.2010-0023
19. Schmidt LS, Linehan WM. Genetic predisposition to kidney cancer. *Semin Oncol* 2016;43:566-74. https://doi.org/10.1053/j.seminoncol.2016.09.001
20. Escudier B, Porta C, Schmidinger M, et al. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2019;30:706-20. https://doi.org/10.1093/annonc/mdz056
21. Downs TM, Schultzel M, Shi H, et al. Renal cell carcinoma: Risk assessment for newly diagnosed patients. *Crit Rev Oncol Hematol* 2008;70:59-70. https://doi.org/10.1016/j.critrevonc.2008.08.006
22. Krabbe LM, Bagrodia A, Margulis V, et al. Surgical management of renal cell carcinoma. *Semin Intervent Radiol* 2014;31:27-32. https://doi.org/10.1055/s-0033-1363840
23. Rendon RA, Kapoor A, Breau R, et al. Surgical management of renal cell carcinoma: Canadian Kidney Cancer Forum Consensus. *Can Urol Assoc J* 2014;8:e398-412. https://doi.org/10.5489/cuaj.1894
24. Wahlgren T, Harmenberg U, Sandström P, et al. Treatment and overall survival in renal cell carcinoma: A Swedish population-based study (2000-2008). *Br J Cancer* 2013;108:1541-9. https://doi.org/10.1038/bjc.2013.119
25. Capitanio U, Montorsi F. Renal cancer. Lancet. 2016;387:894-906. https://doi.org/10.1016/S0140-6736(15)00046-X
26. Resende CAA, Fernandes Cruz HM, Costa e Silva M, et al. Impact of the COVID-19 pandemic on cancer staging: An analysis of patients with breast cancer from a community practice in Brazil. *JCO Glob Oncol* 2022;8:1-7. https://doi.org/10.1200/GO.22.00289
27. Rottoli M, Gori A, Pellino G, et al. Colorectal cancer stage at diagnosis before vs during the COVID-19 pandemic in Italy. *JAMA Netw Open* 2022;5:1-11 https://doi.org/10.1001/jamanetworkopen.2022.43119
28. Castonguay M, El Sayed R, Richard C, et al. COVID-19 impact on diagnosis and staging of colorectal cancer: A single tertiary Canadian oncology center experience. *Curr Oncol* 2022;29:3282-90. https://doi.org/10.3390/curroncol29050268
29. Stevens MN, Patro A, Rahman B, et al. Impact of COVID-19 on presentation, staging, and treatment of head and neck mucosal squamous cell carcinoma. *Am J Otolaryngol - Head Neck Med Surg* 2022;43:17-22. https://doi.org/10.1016/j.amjoto.2021.103263
30. Parikh RB, Takvorian SU, Vader D, et al. Impact of the COVID-19 pandemic on treatment patterns for patients with metastatic solid cancer in the United States. *J Natl Cancer Inst* 2022;114:571-8. https://doi.org/10.1093/jnci/djab225
31. Blay JY, Boucher S, Le Vu B, et al. Delayed care for patients with newly diagnosed cancer due to COVID-19 and estimated impact on cancer mortality in France. *ESMO Open* 2021;6:1-11. https://doi.org/10.1016/j.esmoop.2021.100134
32. London JW, Fazio-Eynullayeva E, Palchuk MB, Sankey P, et al. Effects of the COVID-19 pandemic on cancer-related patient encounters. *JCO Clin Cancer Informatics* 2020;4:657-65. https://doi.org/10.1200/CCI.20.00068
33. Kuderer, NM, Choueiri TK, Shah DP, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet* 2020;395:1907-18. https://doi.org/10.1016/S0140-6736(20)31187-9
34. Zhai G, Zhou J, Woods MO, et al. Genetic structure of the Newfoundland and Labrador population: Founder effects modulate variability. *Eur J Hum Genet* 2016;24:1063-70. https://doi.org/10.1038/ejhg.2015.256
35. Robitaille C, Dai S, Waters C, et al. Diagnosed hypertension in Canada: Incidence, prevalence and associated mortality. *Can Med Assoc J* 2012;184:49-56. https://doi.org/10.1503/cmaj.101863
36. Lytvyak E, Straube S, Modi R, et al. Trends in obesity across Canada from 2005 to 2018: a consecutive cross-sectional population-based study. *C Open* 2022;10:E439-49. https://doi.org/10.9778/cmajo.20210205
37. DiBianco JM, Gomella PT, Ball MW. Pathologic T3a renal cell carcinoma: a classification in need of further refinement. *Ann Transl Med* 2018;6:1-4. https://doi.org/10.21037/atm.2018.12.51
38. Frank I, Blute ML, Cheville JC, et al. An outcome prediction model for patients with clear cell renal cell carcinoma treated with radical nephrectomy based on tumor stage, size, grade and necrosis: The SSIGN score. *J Urol* 2002;168:2395-400. https://doi.org/10.1016/S0022-5347(05)64153-5
39. Frank I, Blute ML, Leibovich BC, et al. Independent validation of the 2002 American Joint Committee on Cancer primary tumor classification for renal cell carcinoma using a large, single institution cohort. *J Urol* 2005;173:1889-92. https://doi.org/10.1097/01.ju.0000158043.94525.d6
40. Guven DC, Sahin TK, Yildirim HC, et al. Newly diagnosed cancer and the COVID-19 pandemic: Tumor stage migration and higher early mortality. *BMJ Support Palliat Care* 2021;0:1-6. https://doi.org/10.1136/bmjspcare-2021-003301
41. Lee-Ying R, O'Sullivan DE, Gagnon R, et al. Stage migration of testicular germ cell tumors in Alberta, Canada, during the COVID-19 pandemic: A retrospective cohort study. *C Open* 2022;10:E633-42. https://doi.org/10.9778/cmajo.20210285
42. Srivastava A, Patel H V., Kim S, et al. Delaying surgery for clinical T1b-T2bN0M0 renal cell carcinoma: Oncologic implications in the COVID-19 era and beyond. *Urol Oncol Semin Orig Investig* 2021;39:247-57. https://doi.org/10.1016/j.urolonc.2020.10.012
43. Chan VWS, Tan WS, Leow JJ, et al. Delayed surgery for localized and metastatic renal cell carcinoma: A systematic review and meta-analysis for the COVID-19 pandemic. *World J Urol* 2021;39:4295-303. https://doi.org/10.1007/s00345-021-03734-1
44. De P, Otterstatter MC, Semenciw R, et al. Trends in incidence, mortality, and survival for kidney cancer in Canada, 1986-2007. *Cancer Causes Control* 2014;25:1271-81. https://doi.org/10.1007/s10552-014-0427-x
45. Cumberbatch MG, Rota M, Catto JW E al. The role of tobacco smoke in bladder and kidney carcinogenesis. *Eur Urol* 2016;70. https://doi.org/10.1016/j.eururo.2015.06.042
46. Ba Z, Xiao Y, He M, et al. Risk factors for the comorbidity of hypertension and renal cell carcinoma in the cardio-oncologic era and treatment for tumor-induced hypertension. *Front Cardiovasc Med* 2022;9:1-12. https://doi.org/10.3389/fcvm.2022.810262

CORRESPONDENCE: Dr. W.C. Ian Janes, Faculty of Medicine, Memorial University, St. John's, NL, Canada; wcij85@mun.ca