Association des Urologues du Québec Congrès Annuel 2024 – Résumés

Session scientifique IV

Vendredi 8 novembre 2024 • Friday, November 8, 2024

Cité comme suit : *Can Urol Assoc J* 2024;18(12S4):S236-9. http://dx.doi.org/10.5489/cuaj.9082

Résumé 11

Understanding the molecular characteristics and vulnerabilities of sarcomatoid/rhabdoid renal cell carcinomas through integrative histological and spatial genomics approaches

Mustafa Soytas[1,4], Kate Glennon[2], Minjun Kim[2], Peixi Liu[2], Eleonora Scarlata[3], Tamiko Nishimura[2], Madeleine Arseneault[2], Senthilkumar Kailasam[2], Fadi Brimo[3], Simon Tanguay[4], Yasser Riazalhosseini[1,2]

[1]Victor Philip Dahdaleh Institute of Genomic Medicine, McGill University, Montreal, QC, Canada; [2]Department of Human Genetics, McGill University, Montreal, QC, Canada; [3]Division of Pathology, McGill University, Montreal, QC, Canada; [4]Division of Urology, McGill University, Montreal, QC, Canada

Introduction: Genomic and immune analyses in sarcomatoid/rhabdoid renal cell carcinoma (S/R RCC) have been limited to bulk tumor analysis and thus lack cellular resolution and spatial perspective. Herein, we use in situ whole transcriptome profiling (WTP) to define molecular differences between tumor regions with and without S/R features, aiming to identify molecular markers of S/R tumors that could lead to better diagnosis or treatments.

Methods: All patients who underwent surgical excision of RCC at the MUHC between 2010 and 2020 were screened by a uropathologist, and histologically defined regions of S/R, ccRCC, papillary, chromophobe RCC, and benign kidney were selected to construct tissue microarrays (TMAs). Whole-exome sequencing (WES) and Compartment-guided spatial WTP were applied for gene and transcriptome analysis.

Results: Our cohort included 56 RCC patients and their TMAs, consisting of 403 cores representing patient-matched tumor areas with and without S/R features. For WES, 47 patients were used to identify copy number variations (CNVs) analysis. Four hundred cores of 55 patients were used for WTP and five groups of clustered with 2000 highly variable genes (HVGs) were constructed. The most variable genes of each tumor type were identified by using digital spatial transcriptome profiling. Whole-exome sequencing was used to identify mutational patterns of tumor cells using a list of specific genes of interest.

Conclusions: According to current and ongoing results, WES and compartment-guided WTP should be used to generate an unprecedented resolution to the molecular and genomic characteristics of S/R RCC tumors and tumor microenvironment.

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Factors predicting opioid requirements of children undergoing outpatient circumcision

Sonia Chahine[1], Bruno Turcotte[1], Katherine Moore[1]

[1]CHU de Québec-Université Laval, Québec City, QC, Canada

Introduction: Healthcare providers are increasingly focused on minimizing opioid usage. Data are limited on factors predicting opioid use in children undergoing outpatient urologic surgeries. We aimed to identify factors that can predict the first 24-hour opioid requirements in prepubertal children undergoing outpatient circumcision.

Methods: We used prospectively collected data from our previous study on 155 patients comparing two different ultrasound-guided blocks during circumcision. Acetaminophen and ibuprofen were systematically given in the addition of the regional block. Five doses of morphine were prescribed at home if needed. Validated pain questionnaires, time to the first postoperative dose of narcotics, analgesic consumption during the first 24 hours after surgery, and satisfaction were collected.

Results: Forty-seven boys (30%) did not require any opioids in the hospital or at home. Most patients (63%) did not receive morphine after discharge. Among the 25 patients who took opioids during their hospital stay, 52% sustained the necessity for opioid at home during the first 24 hours. A Youden threshold value was found to be significant at 45 minutes post-surgery for patients who used in-house opioids. Of the 25 patients with hospital requirements, 10 patients (40 %) received their first opioids <45 minutes post-surgery and among them, two (20 %) sustained the need during the initial 24 hours ($p<0.0147$). In contrast, from the 15 patients (60.0 %) who received their first dose of opioids ≥45 minutes after surgery, 11 of them (73.3%) subsequently required opioids at home. The cumulative FLACC score ≥4 was found to be statistically significant ($p=0.0154$) for the consumption of narcotics in the first 24 hours.

Conclusions: In the first 24-hour postoperative period of pediatric circumcision, non-opioid analgesia on a scheduled basis coupled with a regional block seems to be sufficient for most patients for pain management. Receiving a narcotic dose in the immediate postoperative period seems to influence the subsequent narcotic consumption at home.

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Phase 2 clinical trial to evaluate the early return of urinary continence using a novel hybrid transvesical adapted Retzius-sparing robotic-assisted radical prostatectomy technique

Hend Alshamsi[1], Oleg Loutochin[2], Alexis Rompré-Brodeur[3], Victor McPherson[3]

[1]McGill University, Montreal, QC, Canada; [2]Jewish General Hospital, McGill University, Montreal, QC, Canada; [3]Division of Urologic Oncology, Jewish General Hospital, McGill University, Montreal, QC, Canada

Introduction: Open retropubic radical prostatectomy and standard robotic prostatectomy have substantial effects on postoperative quality of life through resultant urinary incontinence and erectile dysfunction. Retzius-sparing robotic-assisted radical prostatectomy (RS-RARP) has emerged as a technique to improve early return of continence. Alternative strategies, including transvesical approaches, have shown promise in achieving similar continence outcomes. This study aimed to evaluate a novel hybrid technique, transvesical Retzius-sparing robotic-assisted radical prostatectomy (TRS-RARP), at the Jewish General Hospital in Montreal.

Methods: This is a single-arm, prospective, phase 2 clinical trial using Simon's two-stage design (NCT06237114). The primary objective was the rate of urinary continence, defined as 0–1 pad/day, at three months postoperatively. The secondary objectives included continence rates at one and six months, quality of life using EQ-5D-5L, and urinary, bowel, and sexual function through EPIC-CP questionnaires. The study was powered to detect a 65% continence rate (H1) vs. 40% (H0) at three months, with planned 30 patient enrollment. Patients undergoing TRS-RARP were evaluated with baseline demographic data collection. Postoperative assessments were conducted at four weeks, three and six months. Surgical outcomes and pathology results were also analyzed.

Results: As of time of submission, data from an initial 17 enrolled patients was available for analysis and we anticipate having our 30 participants by end of October. The median patient age was 63.5 years. Fifteen patients completed a one-month followup; three-month followup data is expected shortly. The average baseline urinary incontinence according to EPIC-CP questionnaire was 0–1, and 4 at one month. The average number of pads/day was 0 at baseline, and 1–2 pads/day at one month. Quality of life, as measured by EQ-5D, showed 66% of patients had a normal baseline score of 11111, with 50% maintaining this score at one month,

while 30% shifted to a 11121 score. In terms of the EPIC-26, the average overall score was 8 at baseline and 13 at one month.
Conclusions: TRS-RARP represents a novel technique to potentially enhance early urinary continence recovery following radical prostatectomy. Early results suggest promising trends towards achieving the study's primary endpoint of improved early continence rates compared to historical benchmarks.

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Antibiotic use prior to BCG immunotherapy reduces treatment efficacy in non-muscle-invasive bladder cancer

Jalal Laaraj[1,2,3,4,5], Hubert Racine[1,2,3], Roxane Tourigny[1,2,4,5], Gabriel Lachance[1,2,4,5], Souhila Guettou Benmehidi[1,2,3], Prisca Nadège Koné[1,2], Jonathan Fadel[1,2,3], Paul Toren[1,2,3], Alain Bergeron[1,2,3], Yves Fradet[1,2,3], Karine Robitaille[1,2,4,5], Vincent Fradet[1,2,3,4,5]
[1]Centre de recherche du CHU de Québec-Université Laval, Quebec City, QC, Canada; [2]Centre de recherche sur le Cancer de l'Université Laval, Québec City, QC, Canada; [3]Faculty of Medicine, Université Laval, Québec City, QC, Canada; [4]Institute of Nutrition and Functional Foods (INAF); [5]NUTRISS Center - Nutrition, Health, and Society of Université Laval, Québec City, QC, Canada
Introduction: Immunotherapy with live-attenuated bacillus Calmette-Guérin (BCG) is the standard treatment for non-muscle-invasive bladder cancer (NMIBC). Unfortunately, 40% of patients do not benefit clinically from this treatment. It was recently shown that the success of various immunotherapies rely on a healthy gut microbiome, which is negatively altered by antibiotic (ATB) intake; however, the impact of ATB use on BCG treatment is unclear.
Methods: This retrospective study involved NMIBC patients who started a first BCG immunotherapy at CHU de Québec from 2009–2019. We reviewed ATB in prescriptions and medical records. Patients were considered exposed when ATB use lasted at least three days within three months before BCG initiation. The impact of ATB on BCG response was assessed using recurrence-free survival (RFS) and progression-free survival (PFS) using Kaplan-Meier analyses. To test the impact of ATB on BCG efficacy in vivo, C3H mice were randomized to either receive a broad-spectrum antibiotic regimen for one week or continue this ATB treatment throughout the experiment. Mice were subcutaneously injected with MBT-2 bladder cancer cells and received weekly intratumoral BCG treatments.
Results: Of 622 NMIBC patients, 77 (12%) were exposed to ATB before BCG treatment, while 545 (88%) were not. Compared to unexposed patients, ATB-exposed patients receiving BCG had a decreased RFS (HR 0.68, 95% CI 1.38–2.84, p=0.0002) and a trend for decreased PFS (HR 0.68, 95% CI 0.95–4.1, p=0.06). In the preclinical in vivo model, the prolonged use of ATB reduced the anti-tumor activity of BCG immunotherapy compared to controls (p<0.01).
Conclusions: In this first large, single-site, retrospective analysis of ATB use for at least three days before BCG treatment in NMIBC patients, ATB use within three months before BCG reduces treatment response. Prolonged ATB in vivo reduces BCG's anti-tumor activity. Our findings suggest that the gut microbiota may play a crucial role in the efficacy of BCG immunotherapy.

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Improving precision medicine by the use of a human-derived 3D model of prostate cancer

Félix-Antoine Pellerin[1,2], Stéphane Chabaud[1], Frédéric Pouliot[2,4], François Bordeleau[1,2,3], Stéphane Bolduc[1,2,4]
[1]LOEX, Regenerative Medicine Division, CHU de Québec-Université Laval Research Center, Quebec City, QC, Canada; [2]CHU de Québec-Université Laval Research Center (Oncology Division), Quebec City, QC, Canada; [3]Department of Molecular Biology, Medical Biochemistry and Pathology, Université Laval, Quebec City, QC, Canada; [4]Department of Surgery, Faculty of Medicine, Laval University, Quebec City, QC, Canada
Introduction: Prostate cancer (PCa) ranks among the most prevalent cancers in developed nations, yet treatments for advanced stages offer palliative relief. The existing research models for PCa lack fidelity in replicating crucial aspects of its biology, impeding translational potential to clinical applications. Our project's primary objective was to create a human-derived 3D PCa model using tissue engineering techniques.
Methods: Our methodology involves the cultivation of human prostate fibroblasts using the self-assembly method, creating stroma, and subsequent seeding of prostate epithelial cells on this stroma to mature into an epithelium. Specific cell culture conditions, including testosterone incorporation, replicate the hormone-responsive nature of the prostate. We integrated invasive PCa cell lines and spheroids to analyze invasion dynamics, offering a comprehensive platform for studying the tumor microenvironment.
In our process, fibroblasts are initially seeded at confluence in six well plates with a circular paper anchor, held down with a round stainless-steel ingot, and cultured in DMEM medium supplemented with ascorbate to promote collagen deposition over 14 days. Subsequently, these sheets are reseeded with fibroblasts for another 14 days and stacked, aided by rectangular stainless-steel ingots to facilitate stromal layers' fusion. Half of these stromas are cultured using a mixed media, incorporating conditioned media from the DU145 cell line to promote the induction of the fibroblasts into cancer-associated fibroblasts (CAF). Spheroids produced from the LNCAP and DU145 PCa cell lines were deposited onto the stromas. The DU145 line represents invasive PCa cells while LNCAP denotes a non-invasive cell line.
Results: We successfully created manipulatable stromas formed from prostate fibroblasts and from CAFs. Atomic force microscopy (AFM) was performed on the stromas to measure tissue rigidity, and thus ascertain the presence of CAF in the CAF induced stromas. Spheroids from the DU145 and LNCAP PCa cell lines were deposited on these stromas and their invasion of the tissues was analyzed by AFM and immunofluorescence. These techniques were done to allow better visualization of the spheroid invasion into the stroma and its impact on the neighboring cell's rigidity, mimicking the cancer microenvironment, and the CAFs' induction, leading to a higher rigidity.
Conclusions: This groundbreaking model shows great promise in discovering new treatment targets, which could improve patient outcomes and reduce the economic strain of PCa on healthcare systems. Our work in creating a 3D model of prostate cancer using human cells marks a significant advancement in PCa research.

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High-grade prostate cancer: Impact of low PSA levels at diagnosis on disease progression following radical prostatectomy

Jérémie Nadeau[1], Daphnée Bédard-Tremblay[1], Narcisse Singbo[2], Frédéric Pouliot[1]
[1]Département d'urologie, Université Laval, Québec City, QC, Canada; [2]Centre de recherche du CHU de Québec, Université Laval, Québec City, QC, Canada
Introduction: The most impactful prognostic factors in prostate cancer (PCa) involve Gleason score (GS), preoperative prostate-specific antigen (pPSA), and TNM stage. Elevated PSA levels have long been associated with poorer outcomes; however, high-grade (HG) PCa, defined by GS ≥8, can occasionally present with low pPSA (<5 ng/ml). Recent evidence suggests that in HG PCa, lower pPSA levels may correlate with worse outcomes compared to intermediate levels, challenging the linear relationship between pPSA and PCa severity. This study aimed to investigate whether low pPSA levels predict inferior recurrence-free survival and development of lethal PCa post-radical prostatectomy (RP) compared to intermediate pPSA levels in localized HG PCa patients.
Methods: This retrospective cohort study analyzed patients with localized PCa and biopsy-proven HG who underwent RP at our center and PROCURE's biobank between 2011 and 2021. Pathological data from prostate biopsies and surgical specimens were collected, and clinical outcomes were assessed. Statistical analyses were conducted using SAS 9.4 software. Restricted cubic spline with Cox regression, and Kaplan-Meier analysis with log-rank tests were used to compare outcomes among patients with low (<5 ng/mL), intermediate (5–8 ng/mL), and high pPSA (>8 ng/mL) levels. Primary outcome was progression to lethal PCa defined as metastatic disease or PCa-related death.
Results: A total of 729 patients were analyzed, with a median pPSA level of 7.3 ng/ml and a mean followup of 72 months. Pathologic evaluation revealed positive surgical margins in 373 (51%), ≥pT3 in 484 (66%), and pN1 in 175 (24%). Over the study period, biochemical recurrence occurred in 425 (58%), while 115 (16%) developed metastasis and 78 (11%) castration-resistant cancer. No significant statistical difference was observed in progression to lethal PCa between patients with low and intermediate pPSA levels. Restricted cubic spline with Cox regression revealed a direct correlation between PSA and lethal PCa.
Conclusions: In our specific population of HG PCa patients treated with radical prostatectomy, we did not observe a worse impact of low pPSA levels compared to intermediate PSA levels on the progression to lethal PCa, contrary to findings from other studies.

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Effet d'une supplémentation en oméga-3 sur le micro–environnement tumoral du cancer de la prostate

Lucie Leclair[1,2,3,4], Gabriel Lachance[1,2,3], Oscar Molina[1], Hélène Hovington[1], Yves Fradet[1,2,3], Karine Robitaille[1,2,3], Vincent Fradet[1,2,3,4]

[1]Centre de recherche du CHU de Québec – Université Laval, Québec City, QC, Canada; [2]Centre Intégré de Cancérologie (CIC), Université Laval, Québec City, QC, Canada; [3]Centre Nutrition, Santé et Société (NUTRISS) et Institut sur la Nutrition et les Aliments Fonctionne; [4]Faculté de médecine de l'Université Laval, Québec City, QC, Canada

Introduction : Le cancer de la prostate (CaP) est associé à l'inflammation chronique du tissu. Un monoacylglycéride couplé à l'acide eicosapentaénoïque (MAG-EPA), un sous-type d'acide gras oméga-3 aux propriétés anti-inflammatoires, a été testé dans un essai clinique de phase II mené par notre équipe. 130 hommes atteints de CaP ont été randomisés à la prise de MAG-EPA ou d'un placebo pour sept (7) semaines avant leur prostatectomie. Les issues cliniques suggèrent que la supplémentation en MAG-EPA favorise une diminution de l'agressivité du cancer entre la biopsie et la chirurgie (p=0.024) et réduit le risque de récidive biochimique (p=0.048). La présente étude vise à approfondir le rôle du MAG-EPA sur la modulation du microenvironnement tumoral du CaP, en particulier sur le changement de grade histologique.

Méthodes : Des échantillons de tissus prostatiques ont été collectés à la chirurgie et disposés sur des micromatrices tissulaires. Le profilage immunitaire a été réalisé par immunohistochimie et immunofluorescence multiplexée à haut débit. L'analyse quantitative et spatiale des cellules immunitaires a été effectuée en association avec les données cliniques.

Résultats : Comparé au placebo, les patients supplémentés avec le MAG-EPA présentant un changement de grade à la baisse ont un plus grand nombre d'amas lymphocytaires. La composition et l'organisation spatiale du microenvironnement tumoral montrent aussi des différences entre les deux groupes, particulièrement chez les patients avec un changement de grade à la baisse.

Conclusions : La supplémentation en MAG-EPA semble moduler le microenvironnement tumoral associé à une diminution de l'agressivité du CaP. L'analyse plus approfondie des types cellulaires impliqués permettra de mieux comprendre les mécanismes anti-tumoraux. Ces premières observations soulignent le potentiel du MAG-EPA comme agent thérapeutique dans la prise en charge du CaP, en contribuant à une évolution clinique favorable.

Résumé 43

Comparing outcomes of retroperitoneal vs. transperitoneal robotic-assisted partial nephrectomy

Iman Sadri[1], Abdulla Alameeri[1], Simon Tanguay[1], Maurice Anidjar[2], Alexis Rompré-Brodeur[1,2]

[1]Division of Urology, Department of Surgery, McGill University Health Centre, Montréal, QC, Canada; [2]Department of Urology, Jewish General Hospital, McGill University, Montreal, QC, Canada

Introduction: We aimed to describe the surgical efficacy, efficiency, and safety of retroperitoneal robot-assisted partial nephrectomy (R-RAPN) vs. transperitoneal robot-assisted partial nephrectomy (T-RAPN).

Methods: We retrospectively reviewed a prospectively maintained database of a single surgeon's RAPN between September 2022 and February 2024. Baseline and tumor characteristics, as well as operative and perioperative parameters were collected. Thirty-day complications and 3–6-month followup creatinine and hemoglobin were gathered. Descriptive statistics, including means, standard deviations, and frequencies, were calculated for all relevant variables. Normality and homogeneity of variances assumptions were assessed for continuous variables.

Results: A total of 71 patients were included, 32 in the T-RAPN group and 39 in the R-RAPN group. Mean age, BMI, baseline eGFR, Charlson comorbidity index, RENAL nephrometry score, and tumor size were comparable between both cohorts. Both groups had similar rates of endophytic and cystic lesions. The T-RAPN group was comprised of predominantly anterior tumors, while the R-RAPN group had predominantly posterior tumors (p<0.001). Mean OR time was 21 minutes shorter in the R-RAPN group, although failing to achieve statistical significance (186 vs. 165 minutes, p=0.121). Estimated blood loss was significantly lower in the R-RAPN group (328 vs. 173 ml, p=0.047). Clamp time was six minutes shorter in the R-RAPN group, approaching statistical significance (p=0.076). More patients in the R-RAPN group were performed using off-clamp enucleation compared to the T-RAPN cohort (19% vs. 44%, p=0.026). Subgroup analysis for BMI >35 and anterior tumors demonstrated similar outcomes for OR time, estimated blood loss, clamp time, and postoperative day 1 hemoglobin drop between R-RAPN and T-RAPN. In posterior tumors, R-RAPN had shorter operative and clamp time and less estimated blood loss compared to T-RAPN, although failing to achieve statistical significance.

Conclusions: R-RAPN is an efficient and effective approach to performing partial nephrectomy, with potential superior surgical outcomes in those with posteriorly located tumors.

Résumé 29

The incidence of urinary tract infections and urosepsis following holmium laser enucleation of prostate: A meta-analysis

Sepehr Niakani[1], Tarek Benzouak[1], Michael Maalouf[1], Ahmad AlShammari[2], Mélanie Aubé-Peterkin[2], Fadl Hamouche[2]

[1]Faculty of Medicine and Health Sciences, McGill University, Montreal, QC, Canada; [2]Division of Urology, Department of Surgery, McGill University, Montreal, QC, Canada

Introduction: Holmium laser enucleation of the prostate (HoLEP) is the gold standard management for benign prostatic hyperplasia (BPH). The rate of urinary tract infections (UTI) and urosepsis post-HoLEP, however, is unknown. Accordingly, we aimed to measure the incidence of those complications and the effects of patient and procedural parameters on their occurrence.

Methods: Our protocol was registered on Prospero [CRD42022380847]. A comprehensive database search of MEDLINE, Embase, Web of Science, and CINAHL, as well as pre-print manuscripts, was conducted. Observational studies reporting the incidence of UTI and/or urosepsis post-HoLEP were included. Event rate meta-analyses were performed using a random effects model, and the impact of procedural and patient factors on infectious outcomes was measured via meta-regression analyses.

Results: The incidence of UTI and urosepsis post-HoLEP were 4.05% and 0.7%, respectively, as measured across 33 research articles and 11 abstracts (n=20522). Meta-regression analyses identified that higher prostate volumes and higher volumes of resected prostatic tissue were correlated with decreased (b=-0.0332, SE=0.0101, 95% CI -0.0531, -0.0134, z=-3.28, p=0.0010) and increased (b=0.0405, SE=0.0103, 95% CI 0.0203, 0.0608, z=3.93, p<0.0001) rates of UTI, respectively. The effects of other pre- and intraoperative factors on the occurrence of UTI or urosepsis were not significant.

Conclusions: Our study is the first evidence synthesis reporting the incidence of post-HoLEP UTI (4.05%) and urosepsis (0.7%). Indeed, our findings highlight the safety of HoLEP in the treatment of BPH. Additionally, the effects of prostate and resected tissue volumes on the incidence of UTI highlight their importance in determining patients' risk profiles preoperatively for reducing infectious outcomes, particularly in those deemed at risk.

Résumé 40

La radiomique pour prédire l'histologie des masses rénales

Teodora Boblea Podasca[1], Mahdi Ait Lhaj Loufti[2], Marc-Antoine Blais[3], Marie-Lou Gadoury-Campbell[3], Stéphanie Boulet[1], Martin Vallières[2], Patrick O. Richard[1]

[1]Département d'urologie, Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC, Canada; [2]Département d'informatique, faculté des sciences, Université de Sherbrooke, Sherbrooke, QC, Canada; [3]Faculté de médecine et des sciences de la santé, Université de Sherbrooke, Sherbrooke, QC, Canada

Introduction : Présentement, les médecins ne peuvent pas se fier aux imageries pour déterminer avec précision l'histologie d'une masse rénale. La radiomique – l'extraction de données quantitatives provenant d'une imagerie – pourrait aider à résoudre ce problème. L'objectif principal de cette étude était de construire un modèle prédictif utilisant la radiomique sur CT scan et/ou des données cliniques pour distinguer le carcinome rénal à cellules claires (ccRCC) du carcinome rénal à cellules non claires (nccRCC).

Méthodes : Cette étude rétrospective unicentrique a utilisé le système d'information canadien sur le cancer du rein pour identifier les patients opérés pour un carcinome rénal localisé entre 2011 et 2021. Les données cliniques ont été extraites et, pour chaque patient, la masse rénale a été segmentée manuellement sur le scan sans contraste (CT) et avec contraste (CECT). Ensuite, 173 caractéristiques radiomiques ont été extraites. 80% de l'ensemble de données a été utilisé pour créer et tester 5 modèles prédictifs indépendants avec un algorithme

XGboost. Une fois le meilleur modèle choisi, le 20% de données restantes a été utilisé pour tester la performance du modèle final.
Résultats : 326 patients ont été inclus : 76 % avec un ccRCC et 24 % avec un nccRCC. La taille moyenne des tumeurs était de 5,1 ± 3,2 cm. Pour le stade T clinique: 66 % étaient T1, 7 % T2, et 27% T3 ou T4. Après l'analyse des 5 modèles, celui utilisant la radiomique sur CECT a démontré les meilleurs résultats, avec une AUC de 0,83 [IC95% : 0,76, 0,88] et une sensibilité et spécificité de 91% [IC95% : 81,97] et 48% [IC95% : 30, 80] respectivement. Le modèle final avait une AUC de 0,90, avec une sensibilité de 86 % et une spécificité de 80 %.
Conclusions : En conclusion, notre modèle prédictif basé sur la radiomique a démontré une bonne performance pour la distinction des ccRCC et nccRCC sur CECT. Cela soutient l'utilisation de la radiomique pour aider à guider la gestion du cancer du rein.

Résumé 10

Virtual reality in pain management during extracorporeal lithotripsy sessions: A randomized pilot study

Roxann Thériault[1], Marie-Philippe Harvey[2,3], Carmen-Édith Belleï-Rodriguez[2,3], Aurélie Flaive[2,3], Lucas Seggio[2,3], Serge Marchand[3], Guillaume Léonard[2,3], Samuel Lagabrielle[1]
[1]Département d'urologie, Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC, Canada; [2]Centre de recherche sur le vieillissement, CIUSSS de l'Estrie, Sherbrooke, QC, Canada; [3]Faculté de Médecine et des Sciences de la Santé, Université de Sherbrooke, QC, Canada

Introduction: Extracorporeal shockwave lithotripsy (ESWL) is an effective but painful treatment modality for kidney stone disease, which may require the use of opioids. Virtual reality (VR) creates an immersive environment known to reduce the perception of pain. The objective of this randomized pilot clinical trial was to evaluate the feasibility of the protocol and the effect of VR on pain, anxiety, and opioids consumption.
Methods: Patients with radiopaque kidney stones undergoing ESWL for the first time were randomized 2:1 into VR or control group, targeting a sample size of 30 participants. The VR group wore headsets producing a visual and audio stimulation for 20 minutes before ESWL, while the control group had a break in a quiet room. Pain intensity was assessed using a visual analog scale and anxiety using the IASTA questionnaire pre- and post-ESWL. Fentanyl consumption was recorded by dose of 50 mcg injected upon patient's request. Technicians performing the ESWL sessions were blinded to group allocation and followed the same protocol to gradually increase the intensity of the ESWL.
Results: Out of 267 ESWL done in our institution from November 2022 to May 2024, 69 patients (25.8%) were eligible; 30 were included (18 in VR group, 12 in control group; mean age 57, range 21–82 years). VR was well-tolerated, except for one patient who asked to stop after five minutes. Pain intensity was significantly lower in the VR group (3.8/10) compared to controls (5.9/10, p=0.043). No differences were found in the average ESWL power (69 vs. 67%, p=0.669), antalgic doses used (1.4 vs. 1.4, p=0.753), and IASTA questionnaires (p=0.263), in both groups.
Conclusions: Results show promising outcomes of VR during ESWL in terms of pain perception, although antalgic doses and anxiety were not reduced. VR was well-tolerated by patients. The implementation of an adequately powered randomized controlled trial will face a low recruitment rate, and appropriate strategies will have to be elaborated.

Résumé 32

Anesthésie locale en urétéroscopie flexible : Analyse rétrospective des prédicteurs de douleur

Tarek Benzouak[1,2], Ahmad Alshammari[1], Abdulmalik Addar[1], Fadl Hamouche[1], Abdullah Alahmari[1], Sebastien Belliveau[1], Michael Maalouf[1], Rakan Al Haidey[1], Sero Andonian[1], Nada Mohamed[1], Nader Fahmy[1]
[1]Division d'Urologie, Département de Chirurgie, Université McGill, Montreal, QC, Canada; [2]Faculté de Médecine et des Sciences de la Santé, Université McGill, Montreal, QC, Canada

Introduction : L'uréthéroscopie (URS), couramment utilisée dans la gestion minimalement invasive de l'urolithiase et du carcinome urothélial, repose traditionnellement sur l'anesthésie générale pour assurer le confort des patients. Le passage à l'URS flexible, favorisé par les avancées technologiques endourologiques, propose l'anesthésie locale (AL) comme alternative pour réduire les risques périopératoires et améliorer la récupération. Cette étude évalue les résultats rapportés par les patients sous AL en URS flexible, visant à redéfinir les protocoles d'anesthésie pour cette approche.
Méthodes : Nous avons mené une étude rétrospective de cohorte au Centre de santé de l'Université McGill, analysant les procédures d'URS flexible réalisées sous AL par un seul chirurgien de mai 2020 à mars 2023. Les données démographiques des patients, les détails procéduraux et les scores de douleur post-procédurale, mesurés à l'aide d'une échelle visuelle analogique, ont été collectés.
Résultats : Nous avons inclus 61 procédures d'URS sous AL, avec un score de douleur moyen de 2,05, indiquant des expériences de douleur globalement faibles. Les indications pour l'URS incluaient le cancer urothélial des voies urinaires supérieures (47,5 %), les sténoses (32,8 %) et l'urolithiase (19,7 %). La procédure était très tolérable, avec un seul abandon en raison de l'inconfort. Notre modèle multivarié expliquait 31 % de la variance des résultats de douleur (R^2 = 0,314, F(9, 51) = 2,599, p = 0,015). L'utilisation du guide augmentait les scores de douleur de 1,87 unité (β = 1,869, p = 0,004) par rapport à l'URS à main levée. Les patients masculins ressentaient des scores de douleur réduits de 1,38 unité par rapport aux patientes (β = -1,380, p = 0,029).
Conclusions : Ces résultats suggèrent que l'AL pourrait être une alternative viable à l'anesthésie générale pour certaines populations de patients subissant une URS. L'identification de prédicteurs de douleur, tels que l'utilisation de guide et les différences de douleur entre les sexes, suggère que les facteurs patients et procéduraux affectent le confort des patients lors de l'URS sous AL. Des études prospectives et des essais contrôlés randomisés sont essentiels pour valider ces observations et pour élucider pleinement le rôle de l'AL dans l'amélioration des résultats patients en URS flexible.

Résumé 8

Cost-effectiveness of PARP inhibitors for patients with metastatic castration-resistant prostate cancer: The Canadian perspective

Ivan Yanev[1,2], Armen G. Aprikian[3], Brendan L. Raizenne[4], Alice Dragomir[3,5]
[1]Experimental Surgery, McGill University, Montreal, QC, Canada; [2]Centre for Outcomes Research and Evaluation, Research Institute of McGill University Health Centre, Montreal, QC, Canada; [3]Division of Urology, Department of Surgery, McGill University, Montreal, QC, Canada; [4]Division of Urology, Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada; [5]Faculty of Pharmacy, l'Université de Montréal, Montréal, QC, Canada

Introduction: Through phase 3 clinical trials, poly-adenosine diphosphate–ribose polymerase inhibitors (PARPI) have demonstrated outcome improvements in metastatic castrate-resistant prostate cancer (mCRPC) patients with alterations of breast cancer 1 or 2 genes (BRCA1/2). While improving outcomes, PARPI contribute to the ever-growing economic burden of prostate cancer. The objective of this project was to evaluate the cost-effectiveness of PARPIs (olaparib, rucaparib, or talazoparib) vs. the standard of care (docetaxel or androgen-receptor pathway inhibitors ARP]) for mCRPC patients with BRCA1/2 mutations from the Canadian healthcare system perspective.
Methods: Partitioned survival models were created to represent mCRPC disease after progression until death. Survival inputs were extracted from PROfound, TRITON3, and TALAPRO-1 clinical trials, while Canadian-specific costs are presented in 2023 dollars. Outcomes are discounted at 1.5% per year.
Results: PARPIs provide better survival benefit in terms of quality-adjusted life years (QALY) than the current standard of care, but at a higher additional cost (incremental cost-utility ratio of $572 009/QALY). PARPIs required price reductions of up to 83% to meet local willingness-to-pay thresholds (WTP). Results were most sensitive to PARPI acquisition costs and health state utility parameters.
Conclusions: While providing survival benefits to mCRPC patients presenting deleterious BRCA1/2 gene mutations, PARPIs are not as cost-effective and require major price reductions to reach local WTP thresholds.