1. Prostate cancer

1 GDF15 propeptide is a novel blood biomarker for castration-resistant prostate cancer patients with bone metastasis via promoting the vicious cycle

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Background
There is no useful blood biomarker for bone metastasis (BM) in prostate cancer (PCa). Especially in castration-resistant prostate cancer (CRPC), bone scan index (BSI) by bone scintigraphy is a more accurate indicator of BM than PSA. However, this imaging tool is only available in a limited number of facilities, so the purpose of this study was to create a simple and accurate BM biomarker for CRPC patients.
Materials and Methods
We comprehensively examine culture supernatants from 7 prostate, 4 kidney, and 4 bladder cancer cell lines using Orbitrap LC-MS to identify a novel protein specifically secreted by PCa as a biomarker. The effects of this protein will be examined in CRPC cell lines (PC-3 and DU145), osteoblasts, osteoclasts. To evaluate the mechanism of this protein, we created the recombinant protein and injected luciferase gene-transfected PC3 to the tibia of NOD/SCID mice to create BM model. In addition, plasma concentrations of this protein will be measured by Enzyme-Linked Immunosorbent Assay in 185 patients, including 80 mCRPC patients for whom BSI was being measured, and compared with existing biomarkers (PSA, ALP, LDH, OC, BAP, PINP, TRACP 5b).
Results
A total of 2,167 proteins were identified by secretome analysis, and we focused on GDF15 propeptide (GDPP), which is secreted by osteoblasts and osteoclasts as well as PCa cells. GDPP is generated through cleavage by furin from its precursor when secreted extracellularly, and GDPP promotes proliferation, migration, and invasive ability in PC3 and DU145. Furthermore, GDPP enhanced bone formation via increased expression of *RUNX2*, *OSX*, and *ATF4* in osteoblasts, and enhanced bone resorption via increased expression of *NFATc1* and *DC-STAMP* in osteoclasts. In BM mouse model, GDPP aggravated BM with increasing of osteoblast and osteoclast expression. Clinical performance in two cohorts showed that GDPP (both AUC=0.92) was more diagnostic for BM than PSA (AUC=0.78 and 0.59). The amount of change in BSI over time with systemic treatment clearly correlated with that of GDPP (r=0.67), but not with that of PSA (r=-0.041).
Conclusions
GDPP enhances the vicious cycle in the bone microenvironment and is a novel blood biomarker reflecting the aggressiveness of BM in CRPC patients.

1. Prostate cancer

2 Impact of Thienopyridine Class Antiplatelets on Bleeding Outcomes Following Robot-Assisted Radical Prostatectomy: A Cohort Study from a Multicenter Database

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Purpose: This study aims to evaluate the effects of thienopyridine-class antiplatelet agents, including ticlopidine, clopidogrel, and prasugrel, on bleeding complications in patients who underwent robot-assisted radical prostatectomy.

Materials and Methods: This cohort study used a database for robot-assisted radical prostatectomy at 23 tertiary centers nationwide. Among 7700 patients who underwent RARP between 2011 and 2022, patients who received thienopyridines (thienopyridine group) were compared with those who received aspirin monotherapy (aspirin group). The primary outcome focused on the incidence of bleeding complications that required transfusion, additional intervention, or readmission. High-grade complications were defined as Clavien–Dindo grade III or higher. The characteristics of the two groups were adjusted using inverse probability of treatment weighting with propensity scores. The risks of these outcomes were evaluated using weighted regression models.

Results: This study included 520 patients, with 147 in the thienopyridine group and 373 in the aspirin group, respectively. Within the thienopyridine group, 126 (86%) received clopidogrel and 52 (35%) received dual antiplatelet therapy. Thienopyridine therapy was associated with a higher risk of bleeding complications (OR:3.62, 95%CI:1.548.49), transfusion (OR:6.35, 95%CI:1.75–23.0), and readmission (OR:2.96, 95%CI:1.346.54). The increased risks of the thienopyridine group were detected for low-grade bleeding complications (OR:3.20, 95%CI:1.23–8.30) but not for high-grade bleeding complications (OR:5.23, 95%CI:0.78–34.9). The increased risk of bleeding complications was not observed when thienopyridine was discontinued (OR:2.52, 95%CI:0.83–7.70); however, it became apparent when it was continued perioperatively (OR:4.35, 95%CI:1.14–16.61).

Conclusions: This study reveals that thienopyridine increases the incidence of bleeding complications, particularly low-grade bleeding complications, following robot-assisted radical prostatectomy. These bleeding effects emerged when thienopyridine was continued perioperatively.

1. Prostate cancer

3 Preventive measures for port-site hernia in Robotic Assisted Radical Prostatectomy

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Background
With the spread of SARS-Cov-2 infection, the risk of infection due to pneumoperitoneum gas exposure during laparoscopic surgery has been pointed out. In our hospital, robot-assisted urologic surgery is performed with a constant smoke evacuation pneumoperitoneum device (AirSeal®) to manage the gas exchange in a closed circuit. On the other hand, 12mm AirSeal® port site tend to be larger than other ports, and port site hernias often become a problem.
Methods
Due to the occurrence of port-site hernia to the 12mm AirSeal® port, we decided to perform a port suture from the abdominal cavity before the end of insufflation to ensure closure of the peritoneum.
Results
Although this procedure is rather complicated, it can be performed in about 6 minutes on average, regardless of the patient's size or the surgeon's experience. None of the 89 patients who underwent the procedure developed port-site hernias. Port-site hernias are especially noted to occur in ports larger than 10 mm. In pelvic robotic-assisted surgery, port-site hernias are more likely to occur at the lateral side ports that are in close proximity to the intestinal tract and coincide with the Spigelian hernia belt.
Conclusions
Secure suturing from the abdominal cavity may prevent the development of hernias. By standardizing the procedure, suture operations can be performed in a relatively short time without being affected by operating skill or patient body shape. Fascial closure should be aggressively considered for port wounds greater than 10 mm below the arch line.

1. Prostate cancer

4 Differences in incidence and clinicopathologic features of secondary bladder cancer after long-term follow-up of brachytherapy and radical prostatectomy for localized prostate cancer

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Background: Although there studies have been reported that brachytherapy (BT) for prostate cancer is associated with an increased incidence of metachronous urinary bladder cancer (MBC), few studies have clarified differences in the clinicopathological features (CPF) of MBC between BT and prostatectomy (RP). We studied the risk and clinicopathological CPF of MBC between RP and BT groups in our hospital after long-term follow-up.

Methods: Five hundred four patients treated with BT and 471 referred patients treated with RP between 2006 and 2017 in our hospital were reviewed. We compared the incidence of MBC and the CPF including the tumor number, location within the bladder, histology, and time from BT or RP to the MBC occurrence between BT and RP. The differences between the two groups were analyzed. Furthermore, in the BT group, the radiation dose distribution within bladder was estimated.

Results: A total of 11 cases of MBC occurred in the BT group (2.2%) and 7 in the RP group (1.5%) after a median follow-up time of 107 months (13-209). The median time from initial treatments to the occurrences of MBC was 65 months (12-121) in BT and 100 months (4-126) in RP (p=0.469). Average tumor number was not significantly different between the groups (BT:1.4, RP:1.9, p=0.589). The tumor locations of MBC within the bladder for BT vs. RP were 9 vs. 1 in the lateral wall, 0 vs. 4 in the posterior wall, 0 vs. 3 in the dome, and 1 vs. 0 in the trigone. The incidence in the lateral wall was significantly higher in BT than in RP (p=0.001). Their median radiation dose of right wall (15.7±7.74Gy) and left wall (13.0±5.85Gy) showed no significant difference compared to the BT patients without MBC. There were 3 muscle-invasive cases in BT and 1 in RP (p=0.60). High-grade urothelial carcinoma occurred significantly more in BT (10 cases) than in RP (1 case) (p=0.001). According to the criteria, six MBC were judged as radiation-induced secondary bladder cancer.

Conclusions: Long-term follow-up showed that the risk of MBC after BT was similar to that after RP. MBC after BT occurred significantly more frequently in the lateral wall and had a higher grade compared to those after RP.

1. Prostate cancer

5 The efficacy of androgen receptor signaling inhibitor therapies for metastatic hormone-sensitive prostate cancer at Yamaguchi University

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Objective; Androgen receptor signaling inhibitor (ARSI) therapies for metastatic hormone-sensitive prostate cancer (mHSPC) is available since the approval of abiraterone in 2018. We report the efficacy of treatment with ARSI for mHSPC at our hospital.

Methods; Forty-one patients treated with ARSI therapies for mHSPC at Department of Urology, Yamaguchi University, from February 2018 to March 2023 were analyzed, retrospectively.

Results; The median age was 73 years (62-89), median iPSA was 315 ng/mL (4.27-5401), Gleason score was ≥8 in 39 cases (95%), and Gleason grade group 5 was observed in 27 cases (66%). Thirty-four cases (83%) had bone metastases, and 11 cases (27%) had EOD ≥3. Five patients (12%) had visceral metastases. The median Bone Scan Index as measured by BONENAVI® was 0.84% (0-11.12%). The drugs used were apalutamide in 16 patients, abiraterone in 20 patients, and enzalutamide in 5 patients. 6 patients (15%) were diagnosed with CRPC, and time to CRPC was 79.76% at 24 months. Gleason grade group 5 was an independent predictor of time to CRPC (odds ratio 11.54; p=0.01). CTCAE Grade 3 or higher adverse events occurred in four patients (9.8%), with skin rash in 3 patients who received apalutamide and hepatic dysfunction in 1 patient who received abiraterone.

Conclusion; ARSI therapies for mHSPC showed preferable response without life-threatening adverse effect response to treatment, and triplet therapy may be considered in patients in Gleason grade group 5.

2. Bladder Cancer and Upper Tract Urothelial Carcinoma

6 Baseline Tumor Size as a Prognostic factor for Immune Checkpoint Inhibitor Treatment in Metastatic Urothelial Carcinoma Refractory to First-Line Platinum Combined Chemotherapy

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Background: Clinical trials have introduced innovative therapies for metastatic urothelial carcinoma (mUC), primarily immune checkpoint inhibitors (ICIs). However, the relationship between baseline tumor size (BTS) and the effectiveness of ICI therapy in mUC remains unexplored. This study aims to evaluate whether BTS could predict overall survival (OS) and progression-free survival (PFS) in mUC patients (Pts) undergoing ICI treatment.

Methods: We conducted a retrospective analysis of data from 56 Pts with platinum-refractory mUC (PRmUC) who received pembrolizumab (PB) between February 2018 and December 2022 at our institution. We assessed OS rates using Kaplan-Meier curves and the log-rank test. The Objective Response Rate (ORR) and BTS was evaluated using CT scans taken within one month before ICI administration, following RECIST criteria, allowing for up to two measurable lesions per organ and five measurable lesions in total. Target lesions needed to have a diameter of ≥10mm or a short axis of ≥15mm to qualify as lymph node lesions. BTS was estimated using the maximum BTS (mBTS) and total BTS (the sum of the diameters of target lesions). Pts were categorized into two groups based on the cut-off values calculated using the Area Under Curve (AUC) method: tBTS (<50 mm vs ≥50 mm) and mBTS (<30 mm vs ≥30mm).

Results: Among the 56 Pts, median follow-up of 17.4 months, 25 Pts (45%) had succumbed. The median OS was 23.4 months, and the 1-year OS rate was 33%. The ORR was 25%. PFS was notably shorter in Pts with a large tBTS (p=0.015) and a large mBTS (p=0.002). While OS was shorter in Pts with a large tBTS (p=0.355), it significantly reduced in those with a large mBTS (p=0.019), possibly due to subsequent Enfortumab-Vedotin treatment.

Conclusion: In this study, we found that BTS is a valuable prognostic factor in PRmUC Pts treated with PB. Larger both tBTS and mBTS, was associated with significantly shorter PFS. OS was significantly shorter in those with a large mBTS. Pts with PRmUC should be treated with PB earlier before reaching those cutoff values of BTS. Pts with tumor size around the cutoff values for BTS, debulking surgery before ICI treatment may be considered as a therapeutic option.

2. Bladder Cancer and Upper Tract Urothelial Carcinoma

7 A single-institution experience of intra-arterial chemoradiation therapy for non-metastatic bladder cancer

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Object: We investigated the outcome of selective organ preservation in non-metastatic bladder cancer using intra-arterial infusion chemoradiation therapy.

Methods: We examined the outcomes of 18 patients with non-metastatic bladder cancer who underwent intra-arterial infusion chemoradiation therapy between 2016 and 2023. We used radiotherapy to the bladder at 60-66 Gy/30-33 fr and cisplatin 25-100 mg/body administered twice or three times at 3-week intervals through the bilateral bladder arteries. The patients were followed up with clinical and radiographic investigations and bladder biopsy was performed as needed.

Results: The median age of the patients was 80 (46-87) years, 11 were male and 7 were female. 2 patients were at clinical stage Ta, 11 at T2, 3 at T3, 1 at T4, and 1 at Tx. The median follow up were 20 (2-69) months. Overall survival rate was 72%, cancer-specific survival rate was 83% and progression-free rate was 46%. Adverse events included enteritis, dermatitis, cystitis, leukopenia, anemia, and thrombocytopenia; except for one case with grade 3 hematotoxicity, all others were grade 2 or less.

Conclusions: Intra-arterial chemoradiotherapy for bladder cancer is well tolerated and may be a viable option for patients who refuse radical cystectomy.

2. Bladder Cancer and Upper Tract Urothelial Carcinoma

8 Establishment of muscle-invasive bladder cancer models by molecular subtype

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Methods: Recently, molecular subtype classification of muscle-invasive bladder cancer based on gene expression profiles has attracted attention, and currently six subtypes have been proposed, with differences in response rates to chemotherapy and IO (immuno-oncology) treatment reported among the subtypes. Individualized therapeutic selection based on molecular subtypes is considered necessary, but due to the lack of preclinical models, little progress has been made in studying individual treatment strategies. To address this clinical challenge, we are working to establish disease models based on a molecular biological understanding the diversity of bladder cancer.

Results: We focused on organoids, a three-dimensional tissue culture system, as a new model for bladder cancer carcinogenesis. We removed the bladder of mice in which *Trp53* mutation and expression of Cas9-GFP were induced specifically in Krt5-positive cells, which are considered to be one of the origin cells of bladder cancer. GFP-positive cells isolated from the urothelial cells were grown in 3D culture with Matrigel, resulting in the successful establishment of organoids (K5-mUrorganoid; $Trp53^{R172H/+}$). Furthermore, we generated *Pten*-KO organoids (K5-mUrorganoid; $Trp53^{R172H/+}$; $Pten^{-/-}$) by infection with adeno-associated virus (AAV). These cells were transplanted subcutaneously into nude mice and formed tumors that histologically resembled human basal-squamous type with squamous differentiation, and were also found to be viable in immunocompetent mice.

Conclusions: We have successfully established a mouse model of basal-squamous subtype bladder cancer. We are currently investigating factors involved in treatment response and resistance to IO drugs by studying the response of this model. Further studies are needed to establish models for other bladder cancer subtypes.

3. Renal cancer

9 Clinicopathologic analysis of predictive factors for oncological and functional outcomes in minimally invasive treatment for cT1 renal cell carcinoma

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Introduction and objectives:

Tumor-associated factors including tumor complexity play an important role in determining appropriate treatment strategies for small renal cancers. This study aims to evaluate the impact of those on oncological and functional outcomes following minimally invasive treatments for small renal cancers.

Materials and methods:

435 patients with cT1 (<7cm) renal cell carcinoma (RCC) who underwent either robot-assisted partial nephrectomy (RAPN) or percutaneous cryoablation (PCA) divided into training and validation cohort at a ratio of 7:3. All patients were scored according to the modified R (radius, tumor size), E (endophytic properties), N (nearness to the collecting system or sinus), A (anterior or posterior), L (location to the polar line) nephrometry score (m-RENAL score). The primary endpoint was achieving a trifecta, comprising the absence of treatment failure and major complications, as well as preserving renal function. Multivariable logistic regression models were applied to the training cohort. A nomogram was developed using tumor-associated factors and other clinicopathologic factors to predict trifecta achievement. The receiver operating curve (ROC) was utilized to validate the nomogram.

Results:

The trifecta was achieved in 157 (89%) out of 176 RAPN patients and 229 (88%) out of 259 PCA patients, respectively (P=0.8). For developing and validating the nomogram, a total of 305 and 130 patients were assigned to the training and validation cohorts respectively. Multivariate analysis indicated that the L domain of the m-RENAL score was the sole factor associated with trifecta achievement (P=0.009). The resulting nomogram predicting trifecta achievement included the type of intervention, R, E, N, and L domains of the m-RENAL score, histologic subtype, and pretreatment eGFR value. The area under the curve for the ROC was 0.72 for the training cohort and 0.56 for the validation cohort.

Conclusion:

The L domain of the m-RENAL score emerged as the solo independent predictor of trifecta achievement. The nomogram holds the potential to serve as a valuable tool for predicting outcomes for minimally invasive treated cT1 RCC.

3. Renal cancer

10 Comparative Effectiveness of TKI Monotherapy and ICI Combination in First-Line Advanced Renal Cell Carcinoma Treatment

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<Background>
Several drugs, such as TKIs and ICIs, have gained approval for treating advanced renal cell carcinoma (RCC). This study aimed to compare the efficacy between TKI monotherapy and ICI combined therapy as first-line treatments for advanced RCC.
<Methods>
This study included patients who received first-line medical treatment for advanced RCC between April 2007 and November 2023 at our hospital. The progression-free survival (PFS), overall response rate (ORR) and overall survival (OS) were evaluated and compared between TKI monotherapy group and ICI combined therapy group.
<Results>
In 79 patients (59 male and 20 female), median (range) age was 69 years (35-86), 44 had metachronous and 35 synchronous metastasis. The number of patients received TKI monotherapy and ICI combined therapy were 49 and 30, respectively. IMDC risk group distribution was favorable 16%, intermediate 62%, poor 21% (TKI group: 18% / 69% / 12%, ICI combined group: 13% / 50% / 37%). Median PFS was 7.4 months in TKI group and 10.3 months in ICI combined group (p=0.13). The ORR was 0.35 in TKI group and 0.63 in ICI combined group (p=0.02). Median OS was 42.9 months in TKI group, while it was not reached in ICI combined group (p=0.5).
<Conclusions>
ICI combined therapy had significantly higher response rate and tended to be longer time to progression than TKI monotherapy. Our retrospective study indicated that ICI combined therapy was more effective than TKI monotherapy as the first-line treatment for advanced RCC.

3. Renal cancer

11 Development of models of *Neurofibromatosis 2 (NF2)* loss in kidney cancer of Hereditary Leiomyomatosis and Renal Cell Carcinoma (HLRCC)

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Introduction and Objective

Hereditary Leiomyomatosis and Renal Cell Carcinoma (HLRCC) is characterized by cutaneous leiomyomas, uterine leiomyomas, and renal cell carcinoma, caused by a germline mutation in the Fumarate Hydratase (FH) gene. HLRCC patients have aggressive disease with poor outcomes due to limited treatment options. Neurofibromatosis 2 (NF2) is an autosomal dominant disease mainly characterized by high risk of schwannomas. NF2 mutations are identified in 15-20% of HLRCC kidney cancer. As there has been extensive research on Neurofibromatosis-related cancers, we created models of the NF2 deficient HLRCC kidney cancer to assess the biologic effects and therapeutic sensitives to agents that have been investigated in this disease.

Methods

Three isogenic NF2-KO cell lines were generated from NF2 wild-type HLRCC patients derived cell lines (NCCFH1, UOK262, and UOK268), using CRISPR. Protein abundance was analyzed using Western Blot. Gene expression changes were evaluated using the Nanostring nCounter Tumor Signaling 360 gene expression panel and analyzed by ROSALIND™. Cell proliferation, soft agar, scratch wound-healing, and transwell invasion assays were performed. Clonogenic survival assays was performed in NF2-KO HLRCC cell lines treated with Rapamycin, Everolimus, Brigatinib, GSK2256098, and TAK228. We evaluated tumor growth *in vivo*.

Results

Loss of function of NF2 increased kidney cancer cell proliferation, migration, invasion, and colony formation, especially in UOK262 cell line. Gene expression profiling revealed increased activation of mammalian target of rapamycin (mTOR) signaling, Glucose Metabolism, HIF1 Signaling. NF2 deficient NCCFH1 and UOK262 models displayed increased sensitivity to Rapamycin. NF2 deficient UOK262 cells grew much faster as subcutaneous tumor xenografts in NSG mice than cells expressing with sgAAVS1.

Conclusions

Our current data indicated that FH deficient cell lines with NF2 loss of function may have more aggressive potential, and further suggest that mTOR complex-1 (mTORC-1) therapy could play a role into treatment algorithms of NF-2 deficient HLRCC kidney cancers. *In vivo* experiments are planned to test therapeutic approaches.

3. Renal cancer

12 LDH isozyme as a prognostic factor for patients with metastatic clear cell renal cell carcinoma

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Introduction: LDH isozyme is a tetramer of two subunits, H chain and M chain, and is present in all living tissue. Five types of molecular forms characterize the LDH pattern, and tumor tissues relatively consist LDH-4 and LDH-5, composed with a high ratio of the M chain, compared to normal tissues. This study analyzed the association between LDH isozyme and prognosis of mCRCC after nephrectomy.

Material and Methods: Clinical records of mCRCC patients initially diagnosed M0 disease between 2012 and 2016 were retrospectively reviewed. LDH isozyme values before operation and at time of metastasis were checked. Isozyme patterns were classified into 6 types, LDH 1-5 dominant and common type, according to the most composed molecular form.

Results: 38 patients were identified. Median age was 65 years old (36-87). pT1 was seen in 3 cases, pT2 in 4, pT3 in 27, and pT4 in 4. Pathological grade 2 were 9 cases, G3 in 21, and G4 in 8. As for the IMDC risk, favourable was 2 cases (5%), intermediate in 26 (68%) and poor in 10 (26%). Median LDH was 163 IU/L (113-317), and isozyme dominant pattern were as follows: LDH-2 in 9 cases (24%), LDH-3 in 6 (16%), LDH-4 in 4, LDH-5 in 11. 8 cases were common type, and no cases showed LDH-1 dominant. Median time from surgery to recurrence was 10 months (1-104), median follow-up period after recurrence was 18 months (4-72). 16 deaths occurred. No significant correlation was seen between pre-operative LDH isozyme pattern and pathological grade or pT stage. Pre-operative LDH isozyme did not correlate with time to recurrence ($p=0.7420$). Median OS for LDH-4 dominant at the time of metastasis was 10.9 months, significantly shorter than other isozyme types ($P=0.0134$).

Conclusion: LDH-4 dominant isozyme pattern at time of recurrence has a short OS, proposing as a prognostic predictor in mRCC.

3. Renal cancer

13 Elucidation of Transcriptional regulation in Translocation Renal Cell Carcinoma Using CRISPR/Cas9 Genome-Wide Screening

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Objective: Xp11.2 translocation renal cell carcinoma (Xp11.2 tRCC) is a type of renal cell carcinoma caused by the formation of a fusion gene through translocation on the X chromosome, resulting in the constitutive activation of the transcription factor TFE3. We demonstrated the ability of the fusion TFE3 (PRCC-TFE3) to induce renal cell carcinoma through the creation of kidney-specific PRCC-TFE3-expressing mice. However, fusion TFE3 also induces an Oncogene-induced senescence (OIS)-like cell growth inhibition in human renal proximal tubule-derived HK2 cells and human embryonic kidney-derived HEK293 cells. This study aims to elucidate the transcription mechanism of the oncogene fusion TFE3 by identifying the genetic changes necessary for cell growth inhibition induced by fusion TFE3 using CRISPR/Cas9 genome-wide screening.
Methods: We established stable CRISPR/Cas9-expressing HK2 cell lines with inducible PRCC-TFE3. Genome-wide screening using an sgRNA library was conducted in these HK2 cells, and candidate genes were evaluated through RNA sequencing, ChIP qPCR, and immunostaining.
Results: CCNC was identified as an essential gene for cell growth inhibition induced by fusion TFE3 expression. CCNC is a constituent factor of the mediator complex that regulates transcription. Inhibition of the mediator complex by treatment with its inhibitor led to a suppression of cell growth inhibition similar to CCNC KO in response to fusion TFE3. Furthermore, treatment with the mediator complex inhibitor revealed selective control of fusion TFE3 transcriptional activity. ChIP qPCR and immunostaining using CCNC also suggested that the mediator complex selectively regulates fusion TFE3 transcriptional activity.
Conclusion: This study reveals that the transcriptional activity induced by the oncogene fusion TFE3 is selectively controlled by the mediator complex. The mediator complex emerges as a potential novel therapeutic target for Xp11.2 translocation renal cell carcinoma.

5. BPH&LUTS

14 Which affects nocturnal frequency most: Urgency or sleep disorders?

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Introduction & Objectives: There are three major causes of nocturia: bladder storage dysfunction, nocturnal polyuria, and sleep disorders. Although the majority of patients with nocturia have nocturnal polyuria, we have found no reports regarding which of the bladder storage and sleep disorders contributes more strongly to nocturnal frequency. We analyzed whether urinary urgency or sleep disorders more strongly affects nocturnal frequency.

Materials & Methods: We analyzed the symptom severity of male patients with lower urinary tract symptoms/benign prostatic hyperplasia (LUTS/BPH) at their first visits to our outpatient department between April 2014 and May 2018. We evaluated their International Prostate Symptom Score (IPSS) and the original Quality of Sleep Score (QOSS; 1: very good, 2: fairly good, 3: neither good nor bad, 4: fairly bad, 5: very bad) and divided the patients into two groups depending on IPSS question (q)7 (nocturia) and then compared the groups' IPSS and QOSS responses.

Result: Results of 1,478 patients, 360 were excluded due to insufficient questionnaire answers. In 1,018 evaluated cases (age 70.7±8.8 yrs [mean±SD data]), the mean sleep questionnaire score was 3.0±1.1. The IPSS item scores were q1 = 1.8±1.8; q2 = 2.4±1.7; q3 = 1.8±1.9; q4 = 1.7±1.8; q5 = 2.6±1.9; q6 = 1.5±1.8; and q7 = 2.3±1.4. Average total scores were: IPSS 14.1±8.8; IPSS-QOL index 3.8±1.7; and QOSS 2.9±1.1. The median IPSS q7 score was 2.0, and we divided the patients using this cutoff: nocturia ≤2 (n=425) and ≥3 (n=593). Univariate statistics suggested that all of the IPSS and QOSS were significantly associated with nocturia. A multiple regression analysis revealed that IPSS q2 (frequency score: OR 1.21, 95%CI: 1.1–1.4, p=0.001) and q4 (urgency score: OR 1.32, 95%CI: 1.2–1.5, p≤0.001) and the QOSS (OR 1.69, 95%CI: 1.5–2.0, p<0.001) were predictive factors of nocturia. Spearman's rank correlation coefficient revealed that urgency (0.447), and sleep disorder (0.393) were significantly correlated with nocturia.

Conclusion: Both urgency and sleep disorder were strongly correlated with nocturia, but sleep disorder was more important than urinary urgency for LUTS/BPH patients.

6. Urinary Incontinence, Voiding Dysfunction and Prolapse Management

15 Two-photon calcium imaging uncovered that micturition-related neural activity in the cerebral cortex depends on the location, cell-type, and projection pathway

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Introduction & objectives

The mechanism of micturition is complicated and especially in the cerebral cortex, micturition-related neural activity remains poorly understood. Two-photon calcium imaging enables to observe individual neural activities with high spatial resolution. In the present study, we observed the neural activities in the cerebral cortex using two-photon calcium imaging and evaluated the relationship with micturition.

Materials & methods

We genetically expressed calcium indicators in the anterior cingulate cortex (ACC) or the primary motor cortex (M1) of mice. Cell-type patterns were 1) non-selective neurons, 2) layer 5 pyramidal neurons, and 3) certain projection neurons; the ACC to the periaqueductal gray matter (PAG) or the M1 to the pontine micturition center (PMC). Two-photon calcium imaging from the ACC or the M1 was performed with bladder perfusion under urethane anesthesia. Micturition-related neurons were extracted according to neural synchrony with micturition.

Results

The rates of micturition-related neurons per all observed neurons were 1) 6.34%, 2) 10.97%, 3) 9.42% in the ACC and 1) 6.61%, 2) 10.33%, 3) 8.50% in the M1.

The hot spot (high density region) of micturition-related neurons in the ACC (posterior and deep region) were more local than in the M1. The peak timing histogram of 2) activities in the ACC was bimodal (early and delayed peak), and the latter peak was analogous with histogram of 3) activities. Furthermore, the population of the delayed neurons was located in the hot spot of the ACC (posterior and deep region). On the other hand, the patterns of neural activity were uniform among each variation in the M1.

Conclusion

We represented that micturition-related neural activities in the cerebral cortex could be detected individually, which was the first study using two-photon calcium imaging for micturition. Especially in the ACC, the patterns of the activities depend on the cell-type and projection pathway, indicating that the presence of functional clusters. The various neural activity timings would indicate that these neurons play different roles for micturition each other. Utilizing this calcium imaging method would uncover the mechanism of micturition in the future.

6. Urinary Incontinence, Voiding Dysfunction and Prolapse Management

16 Decreased NO production and increased arteriosclerosis cause salt-induced nocturnal polyuria

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Introduction

We have reported that a combination of reduced nitric oxide (NO) production and excessive salt intake induces nocturnal polyuria (NP) in mice. We hypothesized that the same mechanism may cause NP in humans. Moreover, we hypothesized that arteriosclerosis is a predictor of NP associated with excessive salt intake because arteriosclerosis is reported to decrease NO production. The aims of this study were to elucidate the effects of decreased NO production on salt-induced NP and evaluate the predictive value of arteriosclerosis for salt-induced NP in humans.

Materials and methods

Living kidney transplantation donors were included. Twelve-hour Urine collection tests were performed, and urine collected from 10:00 to 22:00 h was defined as daytime urine, and urine from 22:00 to 10:00 h as nighttime urine. The daytime and nighttime urine volume, urinary salt excretion, and urinary nitric oxide (NOx) excretion were evaluated. The nocturnal polyuria index (NPi) was defined as nighttime urine volume/ daily urine volume. The urinary salt excretion was regarded as salt intake. The arteriosclerosis was evaluated by abdominal calcification index (ACI). First, all patients were classified into two groups, high NOx and low NOx group according to NOx excretion, and the correlation between salt intake and NPi was compared between the two groups. Next, the patients were classified into two groups, high ACI and low ACI groups, according to the ACI index, and the NOx excretion was compared between the two groups. Finally, the correlation between salt intake and NPi was compared between the two groups.

Results

Twenty-seven living kidney transplantation donors were included. The NPi was positively correlated with salt intake in the low NOx group ($R=0.65$, $P = 0.02$), but not in the high NOx group ($R=-0.10$, $P = 0.74$)The NOx excretion level in low ACI group was significantly higher than that of high ACI group ($P = 0.05$). The NPi was positively correlated with salt intake in the high ACI group ($R=0.40$, $P = 0.03$), but not in low ACI group ($R=-0.07$, $P = 0.34$).

Conclusion

The decreased NO production and increased arteriosclerosis is involved in salt-induced NP in humans. The arteriosclerosis is suggested to be a predictive value for salt-induced NP.

7. Others

17 Creatine chemical exchange saturation transfer imaging (Cr-CEST) is an innovative method for evaluating intratesticular spermatogenesis

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[Introduction and Objective] The sperm retrieval rate in non-obstructive azoospermia (NOA) is still insufficient. To overcome this problem, an accurate noninvasive method of evaluating testicular spermatogenesis is needed. Chemical exchange saturation transfer (CEST) imaging is a new magnetic resonance imaging (MRI) technique that can image the distribution of trace substances in vivo. We focused on the high creatine (Cr) levels in testes and hypothesized that Cr-CEST could indicate intratesticular spermatogenesis noninvasively.

[Methods] We compared the Cr-CEST signal in testes and testicular spermatogenesis in male infertility model mice, such as the Sertoli-cell-only syndrome model (SCO), and maturation arrest model (MA). To evaluate spatial resolution, we performed Cr-CEST for a partial testicular irradiation model in which the lower half of the testes was irradiated with a single 6Gy dose.

[Results] Cr-CEST signal intensity was enhanced as maturation in the testes progressed in the order of SCO, MA, and normal control (4.0 ± 0.3 vs 5.7 ± 0.2 vs 6.8 ± 0.3, $p<0.05$). In the partial irradiation model, the signal intensity in the irradiated area was significantly lower than that in the non-irradiated area (5.3 ± 1.4 vs 7.6 ± 0.3, $p<0.05$).

[Conclusions] Cr-CEST could noninvasively evaluate intratesticular spermatogenesis both qualitatively and spatially. Cr-CEST can be used as preoperative imaging for evaluating intratesticular spermatogenesis and a navigation system during microscopic intratesticular sperm extraction.

7. Others

18 Isolated calyx caused by robot-assisted partial nephrectomy for neuroendocrine tumor of horseshoe kidney: A case report

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Introduction:
Robot-associate partial nephrectomy (RAPN) has become a standard treatment option for the management of small renal tumors. Surgical assistance robots have enabled us to perform more challenging RAPN procedures that would have otherwise been impossible. While surgical assistance robots have expanded the implementation of partial nephrectomy (PN) surgeries, these procedures can lead to complications that are rarely caused by conventional PN. One potential complication is an isolated calyx which involves the disconnection of the renal calyx and pelvis.
Renal neuroendocrine tumors (NETs) are low-grade tumors with neuroendocrine differentiation, and NETs in the kidney are extremely rare.
We present a case of NET in a horseshoe kidney with an isolated calyx caused by robot-assisted partial nephrectomy.
Case:
A 56-year-old man with a left renal tumor was referred to our hospital. There were no significant findings in blood and biochemistry tests. CT scans revealed a horseshoe kidney and a hypovascularized tumor with a diameter of 19 mm in the ventral side of the left kidney hilum. Off-clamp RAPN was performed. The tumor was easily identified and exposed. After excising the tumor, we found that the renal pelvis was open and closed it using a running suture. However, there was persistent urine leakage from the resection site. We then found a renal papilla that was located some distance from the renal calyx at the resection site, but they were too far apart to anastomose.
The renal papilla was therefore coagulated to prevent postoperative urine leakage. The total operative time was 333 min and total blood loss was 50 ml. The postoperative recovery period was uneventful.
Postoperative pathology findings showed renal NET.

7. Others

19 Poor performance status is a risk factor for higher detection of Gram positive coccus in stone-related pyelonephritis

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Introduction: We aimed to investigate the detection rate of causative organisms in stone-related pyelonephritis and to compare their distribution according to patient backgrounds.

Methods: We retrospectively identified patients with stone-related pyelonephritis. Clinical data were collected between November 2012 and August 2020 at Wakayama Medical University Hospital, including on patient backgrounds and causative organisms. Patients were categorized by Eastern Cooperative Oncology Group performance status (PS) as the good PS group (0, 1) and the poor PS group (2~4). Bacteria were divided into Gram-positive cocci (GPC) or non-GPC groups and logistic regression analysis was used to examine factors that predict detection of GPC.

Results: Seventy-nine patients had stone-related pyelonephritis, 54 (68.4%) in the good PS group and 25 (31.6%) in the poor PS group. In the good PS group, *Escherichia coli* (67%) was followed by *Klebsiella species* (9%), while in the poor PS group, *Escherichia coli* (20%) was followed by *Enterococci* and *Staphylococci* (12%). GPC detection rate was significantly higher in the poor PS group than in the good PS group (40.0% vs 14.8%, p=0.016), and multivariate logistic regression analysis showed that poor PS was an independent factor predicting detection of GPC (OR=6.54, p=0.02).

Conclusions: The distribution of the causative organisms in stone pyelonephritis was similar to that in common complicated urinary tract infections. Poor PS may be an independent predictor of GPC detection in patients with stone pyelonephritis.

7. Others

20 Usefulness of 90m Creatinine Clearance Assay in the Evaluation of Renal Function

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Background: The gold standard for assessing renal function is glomerular filtration rate (GFR) measurement using inulin clearance (Cin), but it has disadvantages associated with the administration of exogenous substances. Twenty-four-hour creatinine clearance (CCr) is widely used for GFR assay using endogenous substances, but it requires long-time urine storage and may overestimate renal function. The aim of this study is to investigate the usefulness of a new CCr assay that can be performed in a short time and less invasive.

Methods: A total of 434 pre-donation donors, post-donation donors, and post-transplant recipients who underwent the Cin measurement were included. Cin was measured using the standard method of three 30-minute cycles. We measured 90minutes CCr (90mCCr) using the same method as for Cin. The predictability of mGFR by 90mCCr was evaluated by single regression analysis and Bland-Altman analysis. We randomly divided these patients into two groups. The regression equation of 90mCCr on mGFR was calculated using the study cohort, and the accuracy of the regression equation was evaluated using the validation cohort.

Results: The coefficient of determination of 90mCCr for mGFR was R^2=0.84 ($p<0.0001$), and the median bias was 30.9(29.7-32.1) mL/min/1.73m^2. The coefficient of determination of adjusted 90mCCr (adj90mCCr) for mGFR was R^2=0.84 ($p<0.0001$), with the median bias of -0.19(-1.45-1.08) mL/min/1.73m^2.

Conclusions: The 90mCCr assay is accurate, short-time, and without exogenous substances method of assessing renal function.

7. Others

21 The MAG3 renal scintigraphy performed on the first postoperative day predicts early postoperative renal function recovery

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Introduction: In our clinical practice, we utilize MAG3 renal scintigraphy on the first postoperative day to ensure adequate blood perfusion in the entire kidney. This procedure also provides insights into excretory patterns, which we have noted vary among different cases. Our hypothesis posits that MAG3 renal scintigraphy can reflect the severity of acute tubular necrosis and, consequently, predict swift renal function recovery post-transplant. Additionally, identifying the factors influencing the variability in MAG3 scintigraphy results could be instrumental in promoting early recovery of renal function.

Methods: From 2010 to 2023, our hospital performed 379 living donor kidney transplants, out of which 307 cases were included in this retrospective cohort study. The patients were categorized into three groups - good, poor, and very poor - based on their excretion patterns as observed in MAG3 renal scintigraphy. We examined renal function trends over a 21-day postoperative period across these groups and assessed potential risk factors.

Results: Among the 307 cases, 204 were classified in the good group, 46 in the poor group, and 57 in the very poor group. Baseline characterization revealed significant differences among the groups in recipient gender, donor age, recipient BMI, and Total Ischemic Time (TIT). There was a significant variation in postoperative eGFR trends among the groups, with the good group exhibiting notably higher eGFR values and the very poor group showing significantly lower values. TIT emerged as a critical risk factor affecting excretion patterns.

Conclusions: MAG3 renal scintigraphy on the first postoperative day serves as a predictive tool for the improvement of graft function following kidney transplantation. By assessing excretion patterns through this scintigraphy, it's possible to anticipate early recovery of renal function, with implications for postoperative patient care and management.