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1 DETECTION RATE OF PROSTATE CANCER IN ANTERIOR ZONE USING TRANSRECTAL ULTRASOUND-GUIDED BIOPSY WITH END-FIRE PROBE

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Introduction/Aim: The anterior zone (AZ) of the prostate is not palpable on digital rectal examination and not targeted commonly by saturation prostate biopsy schemes (1, 2). Recent magnetic resonance imaging data suggest that the AZ can harbour significant cancers (3). We evaluated the detection rate of AZ sampling at the time of repeat transrectal ultrasound-guided saturation prostate biopsy (TRUSbx) using transrectal end-fire probe. Materials and Methods: Between January 2009 and January 2015, 257 consecutive patients underwent TRUSbx at our Department of Urology. Indications for TRUSbx included patients with suspicion of prostate cancer (PCa) even though they had undergone at least one standard (12-14 cores) TRUS-guided biopsy without diagnosis of PCa. TRUSbx was performed under sedoanalgesia with the patient in the left lateral decubitus using a General Electric Logiq 7 machine equipped with a 5-9 MHz multi-frequency convex probe “end-fire”. After imaging the prostate, sampling was carried out with an 18-Gauge tru-cut needle powered by an automatic spring-loaded biopsy disposable gun. Three experienced urologists performed a 24-core biopsy scheme including AZ (two per side). The Gleason grading was based on the recommendations of the 2005 international society of urological pathology consensus conference. All biopsy cores were analysed internally by our Pathology Department that specializes in genitourinary pathology. Results: Statistical analysis of the entire cohort showed a mean age of 62.7±6.93 years, a mean prostate-specific antigen (PSA) of 7.84±4.62 ng/ml, a total volume of the prostate of 53.35±21.77 ml and a body mass index (BMI) of 26.3±3.8 kg/m2. PCa was diagnosed in 93 patients (36.2%). For Gleason score (GS) at biopsy, 57 patients (61.3%) had GS≤6, 29 (31.2%), GS=7 and 7 (7.5%) GS≥8. In 17 patients affected by PCa, cancer in the AZ was found. When cancers detected only by the AZ were compared to all other cancers, there was no statistically significant difference in the patients’ age (p=0.74), PSA (p=0.23), prostate volume (p=0.32), BMI (p=0.27), clinical stage (p=0.55) or GS (p=0.26). Eleven of the 17 patients with AZ positive biopsies had GS≤6 and 6 patients GS=7. Twelve of the 17 patients underwent radical prostatectomy. Two were upgraded to GS7 after being designated GS6 on the biopsy. Without bilateral AZ in TRUSbx, the overall cancer detection rate decreased to 18.3% (17/93) (Table I). Discussion and Conclusion: Since the entire apex is composed of peripheral zone, biopsies performed at the apex or lateral apex might not sample the anterior apex. TRUS end-fire probe permits biopsy cores to be taken more transversely (oriented along an anterior-posterior axis) and has a more oblique-angled trajectory, thereby allowing direct anterior sampling. Based on our experience, we can conclude that the TRUSbx technique using end-fire probe can be used in all cases of repeat biopsy or transperineal saturation biopsy, as TRUSbx provides biopsy schemes with higher PCa detection rates, as well as good patient tolerability and satisfaction.


Table I. Number of positive cores for prostate cancer (PCa) in prostate biopsy.

<table>
<thead>
<tr>
<th>No of cores positive for PCa: 345/2232 (15.5%)</th>
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<td>Lateral plane</td>
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2 INCIDENCE AND PROGNOSTIC SIGNIFICANCE OF PERINEURAL INVASION IN RADICAL PROSTATECTOMY SPECIMENS: A MONOCENTRIC EXPERIENCE

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Introduction/Aim: Perineural space invasion (PNI) is an important mechanism for progression of cancer through the prostatic capsule with a controversial prognostic significance (1, 2). An average of 10% to 20% needle biopsy pathology reports leads to PNI diagnosis (3). The purpose of the present study was to assess the prognostic significance of PNI between prostate biopsy and radical prostatectomy (RP) samples in patients affected by localized prostate cancer (PCa). Materials and Methods: Seventy-five patients undergoing RP with laparoscopic technique, who had PNI on prostate needle biopsy, were retrospectively reviewed. Transrectal ultrasound-guided prostate biopsy (TPB) was performed using a General Electric Logiq 7 machine equipped with a 5-9MHz multi-frequency convex probe “end-fire”. After imaging the prostate, sampling was carried out with a 18-Gauge tru-cut needle powered by an automatic spring-loaded biopsy disposable gun. We excluded patients that received neoadjuvant androgen ablation therapy and/or radiotherapy before RP. To evaluate the correlation between PNI and adverse pathological characteristics of PCa, we examined patients’ age, family history, prostate-specific antigen (PSA) level, biopsy Gleason score (GS), clinical stage (T), extraprostatic extension (EXE), percentage of positive surgical margins (PSM), biochemical recurrence (BR), percentage of positive lymph nodes (PLN) and seminal vesicle invasion (SVI). Follow-up was conducted at 3, 6 and 12 months post-RP during the first year and every six months in the second and third year. PSA level >0.2 ng/ml, by two subsequent measures, was defined as BR. Results: The median age of the 75 patients was 61.3 years (56-76) and the median pre-operative PSA level was 5.8 ng/ml (2.03-15.13), while the median prostate volume was 42.9 ml (17-106). Clinical stage was T1 in 26 (34.6%), T2a/T2b in 31 (41.4%) and ≥T2c in 18 (24%) patients. Biopsy GS was low (GS≤6) in 47 (62.7%), moderate (GS=7) in 22 (29.3%) and high (GS>7) in 6 (8%) patients. At RP, 18 patients (24%) had organ-confined disease, whereas EXE in neurovascular bundle and SVI were present in 57 (76%) and 5 (6.7%) patients, respectively. PSM were shown in 24 (32%) and positive lymph nodes in 13 (17.3%) patients. At a median follow-up of 44 months (12-84), 27 (36%) had BR, 7 (9.3%) developed metastatic disease and 2 (2.6%) died of PCa. GS (≥6) on needle biopsy and the pre-operative PSA level (≥10) were helpful in predicting the patients that were likely to have tumour in the neurovascular bundle (p<0.002). Patients with presence of tumour in the neurovascular bundle were more aggressive, with 38.6% of them having PSM compared to 11.1% of cases without EXE of tumour in neurovascular bundle. However, PLN and SVI occurred less frequently in patients who had tumour in the neurovascular bundle (15.8% compared with 44.5% of patients without tumour EXE, p<0.001). Discussion and Conclusion: This study demonstrated that PNI is not statistically associated with PSM. However, BR, which occurs in 36% of patients, is statistically associated with PNI (p<0.001). PLN involvement was demonstrated in 17.3% of all patients with PNI that underwent RP. We also found that PLN involvement was associated with biologically aggressive PCa (p<0.001). PLN was associated with the pathological stage, GS, PSM, SVI and pre-operative PSA (p<0.002). Based on our experience, PLN involvement was associated with BR after RP on the univariate analysis but not on the multivariate analysis. Additional studies with more detailed exposure measurement are warranted to evaluate questions regarding the percentage of diagnostic biopsies involved with PNI and whether it should be considered in the selection of patients for additional treatment and in planning the follow-up regimen of patients after RP for localized PCa.


3 CAN BODY MASS INDEX INFLUENCE THE BIOCHEMICAL RECURRENCE FOLLOWING RADICAL PROSTATECTOMY?

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Introduction/Aim: Obesity is associated with a number of chronic diseases, such as diabetes, coronary artery disease and hypertension (1). Furthermore, it is frequently linked with tumours of the kidney, breast, colon, endometrium and prostate cancer (2, 3). In this retrospective study, we reviewed patients that underwent radical prostatectomy (RP) for localized prostate cancer (PCa) with negative margins postoperatively and analysed the possible correlation between obesity and biochemical recurrence (BCR). Materials and Methods: We retrospectively reviewed the medical records of 259 patients that underwent RP (118 with laparoscopic technique and 141 with open technique) for clinically localized PCa (stage cT1 to
cT2N0M0) at our Department. Patients with a surgical
treatment of prostatic disease, neoadjuvant therapy, positive
surgical margin status after RP or incomplete clinical data were
excluded from our study. Pre-operative data (age, height,
weight, PSA, prostate volume (PV), clinical stage, digital rectal
examination (DRE) and prostate biopsy Gleason grade) and pathological data (post-operative Gleason Score (GS), pathological stage, seminal vesicle invasion (SVI), lymph node
invasion (LNI)) were collected retrospectively for analysis.
Patients were then categorized with body mass index (BMI)
into three groups, according to the World Health Organisation
(WHO) classification of obesity: 85 patients were found obese
(BMI ≥30 Kg/m²), 86 were overweight (BMI 25 to 30 Kg/m²),
and 88 had normal weight (BMI ≤25 Kg/m²). Patients were
followed-up every 3 months during the first year, every 6
months the second and third years, and yearly thereafter unless
there was evidence of BCR, in which case more frequent
follow-up was required. Recurrence of PCa after RP was
defined as a serum PSA level of ≥0.2 ng/ml for two
consecutive measurements. Results: For the 259 patients that
underwent RP in our study, the mean±SD age was 63.2±6.3.
Median total PSA was 4.8 ng/ml and median PV was 42.8 ml.
A total of 85 (32.8%) patients were classified as obese.
Compared to normal-weight and overweight men, obese men
were older at the time of the surgery (p=0.234) and had
significantly higher grade disease (p<0.002). Moreover, obese
men had a lower PSA concentration (p<0.002) and a large PV
(p<0.001). Obese patients were inclined to have higher stage
disease as 27.1% of those had pT3 disease compared to 10.2%
normal-weight men and 17.4% overweight men. Histological
evaluation of biopsy cores and RP specimens showed that high
GS≥7 was more common in obese men than in normal-weight
patients (p<0.001). Despite this, LNI was more frequently
positive in obese patients than in normal patients (38.9% vs.
29.5%, p<0.001) and SVI was more frequently invaded (16.5%
vs.6.8%, p<0.002). Overall, the mean follow-up time was 52
months (range=12-98 months) during which 68 (26.6%)
patients developed BCR of disease. On multivariate analysis,
for identifying significant pre-operative predictors of BCR,
which included variables of age, PSA, PV, BMI, clinical stage
and biopsy, Gleason grade was not shown to be a significant
predictor of BCR, except BMI (p<0.001). Discussion and
Conclusion: According to our monocentric experience, obese
patients that were older at the time of the RP, had worse
clinical and pathologic outcomes and a greater predicted risk
of recurrence after RP compared to normal-weight patients.
Further randomised clinical trials and additional studies will be
essential in order to establish the effects of obesity on tumour
behaviour and overall PCa outcome.

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4. LAPAROSCOPIC MANAGEMENT OF LOCAL
RECURRENCE OF RENAL CELL CARCINOMA
AFTER RADICAL NEPHRECTOMY

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Introduction/Aim: Local recurrence after radical
nephrectomy (RN) is a rare condition in the natural history
of renal cell carcinoma (RCC). The prevalence has been
reported at between 1% and 2% in different series (1). The
isolated local recurrence of RCC after radical nephrectomy
creates a difficult therapeutic decision because these
patients are at high risk of distant metastatic disease.
Surgical removal of local recurrence in the absence of
metastatic disease appears to be the only theoretically
curative treatment option (2). However, there is no
standard treatment for this rare condition. Open surgery is
a well-established technique that has been successfully
performed for many years (3). In the present report, our
experience with laparoscopic excision of local recurrence of
RCC was examined in light of perioperative and
oncological outcomes. Materials and Methods: This was a
retrospective, single-institutional study of 4 patients with
retroperitoneal recurrence, treated with laparoscopic
surgery from 2010 to 2015. Demographics, clinical and
pathological features, as well as perioperative
complications are reported using descriptive statistics. All
patients were operated in our Division of Urology for their
primary tumors with laparoscopic radical nephrectomy.
Overall and disease-free survival after excision of
recurrence were calculated. Results: The median age at
time of local recurrence was 63.8 (56-72) years. The
median interval between nephrectomy and recurrence was
15.3 months (9-21). None of the patients were
symptomatic when they were diagnosed during regular
follow-up with computed tomography (CT) imaging. The median follow-up time after recurrence surgery was 20.2 months (6-33). All types of primary tumors were RCC. Tumors were mainly on the left side (n=3). Three patients had T3 and one patient had T4 stage tumors with nodal metastases at the time of the RN. Local recurrence involved the operative beds in all cases. The median size of the resected retroperitoneal recurrence was 4.3 cm (1.8-7.3). All of the patients underwent laparoscopic excision of local recurrence through trans-peritoneal approach. The larger vessels were ligated with polymer clips (Hem-o-lok®) and the smaller handled by ultrasonic clamp. The specimen was removed by a small incision below the umbilicus in an appropriate bag. Histopathology revealed RCC in all cases of recurrence specimens and positive surgical margins in one patient post-operatively. The mean operative time, estimated blood loss and length of hospital stay were 110 min (75-155), 305 ml (150-500) and 4.8 days (3-8), respectively. No mortality was observed in any patient during surgery or hospital stay. One patient required two units of blood transfusion and had elongated lymphatic drainage (approximately 1900 cc for 6 days), causing a long hospital stay (8 days). Neoadjuvant therapy was administered in 2 patients. After follow-up, the cancer-specific and overall survival rates were 100%; one patient was administered in 2 patients. After follow-up, the cancer-specific and overall survival rates were 100%; one patient had lung metastasis. Discussion and Conclusion: This study had certain limitations; one of these was the limited size of the study cohort, consisting of 4 patients. This limitation may be explained by the rarity of local recurrence in the natural history of RCC. The other limitation was the short-term oncological follow-up of 20.2 months. Despite the lack of recurrence in all of the patients during this follow-up, long-term follow-up is necessary to describe the success of laparoscopic excision in local recurrence treatment. However, we can conclude that the local recurrence of RCC can be safely operated via laparoscopic technique in early-stage and relatively low-volume of disease. This technique is as feasible as open surgery in the treatment of this well-selected patient group with similar oncological outcomes.


5 RASSF1A QUANTITATIVE METHYLATION-SPECIFIC DROPLET DIGITAL PCR IN URINARY CELLS AS BIOMARKER FOR PROSTATE CANCER DETECTION

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Introduction/Aim: Prostate cancer is the most common cancer in men and the second leading cause of cancer deaths in the USA and Western Europe. The diagnosis of localized prostate cancer may be difficult. In fact, many patients require repeat prostate biopsies to diagnose the disease (1-2) and determination of prostate-specific antigen (PSA) levels alone is neither sensitive nor specific enough for diagnosis. In this context, novel biomarkers for prostate cancer detection represent an important area of research. Aberrant DNA methylation at several known or putative tumor suppressor genes occurs frequently during prostate cancer development and may represent promising tumor markers (2). We investigated urine sediments for aberrant RASSF1A promoter methylation by the use of quantitative droplet digital PCR (DDPCR) to evaluate whether this biomarker could reliably detect prostate cancer. Materials and Methods: Urine samples were collected from patients with benign prostatic hypertrophy (BPH n=38) or localized prostate cancer (PCa; n=35) undergoing fine-needle biopsy and from age-matched patients without evidence of prostatic disease (n=13). The study was approved by the Ethics committee of the University Hospital of Ferrara and all patients gave their written informed consent. Urine sediments were obtained from 50 ml of urine by centrifugation and DNA was extracted with Maxwell® (Promega) and the Blood DNA Kit. After bisulphite conversion (EZ DNA Methylation-Gold™, Zymo Research), 5 μl of DNA was added to a 20 μl PCR reaction for DDPCR. A degenerated primer pair amplified the RASSF1A CpG island, while two specific probes measured the unmethylated and methylated DNA status. For quantification, the level of methylation was calculated from the ratio between methylated and unmethylated DNA. Results: RASSF1A methylation was significantly more frequent (p<0.001) in patients with prostatic disease than control patients. Overall, RASSF1A promoter methylation was detected in the urine samples of
91% of PCa and 89% of BPH patients, while it was detected in 67% of controls. By setting a cut-off value of positivity at 10% (ratio methylated/unmethylated), 63% of PC and 42% of BPH patients exhibited a methylation level higher than 10% (on average, 39±52 and 26±13, respectively), while virtually none of the controls reached the cut-off value. Data showed a positive and significant correlation (p=0.0028) with PSA levels, suggesting that the combination of PSA with RASSF1A methylation could increase specificity in diagnosis of PC. Conclusion: The present study revealed the potential usefulness of the DDPCR approach for the quantification of abnormal methylation in RASSF1A in urine sediments as a non-invasive biomarker for the detection of PCa.


6 MICRORNA501-5P INCREASES AUTOPHAGY IN CLEAR CELL RENAL CELL CARCINOMA

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Introduction/Aim: Clear cell renal cell carcinoma (ccRCC) is the most common histotype of kidney cancer and approximately one third of ccRCC patients develop metastases caused by the inefficacy of conventional chemotherapy (1). Many factors may contribute to the chemoresistance of ccRCC, including the activation of autophagy. Autophagic process may be modulated by different regulators including mTOR kinase and microRNAs (miRs). MiRs dysregulation is associated with progression and drug resistance in various cancers, including ccRCC. In this regard, we have observed an increased expression of miR501-5p in ccRCC cells and tissues that is associated with mTOR activation, as well as with poor prognosis for ccRCC patients (2). Therefore, the effect of microRNA-501-5p dysregulation on autophagy in ccRCC cells was also studied. Materials and Methods: The autophagic process was analyzed in wild type KJ29 kidney carcinoma cells transfected with a recombinant plasmid expressing miR501-5p sequences. Analysis of autophagy was performed by detection of autophagosome and autolysosome with fluorescence microscopy or Western-blot procedures. Microtubule-associated protein light chain 3 (LC3) and p62/SQSTM1 expression were used as specific markers to monitor autophagy. Autophagosomes and the autophagic flux were detected by live fluorescent microscopy using LC3-GFP fluorescent reporter and monitoring the LC3 turnover with the tandem construct LC3-mCherry-GFP, respectively. Results: It is known that the activation of mTOR kinase inhibits canonical autophagy. Surprisingly, however, the up-regulation of microRNA501-5p that induces mTOR activation in ccRCC cells caused a significant increase of autophagy measured by LC3-II increased expression and p62/SQSTM1 down-regulation. Treatment with the mTOR inhibitor rapamycin increased autophagy in control kidney cells but not in cells overexpressing the microRNA501-5p, confirming that this miR stimulates mTOR independent autophagy. Consistently, miR501-5p induces the activation of the AMPK kinase that is functionally active in mTOR-independent autophagy. The increased activity of AMPK could be due to impairment of mitochondrial calcium caused by the down-regulation of the mitochondrial uniporter (MCU) that is a target of miR501-5p. The activation of autophagy in miR501-5p-overexpressing cells was also observed by the formation of autophagosomes and autolysosomes, detected by LC3-GFP and LC3-mCherry-GFP fluorescent probes, respectively. Conclusion: The up-regulation of miR501-5p induces mTOR-independent autophagy and could contribute to poor prognosis and drug resistance in ccRCC patients.


7 LATE TOXICITY AND SIX-YEAR OUTCOMES AFTER HYPOFRACTIONATED STEREOTACTIC RADIOTHERAPY FOR LOCALIZED PROSTATE CANCER

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Introduction/Aim: There is currently no consensus on the best method of treating localized prostate cancer that maximizes the chance of cure while minimizing toxicity. We evaluated the clinical outcome of a cohort of localized prostate cancer patients treated with Cyberknife stereotactic body radiation therapy (SBRT) Materials and Methods: Between July 2007 and October 2010, a retrospective analysis was carried out on 62 consecutive patients with a median age of 74 years (range=60-85), mean prostate volume of 64.7 cc (range=20.64-164.38) and clinically localized prostate cancer treated with Cyberknife stereotactic radiosurgery. The majority of patients (28 (45%) were low-risk, 25 (40%) intermediate-risk and 9 (15%) high-risk using the National Comprehensive Cancer Network criteria. Pre-treatment PSAs ranged from 1.75 to 51 ng/ml (median=7.9 ng/ml). The course of radiotherapy consisted of 3,800 cGy over four fractions given daily to the PTV, which was defined as the prostate (plus seminal vesicles in high-risk patients). Real-time intrafractional motion tracking was used. Results: Acute urinary symptoms (frequency, disuria, urgency, hesitancy and nocturia) were common with 60 % of patients experiencing grade I-II RTOG acute urinary toxicity. No patients experienced RTOG grade 3 acute urinary toxicity; however, in 4 patients (3%) we recorded RTOG grade 3 late urinary toxicity and in 2 of them an additional transurethral resection of the prostate (TUR-P) was performed. No RTOG grade 3 acute and late rectal toxicity was observed. The actuarial median follow-up is 74 months (range=60-85 months). Overall, 12 of 62 patients (19%) died during follow-up for unrelated causes. Overall, 6 (12%) of 50 patients failed biochemically; 4 (8%) of them experienced distant metastases. The six-year actuarial PSA relapse-free survival rate is 92.1% (CI=88.2%-95.8%) with 100% for low-, 88% for intermediate- and 78% for high-risk patients. One patient (2 %) died of prostate cancer (bone metastasis). Conclusion: Cyberknife SBRT produces excellent biochemical control rates for up to 6 years with mild toxicity and minimal impact on quality of life. PSA relapse-free survival rates after Cyberkife radiotherapy compare very favourably with other radiation modalities and strongly suggest durability of our results.

Introduction/Aim: The concept of focal therapy is evolving with the understanding of the biologic variability (clinically aggressive, significant or insignificant) of various prostate cancer lesions that may require different treatment approaches. Minimally invasive, parenchyma-preserving therapies can assume a greater role in the treatment of unilateral or unifocal lesions, representing an alternative approach to the current treatment extremes of whole-gland treatment and watchful waiting. We investigated the role of focal Cyberknife stereotactic hypofractionated radiotherapy (SBRT) in patients with recurrent prostate cancer following external beam radiotherapy (EBRT). Materials and Methods: From November 2012 to July 2015, 26 patients with a median age of 74 years (range=62-89) and a prostate biochemical recurrence following EBRT detected with \[^{11}C\]choline positron emission tomography/computed tomography (PET/CT) were referred to our Department for focal salvage Cyberknife SBRT. Median external beam radiotherapy iPSA was 22.7 ng/ml (4.9-88 ng/ml), initial stage according the National Comprehensive Cancer Network 2008 was defined as low (4 patients) intermediate (6 patients) and high (16 patients), EBRT doses ranged from 74 to 79.2 Gy (median=76 Gy) and the median time from failure to re-irradiation was 60 months (range=19-139). The median pre-reirradiation PSA was 4.64 ng/ml (range=2.23-13.04 ng/ml). To reconstruct CTV and organ at risk, CT scan and magnetic resonance imaging (MRI) with T1-T2 sequences were performed and \[^{11}C\]choline PET/CT images were fuse for prostate target volume definition and delineation. Six patients received 3 fractions of 10 Gy (total dose=30 Gy), 20 patients received 3 fractions of 12 Gy (total dose=36 Gy) delivered to the PET-positive prostate node with a median volume of 14.3 cc (range=5.75-65.04). Results: The treatment was well-tolerated with no RTOG grade 3 acute or late GI and GU toxicity. With a median follow-up of 18 months (range=6-38), we observed no in-field recurrence, with a local control of 100%. In 4 patients, at 11, 14, 16 and 22 months, respectively, after the focal salvage treatment (median time=15 months), \[^{11}C\]choline PET/CT detected a local recurrence with the evidence of a new positive prostate node outside the irradiated field.
9 STEREOTACTIC BODY RADIATION THERAPY IN LOW- AND INTERMEDIATE-RISK PROSTATE CANCER: RESULTS OF PHASE II STUDY

Ciro Franzese, Giuseppe Roberto D’agostino, Rocco Luca Emanuele Liardo, Giacomo Reggiori, Pierina Navarria, Iftode Cristina, Fiorenza De Rose, Davide Franceschini, Angelo Tozzi, Tiziana Comito, Anna Maria Ascolese, Stefano Tomatis, Luca Cozzi and Marta Scorsetti

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Introduction/Aim: Radiation therapy is currently considered a viable approach for the treatment of prostate cancer. Given the low alpha/beta ratio of this cancer, delivery of high radiation doses in few fractions with stereotactic body radiation therapy (SBRT) may improve the therapeutic ratio. This phase II study was aimed at evaluating the efficacy, toxicity and quality of life (QoL) in patients affected by low- or intermediate-risk prostate cancer treated with SBRT. Materials and Methods: Patients affected by prostate adenocarcinoma were enrolled in this trial, provided that they had an initial prostate-specific antigen (PSA)<20 ng/ml, Gleason Score≤7 and international prostate symptom score (IPSS)≤7. The treatment schedule was 35 Gy in 5 fractions, delivered every other day with VMAT technology in FFF modality. Toxicity was recorded according to CTCAE criteria v3.0. Biochemical failure was calculated according to the Phoenix definition. QoL of patients was measured during and after treatment with EPIC questionnaires. Results: Between December 2011 and March 2015, 90 patients were enrolled (53 low-risk, 37 intermediate-risk). Median age was 71 years (range=48-82). Median Gleason Score was 6 (range=6-7) and median initial PSA was 6.9 ng/ml (range=2.7-17.0). Acute toxicity was mild, with 32.2% of patients presenting a G1 urinary toxicity and 31.1% of patients presenting a G2 urinary toxicity, mainly represented by urgency, dysuria and stranguria. Rectal G1 toxicity was found in 15.5% of patients, while G2 toxicity was recorded in 6.6% of patients. In the late setting, G1 proctitis was recorded in 11.1% of patients and G1 urinary in 38.8%; only 2 events of G2 urinary toxicity were observed (transient urethral stenosis, resolved by a 24-hour catheterization). At a median follow-up of 27 months (range=6-62) only two intermediate-risk patients experienced a biochemical failure (22 and 24 months after radiotherapy, respectively). Regarding QoL, compliance to treatment was good with a slight worsening in the urinary domains during treatment, with a return to baseline three months after treatment. Conclusion: Stereotactic body radiotherapy seems to be a valid therapeutic option in low- and intermediate-risk prostate cancer patients, warranting an adequate control of disease, with mild toxicity profiles and good patient-reported QoL perception.

10 TIMING OF BLOOD TRANSFUSION AND NOT ABO BLOOD TYPE IS ASSOCIATED WITH SURVIVAL IN PATIENTS TREATED WITH RADICAL CYSTECTOMY FOR NON-METASTATIC BLADDER CANCER: RESULTS FROM A SINGLE HIGH-VOLUME INSTITUTION

Marco Moschini1, Stefano Luzzago1, Giorgio Gandaglia1, Paolo Dell’oglio1, Nicola Fossati1, Vito Cucchiara1, Giusy Burgio1, Rocco Damiano2, Andrea Salonia1, Francesco Montorsi3, Alberto Briganti1, Andrea Gallina1 and Renzo Colombo1

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Introduction/Aim: Radical cystectomy (RC) is the treatment of choice for muscle invasive and high risk non-muscle invasive bladder cancer (BCa) patients. However, 5-year survival is not optimal, ranging from 42% to 58%, according to the stage of the disease. Recently, several biochemical or hematological parameters have been described as possible predictors of survival in BCa patients treated with RC. Specifically, perioperative transfusions have been recently associated to poor outcomes as an indirect consequence of immuno-hematological changes related to transfusion itself and blood type. We tested the role of blood transfusion on cancer-specific mortality (CSM) and overall mortality (OM), considering the impact of ABO system, Rh factor and timing of transfusions. Materials and Methods: The study focused on 728 BCa patients treated with RC at a single tertiary care referral center between January 1995 and August 2013 with complete ABO blood type information. Kaplan-Meier was used to assess the effect of transfusions, stratified according to ABO type and Rh status, on CSM and OM. The same end-points were tested in Cox regression models, after adjusting for year of surgery, age, gender, Charlson comorbidity index, intra- and post-operative transfusions, Rh status, pre-operative anemia, number of nodes...
removed, pathological T and N stage, surgical margins and adjuvant chemotherapy. Results: A total of 341 (46.8%), 277 (38.0%), 83 (11.4%) and 27 (3.7%) patients had blood type O, A, B and AB, respectively. Overall, 630 (86.5%) and 98 (13.5%) were Rh- and Rh+, respectively. At a median follow-up time of 65 months, 225 (30.9%) and 282 (38.7%) patients recorded CSM and OM, respectively. At univariate analyses, ABO blood type and Rh status were not associated to either CSM or OM (all \( p > 0.2 \)). Similar results were observed when ABO blood type and Rh status were tested in multivariate models (all \( p > 0.3 \)). Conversely, Charlson score, age, number of nodes removed, pathological T stage, pathological N stage, anemia status and surgical margin status were associated to both CSM and OM (all \( p < 0.05 \)). Interestingly, intra-operative transfusion (all \( p < 0.045 \)) but not the administration of blood units in the post-operative period (\( p > 0.4 \)) were associated with an increase of CSM and OM. Conclusion: Although ABO type and/or Rh factor were associated with several adverse outcomes in many cancers, we were not able to confirm this association in BCa. Based on our results, the impact of transfusion on survival is independent by ABO type but is associated to the timing of blood supply administration. It may be argued that intra-operative transfusion may represent a proxy for more complex surgery and, in turn, for more advanced disease, which may translate into a reduction of survival after surgery.

11 PRE-OPERATIVE FAVORABLE CHARACTERISTICS IN BLadder CANcer PATIENTS CANNOT SUBSTITUTE THE NECESSITY OF EXTENDED LYMPHADENECTOMY DURING RADICAL CYSTECTOMY: A SENSITIVITY CURVE ANALYSIS

Marco Moschini\(^1\), Stefano Luzzago\(^1\), Giorgio Gandaglia\(^1\), Paolo Dell’Oglio\(^1\), Nicola Fossati\(^1\), Vito Cucchiara\(^1\), Giusy Burgio\(^1\), Rocco Damiano\(^2\), Andrea Salonia\(^1\), Francesco Montorsi\(^1\), Alberto Briganti\(^1\), Andrea Gallina\(^1\) and Renzo Colombo\(^1\)

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Introduction/Aim: The clinical significance of pelvic lymph node dissection (PLND) is under discussion but is related to two main aspects: (i) therapeutic and (ii) staging procedure. On the other hand, PLND is not free of drawbacks, such as increased perioperative morbidity and operating time. A tendency to avoid or to limit the extension of lymphadenectomy, when bladder cancer (BCa) is considered less aggressive, has been recorded by some series that reported as 25% of patients submitted to RC due to BCa did not receive any PLND. Considering only patients submitted to radical cystectomy (RC) due to pTa or carcinoma in situ and pT1 this rate increases to 50% and 35%, respectively. No data exist about the possibility to limit the extension of PLND on the basis of pre-operative or intraoperative parameters without losing accuracy in the staging procedure. Considering these points, we investigated the hypothesis that a limited PLND can be offered in patients with particularly favourable clinical and pathological real scenarios. Materials and Methods: Between 1995 and 2012, 1,016 RC due to BCa were performed at a single tertiary care institution. The relationship between the number of nodes removed and the probability to find node metastases at final pathology examination was assessed using receiver operating characteristic (ROC) analyses. Different clinical and pathological scenarios were investigated, such as pathological stage at last transurethral resection, primary or progressive status at the time of last transurethral resection, clinical radiological N status and pathological T stage at RC. Results: Among the patients who underwent RC plus PLND, the median number of nodes removed were 18 and the lymph node metastases (LNM) prevalence was 35.7% (363 of 1,016), ROC curve analyses were used to explore graphically the relationship between the numbers of removed and examined nodes and the probability of finding one or more metastatic nodes in the overall population. The curve indicated that 25, 35 and 45 nodes needed to be removed to achieve 75, 90% and 95% probability respectively of detecting one or more LNM. When the analyses were stratified according to pre-operative characteristics, only slight differences were recorded among the sensitivity analyses stratified for pathological stage at last transurethral resection (TUR), primary or progressive status, radiological N status or pathological stage at RC. Conclusion: Our results showed that it is necessary to extend PLND in order to improve the ability to stage accurately node metastases. Pre-operative parameters can minimally change this indication and an extended PLND should be always performed.

12 IMPACT OF STAGE MIGRATION ON BLadder CANcer: A SLOW BUT STEADY IMPROVEMENT IN THE LONG TERM SURVIVAL RATES AFTER RADICAL CYSTECTOMY IN THE LAST 25 YEARS

Marco Moschini\(^1\), Stefano Luzzago\(^1\), Giorgio Gandaglia\(^1\), Paolo Dell’Oglio\(^1\), Nicola Fossati\(^1\), Vito Cucchiara\(^1\), Giusy Burgio\(^1\), Rocco Damiano\(^2\), Andrea Salonia\(^1\), Francesco Montorsi\(^1\), Alberto Briganti\(^1\), Andrea Gallina\(^1\) and Renzo Colombo\(^1\)

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Introduction/Aim: Bladder cancer (BCa) is a heterogeneous disease with up to 25% of incidental diagnoses reported to be found muscle-invasive at first episode. Numerous markers and an increased awareness have been recorded in recent years. We sought to evaluate if those considerations may determine a change in BCa clinical presentation at radical cystectomy (RC) over the years in a single high-volume tertiary referral center.

Materials and Methods: The study relied on 2,003 consecutive BCa patients treated with RC and extended pelvic lymphadenectomy (PLND) at a single institution between January 1990 and December 2014. Patients were stratified into tertiles according to the year of surgery (1990-2000 vs. 2001-2009 vs. 2010-2014). ANOVA and chi-square trend tests were used to report the clinical and pathological characteristics of the cohort over time. Multivariate Cox regression analysis was used to test the relationship between year of surgery and recurrence, cancer-specific mortality (CSM) and overall mortality (OM). Results: When considering clinical characteristics, patients’ age (66.7 vs. 66.5 vs. 67.6 years, p=0.1) and gender (81.9% vs. 82.7% vs. 85.4% male, p=0.2) resulted steady over the three tertiles. Conversely, body mass index (BMI) (24.7 vs. 25.6 vs. 26.0, p<0.005) increased over the studied period. Considering pathological features, carcinoma in situ (CIS) detection (8.8% vs. 19.8% vs. 34.4%, p<0.001) showed an increasing rate, while pathological T3-4 stage (64.1% vs. 48.6% vs. 51.6%, p=0.005) expressed a decreasing trend. The number of nodes removed increased during tertiles (16.8 vs. 22.7% vs. 26.78, p<0.001) resulting in an increased number of positive nodes over years (5.1 vs. 7.1 vs. 7.8, p<0.001). However, lymph node invasion (34.6% vs. 29.8% vs. 33.7%, p>0.1) remain stable across years in the overall population. At multivariable Cox regression analyses, year of surgery represent a predictor of recurrence (hazard ratio (HR)=0.97), CSM (HR=0.97) and OM (HR=0.98), with a slight but constant reduction in all survival outcomes (all p<0.04). Conclusion: A significant increase of BMI over years has been recorded in patients affected by BCa treated with RC.

Considering pathological characteristics, higher rates of CIS but lower rates of pathological advanced disease were recorded in recent years, with a reduction in the prevalence of pT3/pT4 disease. These variations directly reflect the differences in terms of long-term survival expectations recorded in our series during the last 25 years.

Aim: To retrospectively evaluate external beam re-irradiation (re-EBRT) delivered to either the prostate or prostatic bed for local recurrence after radical or adjuvant/salvage radiotherapy. Materials and Methods: Between February 2008 and March 2015, 59 patients received re-EBRT. Median age was 63.8 years (range=47.1-81.7) and median prostate-specific antigen (PSA) at the time of relapse was 20.2 ng/ml (range=4.4-110). All patients had clinical and/or radiological local relapse in the prostate or prostatic bed and no distant metastasis at the time of re-EBRT. A concomitant hormonal treatment was administered to 18 patients. Re-EBRT was delivered mainly with image-guided stereotactic technology including Rapid Arc®, VERO® and CyberKnife® to a total dose of 15-32 Gy in 3-6 fractions. Toxicity was evaluated using RTOG/EORTC criteria. Biochemical control was assessed according to Phoenix definition. Results: Only one patient experienced an acute GI event >G3, while two patients had late ≥G3 urinary toxicity. At a mean and median follow-up of 24.1 and 19.8 months, respectively (range=2-65.5), 27 patients (45%) show no evidence of disease, 26 (44%) are alive with biochemical or clinical disease and 2 have been lost at clinical follow-up. Four patients (7%) died: 2 of disease progression and 2 of other causes. Mean and median time-to-progression are 12.1 and 9.8 months, respectively (range=2-53). Discussion and Conclusion: Re-EBRT, using stereotactic approach, is a feasible option for local prostate cancer recurrence achieving tumour control in 45% of the patients and an acceptable progression-free interval (1). Toxicity of re-EBRT appeared to be very low (2, 3). Future studies are needed to identify those patients that would benefit the most from this treatment.


14 THE ROLE OF IALURIL SOFT GEL® DURING RADICAL HYPOFRACTIONATED RADIOTHERAPY IN PROSTATE CANCER: PRELIMINARY EXPERIENCE ON GENITOURINARY TOXICITY PROFILE

Sergio Fersino1, Alba Fiorentino1, Niccolò Giag Levra1, Rosario Mazzola1, Francesco Ricchetti1, Gioacchino Di Paola2, Stefano Cavalleri3 and Filippo Alongi1

1Radiation Oncology Department, Sacro Cuore Don Calabria Hospital, Negar (VR), Italy; 2Statistic Science Faculty, Statistic Science Faculty, Negar (VR), Italy; 3Urologia, Sacro Cuore Don Calabria Hospital, Negar (VR), Italy

Aim: To evaluate the impact of Ialuril soft Gel® in reducing acute genito-urinary (GU) toxicity in patients with prostate cancer treated with volumetric modulated arc radiotherapy (VMAT). Materials and Methods: Forty patients were prospectively recruited. A moderate hypofractionation in 28 fractions ("Hypo-moderate") was prescribed in 20 patients, while an extreme hypofractionated ("Hypo-extreme") in 5 fractions was prescribed in 20 patients. International prostate symptom score (IPSS) questionnaire was administered in all cases before and after radiotherapy (RT). GU toxicity was evaluated according to CTCAE v4.0. Patients of each group ("Hypo-moderate" and "Hypo-extreme") were randomized (1:1) to receive RT alone or RT combined with Ialuril soft Gel®. Results: In "Hypo-moderate" patients treated with Ialuril soft Gel® the following GU toxicities were reported: G0 3, G1 6, G2 1, G3 0. In the arm without Ialuril soft Gel® the results were G0 0, G1 7, G2 2, G3 1. In the "Hypo-extreme" arm with Ialuril soft Gel® it the following GU toxicity was recorded: G0 7, G1 2, G2 1, G3 in 0; while in the arm without Ialuril soft Gel® G0 5, G1 2, G2 2, G3 1. IPSS was unchanged in "Hypo-moderate" and "Hypo-extreme" and patients undergoing Ialuril soft Gel®, with a median value of 6 and 5 respectively. In patients without Ialuril soft Gel®, an increased IPSS was reported in "Hypo-moderate" and "Hypo-extreme" from 6 to 8 and 3.5 to 4.5, respectively. Statistical analysis (Fisher's exact text) showed that Ialuril soft Gel® was associated with IPSS improvement (p=0.03). Conclusion: Ialuril soft Gel® seems to have an encouraging role in reducing GU toxicity without worsening of the IPSS score.

15 SOLITARY FIBROUS TUMOR OF THE KIDNEY: CASE REPORT, HISTOPATHOLOGICAL APPROACH AND REVIEW OF THE LITERATURE

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Introduction: A solitary fibrous tumor (SFT) is a rare mesenchymal neoplasm characterized by the proliferation of spindle cells, originating from fibroblasts and primitive mesenchymal cells. It occurs generally in the pleura but, in recent years, extrapleural localizations have been also reported in literature (1-17) (Table I). Its occurrence in kidney is extremely rare, with only 47 cases being reported in the literature from 1996 to 2014 (18-34). The median age is 52 years (range 28-83 years), with no difference in incidence between men and women (Table II). Case: A 77-year-old woman was referred to our Department with a 2-month history of dull pain in the right lumbar region. Abdominal computed tomography (CT) scan showed a mass with irregular enhancement at the lower third of the right kidney (Figure 1). Radical nephrectomy was performed and immunohistochemical study was the key for diagnosis of solitary fibrous tumor of kidney (Figure 2) (Table III). A regular 4-month radiographic TC-based post-operative follow-up was performed (Figure 3). Thirteen months after surgery, no radiographic signs of recurrence are present and the patient is still asymptomatic. Conclusion: This case-report requires attention from the scientific community because it improves knowledge of a rare disease and suggests a multidisciplinary management for the best therapeutic choice of renal SFT.
Figure 1. Abdominal CT at diagnosis (August 2014).

Figure 2. Histopathological features. Detailed histological diagnosis: nodule 6×6×6 cm in size, tumor of mesenchymal origin with hemangiopericytoma-like vascular pattern; large areas of necrosis and thick fibrotic bands; microscopically, it consists of fusiform elements, arranged in a sorted pattern, and markedly pleomorphic polygon elements. The tumor diffusely infiltrates the perirenal adipose tissue until the end, while there are no cancer cells in the context of the piece of analyzed muscle tissue in the hilum, ureter and adrenal gland. The tumor is positive for vimentin with a Ki 67 equal to 15%.

Table I. Extrapleural SFT reports.

<table>
<thead>
<tr>
<th>Author</th>
<th>Site</th>
<th>Year</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alves Filho W</td>
<td>Thyroid</td>
<td>2014</td>
<td>17</td>
</tr>
<tr>
<td>Debs T</td>
<td>Liver</td>
<td>2014</td>
<td>15</td>
</tr>
<tr>
<td>Yoh T</td>
<td>Retroperitoneal</td>
<td>2014</td>
<td>3</td>
</tr>
<tr>
<td>Hudson TM</td>
<td>Bone</td>
<td>1993</td>
<td>4</td>
</tr>
<tr>
<td>Yang LH</td>
<td>Breast</td>
<td>2014</td>
<td>6</td>
</tr>
<tr>
<td>Toniato A</td>
<td>Adrenals</td>
<td>2014</td>
<td>5</td>
</tr>
<tr>
<td>Ali MJ</td>
<td>Eye sockets</td>
<td>2013</td>
<td>12</td>
</tr>
</tbody>
</table>

Table II. Clinical characteristics of renal SFTs reported in the literature.

<table>
<thead>
<tr>
<th>Number of cases</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>4-18 years</td>
<td>2</td>
</tr>
<tr>
<td>19-30 years</td>
<td>4</td>
</tr>
<tr>
<td>31-65 years</td>
<td>29</td>
</tr>
<tr>
<td>66-85 years</td>
<td>12</td>
</tr>
<tr>
<td>Kidney</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>26</td>
</tr>
<tr>
<td>Left</td>
<td>19</td>
</tr>
<tr>
<td>Bilateral</td>
<td>2</td>
</tr>
<tr>
<td>Localization</td>
<td></td>
</tr>
<tr>
<td>Parenchymal</td>
<td>26</td>
</tr>
<tr>
<td>Other (polar, hilar…)</td>
<td>21</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>22</td>
</tr>
<tr>
<td>Female</td>
<td>25</td>
</tr>
</tbody>
</table>
Table III. Immunostaining positivity rates of the SFT according to the literature.

<table>
<thead>
<tr>
<th>Immunohistochemistry</th>
<th>Positivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD 34</td>
<td>90-95%</td>
</tr>
<tr>
<td>CD 99</td>
<td>70%</td>
</tr>
<tr>
<td>BCL2</td>
<td>20-35%</td>
</tr>
<tr>
<td>EMA</td>
<td>20-35%</td>
</tr>
</tbody>
</table>

Vittorio Schweiger1, Tania Processali2, Davide De Marchi2,  
1Urology Clinic, Department of Surgery, AOUI Verona,  
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Introduction/Aim: Radical cystectomy represents the gold  
standard treatment in muscle-invasive bladder cancer and  
is one of the most challenging procedures in urologic surgery.  
This procedure is associated with significant perioperative  
morbidity and mortality, ranging from 20 to 64% and from 0.3  
to 5.7%, respectively. The considerable inter-individual  
variability of perioperative mortality has led to the  
development of several models of individual perioperative  
mortality prediction for patients undergoing radical  
cystectomy. The aim of our study was to evaluate the  
predictive accuracy of the nomograms of Isbarn and Aziz and  
the identification of perioperative mortality risk factors in a  
series of patients undergoing radical cystectomy for muscle  
invasive bladder cancer at our institution. Patients and  
Methods: We retrospectively reviewed data regarding 145  
consecutive patients who underwent radical cystectomy and  
urinary diversion for urothelial bladder cancer at our Institute  
between 2002 and 2012. The following pre-operative  
variables, such as age at intervention, gender, body mass index  
(BMI), operative volume, Charlson comorbidity index,  
presence of carcinoma in situ (CIS) to endoscopic resection  
bladder (TURV), American society of anesthesiologists (ASA)  
score, clinical stage according to the TNM and 90-day  
mortality, were collected and analyzed. The Isbarn and Aziz  
nomograms were, moreover, applied to our cohort. Results:  
Median age at radical cystectomy was 68 years and 85% of  
patients were male, with a median BMI of 26 (IQR=25-27).  
The most represented ASA score was 2, whereas the most  
frequent Charlson score (62.76%) was 0. Median in-hospital  
stay was 15 days, with a range between 7 and 35 days. Median  
follow-up was 26 months (IQR=11-45); five deaths were  
registered within 90 days (3.4%). Applying the nomograms of  
Aziz and Isbarn to our patients, we obtained an average  
mortality risk <10% and of 2.4%, respectively. At multivariate  
analysis, no variable was independently related to  
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the single variable with the highest accuracy in predicting  
90 days mortality. Results: In our series, at the multivariate  
analysis, none of the variables resulted as an independent risk  
factor for 90-day mortality; however, only ASA score seemed  
to have a trend in this sense. This retrospective study has a  
small number of participants with few events, thus making the  
multivariate analysis unreliable. Conclusion: In our series, 90-  
day mortality after radical cystectomy was 3.4% (5/145  
patients). On univariate analysis, only Charlson comorbidity  
index (ref. 0-2; p=0.019; 0.013), ASA score (p=0.004) and the  
adjusted ICC age (0.022) were independent risk factors of 90-

90-DAY MORTALITY AFTER RADICAL  
CYSTECTOMY FOR BLADDER CANCER  

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day mortality after radical cystectomy was 3.4% (5/145  
patients). On univariate analysis, only Charlson comorbidity  
index (ref. 0-2; p=0.019; 0.013), ASA score (p=0.004) and the  
adjusted ICC age (0.022) were independent risk factors of 90-

AGE AS INDEPENDENT RISK FACTOR OF  
RECURRENT AFTER NEPHROURETERECTOMY  
OR SEGMENTAL URETERECTOMY:  
MULTICENTER RETROSPECTIVE EVALUATION  

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Abstracts of the 26th Annual Meeting of the Italian Society of Uro-Oncology (SIUrO), 9-11 June, 2016, Florence, Italy
Introduction/Aim: Nephroureterectomy (NU) is considered the gold standard treatment for invasive and non-metastatic upper tract urothelial carcinoma (UTUC). We evaluated the role of age as independent predictive risk factor of recurrence-free survival (RFS) and cancer-specific survival (CSS) in patients with UTUC who underwent NU or segmental ureterectomy (SU). Patients and Methods: We evaluated 412 patients with UTUC from 2001 to 2013 from 5 urological academic centers. A large number (324/412 (79%)) of patients underwent NU, while 88/412 (21%) were treated by SU. Clinical and pathological characteristics were analyzed with reference to age (≤70 vs. >70 years), gender (male vs. female), type of surgery (NU vs. SU), pTNM-stage (pT0-pT2 vs. pT3), grading (G0-G2 vs. G3) and synchronous bladder cancer (yes vs. no). Univariate and multivariate analysis were performed to assess clinical and pathological characteristics as predictors for RFS and CSS by using Cox proportional model (hazard ratios (HR) and 95% confidence interval (CI)). Results: No significant differences were found between the two types of surgery with reference to male gender (73.5% (38/324) vs. 78.4% (69/88), respectively), mean age (71.4±9.3 vs. 69.6±9.0 years, respectively), mean follow-up (35.4±28.7 vs. 31.9±31.7 months, respectively) and number of recurrence (44.4% (144/324) vs. 44.3% (44/88), respectively). By contrast, we found a higher percentage of mortality in the NU group 28.1% (91/324) vs. SU group 11.4% (10/88) (p=0.001) and in the percentage of cause-specific mortality (14.8% vs. 4.6% respectively for NU and SU, p=0.01). At univariate and multivariate analysis, age, pTNM-stage and synchronous bladder cancer were significant predictor risk factors for RFS. The risk for recurrence was as follows, age >70 vs. ≤70 years: 1.49 (95% CI=1.10-2.03), p=0.01; pT3 vs. pT0-pT2: 1.60 (95% CI=1.18-2.18), p=0.003; and synchronous bladder cancer yes vs. no: 1.94 (95% CI=1.35-2.79), p=0.003. For CSS at univariate analysis, age, type of surgery, pTNM-stage, grading and synchronous bladder cancer were statistically significant and only three of them remained statistically significant at multivariate analysis. The risk for CSS (HR) was, for age >70 vs. ≤70 years: 2.07 (95% CI=1.14-3.77), p=0.02; for pT3 vs. pT0-pT2: 3.13 (95% CI=1.68-5.84), p=0.003; and for grading G3 vs. G0-G2: 9.72 (95% CI=2.87-32.95), p=0.003. At three years the probability of RFS was 91% and 81% for ≤70 years vs. >70, respectively. Conclusion: NU with bladder cuff removal remains the gold-standard treatment for UTUC but the identification of predictive risk factors remains uncertain. Tumor stage and grading are used as predictors of prognosis, while age seems to be associated to more aggressive kind of UTUC. Age could be an independent predictive factor for RFS and CSS in patients with UTUC.

18

HRQOL IN ELDERLY PATIENTS RECEIVING ILEAL CONDUIT OR ORTHOTOPIC NEOBLADDER

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1Urology Clinic, Department of Surgery, AOUI Verona, University of Verona, Verona (VR), Italy; 2Department Time Space Image Society, Sociology Section, European Organisation for Research and Treatment of Cancer (EORTC) instruments quality of life questionnaire C30 (QLQ-C30) and QLQ muscle-invasive bladder cancer module (QLQ-BLM), Results: IC and IONB groups were comparable for all but one (gender) demographic and clinical variables. Actually, in the IC group, the number of females was significantly higher (12 versus 1, p=0.029). At a mean follow-up of 60.91±42.19 months, mean scores in the IONB group were significantly better (higher in functional items and lower in symptoms items) in the following domains: cognitive functioning (95.87 vs. 91.16, p=0.002), role functioning (97.58 vs. 88.65, p=0.001), emotional functioning (95.87 vs. 91.16, p=0.002), social functioning (97.58 vs. 88.65, p=0.001), physical functioning (97.58 vs. 88.65, p=0.001), pain (3.97 vs. 4.68, p=0.001), fatigue (18.95 vs. 25.33, p=0.001), constipation (14 vs. 42.48, p=0.001) and financial
difficulties (1.28 vs. 7.84, \( p=0.043 \)). Considering only male patients, HR-QoL showed significant more favourable outcomes only in two symptoms items (constipation and appetite loss, \( p=0.001 \) and \( p=0.021 \), respectively).

**Conclusion:** The results of our retrospective analysis suggest that, in terms of HR-QoL, IONB, when compared to IC, can be a suitable diversion for elderly patients with better favourable score for some functional and symptoms' aspects. These results may be affected by gender.

**19 ASSOCIATION BETWEEN PHYSICAL ACTIVITY AND QUALITY OF LIFE IN PROSTATE CANCER PATIENTS FOLLOWING ACTIVE SURVEILLANCE**

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**Introduction/Aim:** Patients diagnosed with low-risk, potentially not aggressive, prostate cancer may choose to not treat cancer and benefit from active surveillance (AS) (1). For these patients, treatment-related complications are avoided; however, quality of life outcomes can be lowered by potential anxiety and distress related to cancer course (1). Although there is overwhelming evidence that lifestyle modification and, in particular, physical activity (PA), is beneficial for oncological patients (2), few studies investigated its potential to improve quality of life and psychosocial outcomes among men with prostate cancer in AS (3). Thus, we aimed to investigate if men undergoing AS, who actively manage their health, *i.e.* by engaging in PA, may also improve their health-related quality of life.

**Patients and Methods:** Men with prostate cancer enrolled in the Prostate cancer Research International: AS (PRIAS) protocol, in one of the PRIAS European Centers, and accepting to participate in an ancillary study on health-related quality of life (HRQoL) were enrolled. PA and HRQoL -both generic and disease-specific- were self-reported and measured through the International Physical Activity Questionnaire (IPAQ), the Short Form 36 (SF-36) and the Functional Assessment of Cancer Therapy scale - Prostate Version (FACT-P). Questionnaires were completed at 10 months after diagnosis. Descriptive analyses were conducted and stepwise multiple regression analyses were performed to examine the impact of exercise type and activity on the HRQoL scores. Statistical significance was established at \( p<0.05 \).

**Results:** Between 2013 and 2015, 71 patients completed the questionnaires. Mean age of participants was 64+7 years (range=42-79) (see Table I for further details about physical activity scores of participants).

Regression analyses revealed that high PA was associated with greater physical wellbeing (FACT-P) \( (p=0.018; \ R^2=0.085; F=5.294; \beta=0.291) \) (Table II) and higher mental health scores (SF-36) \( (p=0.025; \ R^2=0.071; F=5.268; \beta=0.266) \) (Table III). Furthermore, higher levels of vigorous activity were related to higher FACT-P functional wellbeing scores \( (p=0.025; \ R^2=0.075; F=5.253; \beta=0.273) \) (Table IV).

**Table I. Descriptive analysis for physical activity scores.**

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
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<tbody>
<tr>
<td>Walking</td>
<td>67</td>
<td>855.28</td>
<td>921.32</td>
<td>594</td>
<td>0</td>
<td>4752</td>
</tr>
<tr>
<td>(min/week)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>68</td>
<td>1106.85</td>
<td>2243.83</td>
<td>240</td>
<td>0</td>
<td>15000</td>
</tr>
<tr>
<td>(min/week)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vigorous</td>
<td>69</td>
<td>1594.35</td>
<td>3402.65</td>
<td>320</td>
<td>0</td>
<td>15360</td>
</tr>
<tr>
<td>(min/week)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>71</td>
<td>3415.93</td>
<td>4923.41</td>
<td>1554</td>
<td>0</td>
<td>20052</td>
</tr>
</tbody>
</table>

**Table II. Regression equation for physical activity and physical wellbeing scores.**

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Coefficient</th>
<th>Std. Error</th>
<th>Beta</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>3.848</td>
<td>0.027</td>
<td>141.531</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>PA total scores</td>
<td>1.107E-005</td>
<td>0.000</td>
<td>0.291</td>
<td>2.434</td>
<td>0.018</td>
</tr>
</tbody>
</table>

a. Dependent variable: physical wellbeing, T1

**Table III. Regression equation for physical activity and mental health scores.**

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Coefficient</th>
<th>Std. Error</th>
<th>Beta</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>77,836</td>
<td>2.257</td>
<td>34.48</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>PA total scores</td>
<td>0.001</td>
<td>0.000</td>
<td>0.266</td>
<td>2.295</td>
<td>0.025</td>
</tr>
</tbody>
</table>

a. Dependent variable: mental health, T1
progress after an initial response to treatment with luteinizing hormone-releasing hormone (LH-RH) (1, 2). Recent data suggest that the androgen receptor (AR) signalling pathway remains a key driver of prostate cancer progression despite castrate levels of testosterone in advanced disease (3-5).

Various drugs have been shown to benefit patients with mCRPC: the therapeutic approach is complex and less clear than in the past. Abiraterone is a potent, selective and irreversible inhibitor of CYP17 (6, 7), a key enzyme in the androgen and estrogen synthesis process, which has been shown to significantly prolong overall survival (OS) of patients with mCRPC, in post- and in pre-docetaxel setting (8, 9). The aim of our retrospective study is to evaluate the efficacy and the safety of abiraterone in our patients affected by mCRPC and study potential predictive factors of response to treatment. **Patients and Methods:** We report data about 40 patients affected by mCRPC, progressed after first-line chemotherapy with docetaxel, treated with abiraterone acetate (AA) from September 2012 to February 2015. Abiraterone was administered at the standard dose of 1,000 mg/day, given concurrently with prednisone, 5 mg twice daily. Twenty-four patients (60.0%) underwent concomitant hormonal therapy with LH RH agonist, while 16 patients (40.0%) with LH RH antagonists. All patient received a first-line chemotherapy with docetaxel; 27 patients received AA as a second-line therapy. Only 4 patients presented visceral metastases; the others had a bone/lymphnode involvement. We evaluated progression-free survival (PFS), defined as the time from beginning of AA to either biochemical or radiographic progression according to PCWG 2 (10, 11). Other outcomes reported are prostate-specific antigen (PSA) response and adverse events (AE), defined as any AE that required suspension or interruption of AA therapy. **Results:** With a median follow-up of 12 months (range=0.7-29.5), 3 patients (7.5%) died and 22 patients (55%) had progressive disease (PD). The median time of duration of abiraterone therapy was 8.33 months (range=1-20); median PFS was 10.3 months (range=1.4-18.7). Results showed that four parameters were associated with a better PFS: response to docetaxel ($p=0.031$), baseline PSA ($p=0.014$), baseline Hb ($p=0.008$) and PSA reduction>50%. Univariate analysis confirmed the statistically significant effect of baseline PSA ($p=0.027$), baseline Hb ($p=0.016$) and PSA reduction >50% ($p=0.017$). At the multivariate analysis, only baseline Hb>10 g/dl ($p=0.038$) and PSA reduction>50% ($p=0.002$) remained significant. Of note, no difference was noted in terms of PFS ($p=0.17$) and OS ($p=0.91$) between patients treated with concomitant LH RH agonist or LH RH antagonist. Overall, treatment was well-tolerated; 5 patients (12.5%) interrupted therapy; 2 patients due to cardiovascular events (1 NSTEMI, 1 arrhythmia), one patient had intestinal occlusion, 1 patient had herpetic dermatitis and 1 had diffuse atopic erythema. **Conclusion:** Our data show the safety and activity of AA confirming the findings of the post-docetaxel pivotal trial in"
the patients as a whole population. Due to the relationship between baseline PSA and treatment response, it appears that therapy for mCRPC has to begin as early as possible. AA was a well-tolerated therapy: no unexpected AEs were recorded during the treatment.


22 HRQOL IN PATIENTS WITH ILEAL CONDUIT OR ORTHOTOPIC NEOBLADDER: A COMPARATIVE PROPENSITY SCORE MATCHED ANALYSIS

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2Department Time Space Image Society, Sociology Section, University of Verona, Verona, Italy;
3Urology Clinic, University of Padua, Padua, Italy;
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Introduction/Aim: Bladder cancer (BC) is a disease playing an important role in urological clinical practice. When a radical cystectomy (RC) is indicated, the ideal urinary diversion after RC should be easy to prepare and easy to handle, presenting few complications, low mortality and morbidity; moreover, it should protect the upper urinary tract function and should be well-accepted by the patient, thereby ensuring the best health-related quality of life (HR-QoL) as possible. The aim of this study was to compare HR-QoL domains with two forms of
urinary diversions, including ileal conduit (IC) and ileal orthotopic neobladder (IONB) in patients with BC. Patients and Methods: This retrospective multicentre cohort study included 148 (115 males and 33 females; mean age=70.76±8.27 years) and 171 (156 males and 15 females; mean age=64.33±9.38 years) patients who underwent RC and urinary diversion with an IC and an IONB, respectively. Different domains of patients' HR-QoL were assessed postoperatively using the EORTC QLQ C-30 and the EORTC QLQ BLM-30 as validated questionnaires. A comparative analysis using propensity score matching was performed with matching variables of age, gender, number of underlying diseases and pathologic T and N stages, for comparison of HR-QoL between IC and IONB. Results: In this series, at a mean follow-up of 48.35±39.21 months, in questions addressing physical functioning (PF), emotional functioning (EF), cognitive functioning (CF), symptoms of fatigue (FA), dyspnoea (DY), appetite loss (AP), constipation (CO) and abdominal bloating and flatulence (AB), patients with IONB had a significant more favourable outcome (p=0.006, p=0.023, p=0.000, p=0.001, p=0.007, p=0.012, p=0.000 and p=0.000, respectively). Interpretation of Results: After propensity score matching, the best results of IONB—in terms of HR-QoL—were confirmed, thus adding other two aspects in favour of IONB (pain and sleep disturbance, p=0.007 and p=0.003, respectively). Conclusion: Ileal orthotopic neobladder after radical cystectomy proves, in many aspects, better results of HR-QoL as compared with ileal conduit diversion.

24
MR-TARGETED VS. TRUS-GUIDED PROSTATE BIOPSY IN PATIENTS WITH HIGH PSA VALUES: A RANDOMIZED CONTROLLED TRIAL

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Introduction/Aim: Nowadays, most prostate biopsies are driven by prostate-specific antigen (PSA) testing. However, as the positive predictive value of PSA has been significantly reduced over the last several years, more unnecessary prostate biopsies are performed annually on millions of men worldwide (1). Moreover, transrectal ultrasound (TRUS)-guided biopsy, which is the standard procedure for prostate histological sampling, has a detection rate of about 40%, with a false negative rate of about 20% (2). In this scenario, more accurate methods need to be found to detect significant prostate cancer (PCa) or rule out patients with elevated PSA levels and insignificant lesions. In the last decade, with the aid of multiparametric magnetic resonance (mp-MR) imaging, clinical relevant PCa foci could be better identified, sampled and treated than in the past. Hence, more efforts are being made to incorporate mp-MR imaging into routine prostate biopsy, including cognitive, fusion and in-bore MR-guided techniques (3). Aim of this study is to compare PCa detection rate of in-bore MR-targeted biopsy with the detection rate of TRUS-guided prostate biopsy in patients with high PSA values and at least one suspicious region identified by the radiologist at mp-MR imaging. Materials and Methods: The dataset of this study comprised 223 subjects referred for clinical suspicion of PCa who underwent mp-MR imaging. Of these, 51 patients (23%, median age=68.4 years, median PSA=7.5 ng/ml) showed at least one suspicious lesion at mp-MR imaging (median lesion diameter=10 mm), with the characteristics of a clinically significant disease. Among these patients, 32 had at least one prior negative TRUS-guided biopsy (median of one session per patient, range=1-3). Then, they were randomly divided into two groups balanced with respect to age, PSA value, lesion size and location. Group A included 26 patients who underwent MR-targeted biopsy towards the MR findings. Two targeted cores were obtained from each lesion defined by the radiologist. Group B included 25 patients who underwent a TRUS-guided biopsy with saturation scheme. biopsy specimens were fixed in formalin and underwent pathologic evaluation to define PCa presence and Gleason score. Results: In group A, PCa was detected in 20/26 (77%) cases, 6 of which were located in the transition zone (TZ). Five negative findings in group A were located in the peripheral zone (PZ) and one was found in the TZ. In group B, we found 18/25 (72%) PCa, 6 of which were in the TZ. Six negative findings in group B were located in the PZ and one in the TZ. Detection rates between the two groups were not significantly different (p>0.93). An example of one patient in group A (imaging and MR-guided biopsy) is illustrated in Figure 1. Results of pathologic evaluation are reported in Table I. Discussion and Conclusion: The results obtained from a dataset of 51 patients suggest that introducing a mp-MR exam before scheduling a prostate biopsy increases the detection rate of clinically significant PCa, whatever the biopsy technique used for sampling. This study also has some limitations: first, results may not be generalized as this was a single-center trial. Second, we included men without considering previous number of prostate biopsies performed. Finally, in the TRUS-guided arm, cognitive targeting could not be avoided. Thus, this randomized controlled trial demonstrated that PCa detection rate of the MR-targeted arm and the saturation one are not statistically different, provided that an additional mp-MR examination is performed before biopsy.
25
A CASE OF SKIN METASTASIS IN CASTRATION-RESISTANT PROSTATE CANCER: CASE REPORT AND LITERATURE REVIEW

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Introduction/Aim: The common sites of metastasis of prostate cancer are bones, liver and lung. The cutaneous metastases are very rare (1-6). In this case presentation, we describe a patient who presented with cutaneous metastases on his left leg secondary to castration-resistant prostate cancer. Case Presentation: An 84-year-old Caucasian man with a history of castration-resistant prostate cancer, treated 8 years before with radiation therapy, presented with significant bilateral enlargement of inguinal nodes and cutaneous nodules on the medial part of the upper leg. The prostate-specific antigen (PSA) was 42 after 4 cycles of docetaxel. A punch biopsy evidenced cutaneous metastases, with histological confirmation, with positive staining for cytokeratin and PSA.

Table I. Results of pathologic evaluation.

<table>
<thead>
<tr>
<th>Gleason Score</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cancer</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>3+3</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>3+4</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>4+3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>4+4</td>
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<td>4</td>
</tr>
<tr>
<td>4+5</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>5+5</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>
Conclusion: Although the overall rate of cutaneous metastases from prostate cancer (PCa) is low, there is a possibility that a skin lesion may represent an undiagnosed metastasis. Obstruction of cutaneous lymphatic channels can result in retrograde regurgitation of small tumor emboli and facilitate deposition of tumor cells in the skin. This mechanism is supported by the histopathologic findings of nodules of metastatic cells in the dermis. In the absence of a clear history of prior malignancy, the clinical changes may mimic a lymphovascular neoplasm or even an inflammatory skin condition. Therefore, in case of skin nodules in patients with long history of PCa, a diagnosis of metastasis should be considered.


TESTICULAR METASTASIS OF UROTHELIAL BLADDER CANCER: CASE REPORT AND LITERATURE REVIEW

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Introduction: Testicular metastasis of carcinoma is rarely reported in literature, with a total of almost 200 cases (1, 2). The most frequent primary localization of tumour is prostate, lung and gastrointestinal tract. To our knowledge, there are only three cases of testicular metastasis of urothelial bladder cancer. Materials and Methods: Case report and English-literature review. Case Report: A 60-year-old man with a story of diabetes mellitus type II and hypertension was diagnosed with T1 high grade urothelial carcinoma of the bladder when he was 55 years old. He underwent instillations, first with mitomycin and, successively, with BCG. He was diagnosed with recurrence Ta low grade four years later. The therapeutic suggestion was another cycle of BCG, two years after the first
one; however, administration of the drug was not possible because of several recurrent urinary tract infections. A new transurethral resection documented an urothelial carcinoma, T1 high grade, but located in the prostatic urethra. Similarly, the patient did not assume BCG because of recurrent urinary tract infections. The patient showed right orchi-epididymitis two months after the last operation, with multiple antibiotics' resistance. Additionally, the pathologist documented necrotic flogosis of the testicular parenchyma, with a group of epithelial-like cells with a maximum diameter of 3 mm, located proximally to rete testis (GATA 3+, P63-, PAX8-, CK34 E12 –/+ ) compatible with urothelial primary tumour. Computed tomography and positron emission tomography did not document any metastasis. The patient is still on follow-up. Conclusion: The testis can be the site of distant metastasis of prostate, lung and gastrointestinal tract. The primary neoplastic site in bladder is extremely rare. The dissemination way can be identified in the seminal tract, due to the first involvement of prostatic urethra. In case of hardening or swelling of the testis in patients with recurrent bladder cancer with involvement of the prostatic urethra, the hypothesis of metastasis has to be taken into account.


28 MANDIBULAR METASTASIS OF UROTHELIAL CARCINOMA OF THE BLADDER: CASE REPORT AND LITERATURE REVIEW

Carmen Maccagnano1, Agazio Ussia2, Laura Longhi3, Carlo Patriarca2, Stefano Valsecchi4 and Giario Conti1

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Introduction/Aim: Mandibular metastasis is mostly related to primary oral neoplasms having an incidence inferior to 1% (1-4). In this case presentation, we describe a patient who presented firstly with bladder cancer and, successively, rapid diffusion to jaw. We also review English literature about mandibular involvement in urothelial bladder cancer. Case Report: The case concerns a 79-year-old woman with a history of Chron’s disease and therapy with mesalazine. She reported several episodes of gross haematuria during the last four months. The patient executed trans-urethral resection of both extended lesion in the whole bladder neck and another big lesion localized in the whole right wall, with infiltrating appearance. The pathologist evidenced urothelial carcinoma, T1e according Van Rhijn, high grade and focal vascular invasion. The muscle layer was uninjured. Computed tomography (CT) documented enlargement of multiple retroperitoneal and right external iliac nodes, with a maximum diameter of 25 mm. Thus, two nephrostomies were positioned because of the CT diagnosis of bilateral hydronephrosis. Simultaneously, carbapenemases were administered because of concomitant urosepsis. After 20 days of recovery, a significant hardening and swelling of the right jaw was noted, with worsening during the following 24 hours, with concomitant persistent fever (>38°C). A facial CT with contrast medium evidenced a voluminous lesion of the right jaw, with a maximum diameter of 5 centimeters, with complex densitometry due to the presence of colliquative areas, peripheral calcifications, bone erosion and involvement of pterygoid and masseter. The exam also showed oval enlargement of local nodes, according to II level of Robbins. Biopsy of the lesion revealed localization of carcinoma with morphologic and immunohistochemical appearance compatible with primary urothelial bladder cancer (GATA3+, p63+). Bone scan was negative and the patient died one month after diagnosis, in palliative regimen. Conclusion: Only nine cases of mandibular metastasis of urothelial bladder cancer have been reported in literature. According to the published data, we hypothesized that the localization of the metastasis -distally from the primary tumour- can be explained by hematogenous spread, trough the vena cava, in the context of a metastatic disease just at the first diagnosis, as evidenced by the enlargement of nodes in multiple and different locations. The prognosis is not good with a four-year survival of about 10%. The exitus is rapid, with few possibilities of chemo- or radiotherapies, and only with palliation intend.

SYNCHRONOUS LIVER METASTASES OF RENAL ONCOCYTOMA: A CASE REPORT AND LITERATURE REVIEW

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Introduction/Aim: The 2004 WHO classification of renal tumors in adults described renal oncocytoma (RO) as benign epithelial neoplasia deriving from intercalated cells. The benign nature of this tumor was established in the 1990s. The term “oncocytoma” was initially used to describe lesions in parathyroid glands, thyroid glands and salivary glands. The first case of RO was described by Zippel in 1942. This kind of lesion comprises 3-9% of all renal tumours, with prevalence in male gender. At present, few clinical cases of metastatic oncocytomas are reported in literature. We describe a patient with synchronous liver metastases of RO. Case Report: We report a case of a 62-year-old woman affected by left renal mass and 10 liver nodules identified by computed tomography scan. A left radical nephrectomy with excision of 2 of the 10 liver nodules was carried out. Macroscopically, the renal neoplasm extended into the renal pelvis and vascular invasion of minor renal venous branches were reported. By histopathological evaluation, the renal and hepatic nodules were composed of solid nests of round to polygonal cells with densely granular eosinophilic cytoplasm, round uniform nuclei and scattered nucleoli. An area of oedematous fibrous stroma was present in the central part of the lesions. Neither mitosis nor necrosis could be seen. Renal and hepatic lesions shared the same immunophenotypical profile showing partial positivity for S100A1, CD10 and CD117 and diffuse positivity for PAX-8 and succinate-dehydrogenase. On the contrary, the neoplasms were negative for carbonic anidrase IX, CD13, cytokeratin 7, parvalbumin, vimentin, anti-HEPAT, TTF1, thyroglobulin and HMB45. A fluorescence in situ hibridization (FISH) was suggestive of RO with liver metastasis. Materials and Methods: A research on PubMed was performed with the falling strategy: renal oncocytoma, metastatic renal oncocytoma, renal adult tumours. Discussion: RO is a benign renal tumour, commonly asymptomatic, discovered incidentally with diagnostic imaging. The standard treatment for RO is the surgical excision or radical nephrectomy. More recently, minimally extensive and ablative renal sparing techniques, such as partial nephrectomy, radiofrequency or cryoablation have been alternative options. RO, sometimes, co-exists with a malignant neoplasm that may be present within or adjacent to the oncocytoma; rare cases of metastatic RO have been reported simulating a malignant course. Nevertheless, more than 20 cases with invasive histopathological features are described, 5 of them with distant metastases (liver, skeleton, lungs). Only liver metastases were confirmed at immunohistochemical staining. Review of the literature showed that oncocytomas sharing genetic or molecular features of chromophobe carcinoma may exist, explaining these rare instances of metastases. Conclusion: In the reported case, we provide additional evidence that RO, in extraordinarily rare cases, can have a metastatic potential as it is the only one with a synchronous pathway in the literature. In our case, as well in all the cases previously described, the liver was the organ involved in metastasis, while the presence of metastasis did not seem to affect prognosis.

A NOMOGRAM PREDICTING SEVERE LATE RECTAL BLEEDING IN A LARGE POOLED POPULATION AFTER RADIOThERAPY FOR PROSTATE CANCER

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Aim: To develop a nomogram based on a model for grade 3 (G3) late rectal bleeding (LRB) after radical radiotherapy (RT) for prostate cancer. The proposed model was derived from a pooled population made up of two large prospective
trials: Airopros0102 (Fellin RO2014) and TROG 03.04 RADAR (Ebert IJROBP2015). Materials and Methods: Both trials included patients (pts) treated with three-dimensional conformal radiation therapy (3DCRT) at 66-80 Gy, conventional fractionation. Planning data were available for all pts. G3 LRB was prospectively scored using the SOMA/LENT questionnaire, with a minimum follow-up of 3 years. Rectal dose-volume histograms were reduced to equivalent uniform dose (EUD) calculated with volume parameter n derived by 3 studies: n=0.06 (Rancati RO2004), n=0.05 (Rancati RO2011) and n=0.018 (Defraene IJROBP2011). EUD was inserted into multivariable logistic regression (MVL) model together with clinical and treatment features. Irradiation of seminal vesicles (SV), irradiation of pelvic nodes, hormonal therapy, hypertension, previous abdominal surgery (SURG), use of anticoagulants, diabetes, cardiovascular diseases and presence of acute toxicity were considered as potential dose-modifying factors. Goodness of fit was evaluated with Hosmer-Lemeshow test (HL), calibration through calibration slope and area under the curve (AUC) was used for discrimination power. The results of multivariate analyses were used to develop a nomogram to predict long-term toxicity. All computations were performed using r-project (http://www.r-project.org) software. Results: 1,337 pts were available: 668 from RADAR trial and 669 from Airopros 0102. G3 LRB was scored in 95 pts (7.1%): 62 RADAR and 33 Airopros 0102. EUD calculated with n=0.06 was the best dosimetric predictor for G3 LRB. A 4-variable MVL model was fitted including EUD (odds ratio (OR)=1.07 p=0.16), SV (OR=4.75 p<0.001), SURG (OR=2.30 p=0.02) and cardiovascular disease (OR=1.42 p=0.18). Predicted toxicity curves together with observed toxicity rates, as a function of EUD and clinical risk factors, are presented in Figure 1. The coefficient derived from the logistic model was used to develop a nomogram for prediction of severe bleeding (Figure 2). The AUC of the model was 0.63, calibration slope=0.99 (R^2=0.89) and p for HL=0.43. Inclusion of acute toxicity (OR=2.34 p<0.001) slightly improved AUC (0.65), thus confirming a possible role of consequential injury. Conclusion: EUD with n=0.05 was predictive of G3 LRB in this pooled population, confirming the importance of sparing the rectum from high doses. Irradiation of seminal vesicles together with cardiovascular disease and previous abdominal surgery were relevant dose-modifying factors highly impacting the incidence of G3 LRB. The study was funded by: AIRC IG16087, Fondazione Monzino, NHMRC (300705, 455521, 1006447).
A LONG-TERM RESPONSE IN TRANSITIONAL CELL CARCINOMA OF THE BLADDER TREATED WITH VINFLUNINE

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Introduction: There is no established treatment for patients with advanced bladder cancer who experience progression after first-line platinum-based regimen. Vinflunine (VFL) seems to be a valid option for transitional cell carcinoma of urothelial tract (TCCU) in second-line treatment (1). Nevertheless, TCCU patients who progress after platinum-based chemotherapy have a very poor prognosis with a life expectancy just above 6 months. Recently, anaemia, poor performance status and liver metastases have been validated as independent, adverse prognostic factors for survival (2).

Patients and Methods: We present the case of a 57-year-old woman, who was submitted to a left nephrouretectomy for a transitional cell carcinoma (stage II - pT2 pN0, Grading 3), with the involvement of the proximal ureter, in February 2002. Then, she underwent adjuvant chemotherapy with 1,000 mg/m² gemcitabine d1, 8, 15 q28 for 6 cycles. In April 2011, after 9 years of follow-up, a pelvic magnetic resonance (RM) was performed for the occurrence of
pulmonary disease and oedema in the left leg. The pelvic RM showed a mass of 42 mm in diameter between the obturator artery and the ureter, causing stenosis of both left iliac and hypogastric arteries. Moreover, the omolateral ureter was thickened and infiltrated by the pathologic tissue. On May 2011, she started first-line chemotherapy with cisplatin and gemcitabine. After 4 cycles of treatment, the patient experienced a partial response with a reduction of more than 30% in the pelvic mass. Regardless of the good response, the surgeon evaluated the patient inoperable, thus, in March 2012, she underwent a definitive radio-chemotherapy with infusional 5-fluorouracil, followed by a screening program. She was negative for relapse of disease until February 2014 when anemia and macrohematuria appeared. Cystoscopy showed a relapse of disease and 18-FDG PET scan revealed a pathologic captation in carinal lymphadenopathy, VIII/IV hepatic segment in pelvic left side. Considering the time elapsed since the previous platinum-based chemotherapy (>12 months), as such a platinum-sensitive, a second-line treatment with carboplatin and paclitaxel was started. However, treatment was interrupted for a drug adverse reaction after the first cycle. Therefore, we decided to switch her to VFL. By March 2014, the patient received 20 cycles with a progression-free survival (PFS) of 18 months. The best response was a partial reduction in mediastinal lymphadenopathy and in pelvic mass and a complete response in hepatic metastasis. Moreover, haematuria resolved after the fourteenth cycle. The maximal toxicities reported were grade 1 constipation and grade 3 non-febrile neutropenia. Prophylactic granulocyte colony-stimulating factor was introduced in the last 6 cycles with complete control of haematological toxicity. Discussion and Conclusion: In this case, the use of VFL in second-line setting achieved an objective response with a complete regression of hepatic disease together with a significantly improvement in PFS, also maintaining a good toxicity profile. We can conclude that VFL may also be a suitable choice both in presence of adverse prognostic factors, such as anaemia and/or liver metastasis, and in platinum-sensitive disease. Further studies are needed to confirm these data.


32 COMPLETE RESPONSE BY TEMSIROLIMUS IN POOR RISK METASTATIC RENAL CELL CARCINOMA WITH SARCOMATOID HISTOLOGY

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Introduction: Temsirolimus, a mammalian target of rapamycin (mTOR) inhibitor, is approved for first-line treatment in metastatic renal cell carcinoma (mRCC) patients with poor prognosis (1). Its role in systemic therapy for patients with non-clear-cell or sarcomatoid histology was evaluated in several studies (2). Patients and Methods: In this case, we report a complete radiological response by temsirolimus in an 81-year-old patient with mRCC. A pre-operative abdomen computed tomography (CT) scan has shown a renal mass in the right kidney with thrombosis of renal vein and two liver metastases. The patient underwent a radical right nephrectomy and histology confirmed a sarcomatoid RCC with a component of clear cell and papillary form (Furhman grade 4). The liver metastases were considered inoperable at surgical evaluation. According to the MSKCC and Heng’s score criteria, we evaluated the patient as a poor risk for the presence of ≥3 prognostic factors: low Karnofsky performance status (70%), serum hemoglobin less than the lower normal limit (10 g/dl), time to diagnosis to treatment of less than 1 year (2 months) and high lactate dehydrogenase (305 U/l). Considering the prognostic analysis and the histology, we decided to start first-line systemic therapy with 25 mg/week temsirolimus (3). After XI cycles of therapy, adverse events were not registered, except for grade 1 mucositis; a CT scan did not show hepatic metastases anymore. Currently, the progression-free survival is 7 months and therapy is ongoing. Discussion and Conclusion: This case describes a complete radiological response by temsirolimus in poor risk mRCC with rare and aggressive histology. Currently, few data exist in literature on modality of treatment in this subgroup of patients with aggressive features. Indeed, further trials are needed in this setting.


33 STEREOTACTIC RADIOTHERAPY FOR BRAIN METASTASES FROM PROSTATE CANCER: A CASE REPORT

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Introduction: Nowadays, brain metastases from prostate cancer (PCa) seem to be more frequent, probably due to recent introduction of innovative treatments in clinical routine. Particularly, patients with castration-resistant PCa have prolonged their survival. This is the case report of a 68-year-old patient with clinical recurrence of prostate cancer, who reported a secondary brain lesion treated with stereotactic ablative radiotherapy (SABR). Materials and Methods: The patient, with an initial prostate-specific antigen (PSA) level of 32.6 ng/ml, underwent prostatectomy and lymphadenectomy in 2004. Final pathology revealed a Gleason Pattern score 6 (3+3) prostatic adenocarcinoma (final Stage pT2b pN0 M0). In 2005, the patient was treated with total androgen deprivation therapy (ADT) (bicalutamide 50 mg and degarelix 3.75 mg) due to an increase of PSA level. After biochemical progression disease in September 2007, the patient underwent subcapsular bilateral orchiectomy followed in 2009 by surgical removal of a suspicious solid pelvic suprapubic neoplasm. Final pathology was positive for metastasis from prostatic adenocarcinoma. The patient underwent regular follow-up until 2012 when he was referred to our institution for radiotherapeutic advice. At the moment of SABR, the patient was in good general condition (Karnofsky performance status=100) and without neurological symptoms. On 24/07/2015, the patient underwent SABR of the brain lesion using IG-IMRT Tomotherapy. We delivered 25.5 Gy in 3 fractions (8.5 Gy/die) according to International Commission on Radiation Units & Measurements (ICRU) 83. Delivery treatment time was 12 minutes for each session with a total machine time of 20 minutes. Treatment ended on 28/07/2015; it was well-tolerated without side effects. The MRI of revaluation showed size reduction of the known secondary lesion involving genu of the corpus callosum, re-expansion of frontal horns of the lateral ventricles and reduction of peritumoural oedema. The first post-SABR PSA level was 6 ng/ml and last PSA level (28/08/15) was 31.21 ng/ml due to extracranial progression of disease. Conclusion: SABR, using Tomotherapy, has been proven feasible as non-invasive exclusive treatment (1, 2) for castration-resistance prostate cancer, even for brain metastases (3) not showing significant acute and late toxicity.


integrated boost (SIB) with Tomotherapy. In 2013, due to the appearance of pulmonary and bones metastasis secondaries the patient was treated with first-line chemotherapy (cabazitaxel) associated to ADT obtaining pathological complete response. PSA levels remained satisfactory until June 2015 when a rise was shown (PSA=5.07 ng/ml). The patient was submitted to 18FC-PET that showed “hyperaccumulation of radiotracer in left corpus callosum region, no other secondary lesions”. Magnetic resonance imaging (MRI) confirmed the presence of one cystic-necrotic parasagittal lesion (diameter of about 3 cm) marking the frontal horns of the lateral ventricles with deviation to the right of the septum pellucidum suspected for high grade glioma. Then, a cerebral stereotactic biopsy was performed and pathology revealed metastasis from prostatic adenocarcinoma. Results: In July 2015, the patient was referred to our institution for radiotherapeutic advice. At the moment of SABR, the patient was in good general condition (Karnofsky performance status=100) and without neurological symptoms. On 24/07/2015, the patient underwent SABR of the brain lesion using IG-IMRT Tomotherapy. We delivered 25.5 Gy in 3 fractions (8.5 Gy/die) according to International Commission on Radiation Units & Measurements (ICRU) 83. Delivery treatment time was 12 minutes for each session with a total machine time of 20 minutes. Treatment ended on 28/07/2015; it was well-tolerated without side effects. The MRI of revaluation showed size reduction of the known secondary lesion involving genu of the corpus callosum, re-expansion of frontal horns of the lateral ventricles and reduction of peritumoural oedema. The first post-SABR PSA level was 6 ng/ml and last PSA level (28/08/15) was 31.21 ng/ml due to extracranial progression of disease. Conclusion: SABR, using Tomotherapy, has been proven feasible as non-invasive exclusive treatment (1, 2) for castration-resistance prostate cancer, even for brain metastases (3) not showing significant acute and late toxicity.


FACING UNTREATED PROSTATE CANCER ON ACTIVE SURVEILLANCE: WHO IS AT RISK FOR INCREASED ANXIETY?

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Introduction/Aim: The still-debated issue about active surveillance (AS) is whether “living with untreated” prostate cancer (PCa) could cause anxiety. Although the majority of AS patients seems not to report heightened anxiety (1), high levels of anxiety may negatively impact patients’ health-related quality of life (HRQoL) (2). To date, it is still scarcely understood which issues are related to anxiety. The aim of this analysis was to further investigate factors associated with higher level of PCa-related anxiety during AS. Patients and Methods: Patients enrolled in one of the European centres that offer participation to the Prostate Cancer Research International: AS (PRIAS) protocol and consented to participate in the ancillary PRIAS QoL study were considered. Socio-demographic features, HRQoL domains (Short Form-36, SF-36; Functional Assessment of Cancer Therapy – Prostate, FACT-P), coping with cancer (Mini-Mental Adjustment to Cancer, Mini-MAC), decisional data (Decisional Conflict Scale, DCS) and personality (Eysenck Personality Questionnaire, EPQR-A) were assessed at entrance in AS (T0). PCa-related anxiety was measured by the memorial anxiety scale for PCa (MAX-PC) according to the Italian cultural adaptation at 2 months before the first protocol re-biopsy (T1). Compared to the English version of MAX-PC, the Italian one is based on a new three-factor structure derived from 15 items, which does not include the questions related to the original PSA-anxiety subscale (i.e. items 12, 13, 14) due to their strong floor effect (76%). Descriptive analyses were conducted and multivariate logistic models were performed to detect factors associated with high levels of anxiety, i.e. MAX-PC total score > average score of 1.5 on the 0-3 rating scale (3).

Results: Between 2010 and 2015, 168 patients completed MAX-PC at T1. Mean age was 64±7 years (42-79 years). Table I summarizes the socio-demographic and clinical characteristics of the sample. Table II illustrates the

Table I. Sample’s characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients</td>
<td>168</td>
<td></td>
</tr>
<tr>
<td>Socio-demographic characteristics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher Education (High school)</td>
<td>113</td>
<td>67%</td>
</tr>
<tr>
<td>Employed</td>
<td>71</td>
<td>42%</td>
</tr>
<tr>
<td>Retired</td>
<td>97</td>
<td>58%</td>
</tr>
<tr>
<td>Married or living with a partner</td>
<td>149</td>
<td>89%</td>
</tr>
<tr>
<td>Months between diagnosis and entrance in AS</td>
<td>152</td>
<td>90%</td>
</tr>
<tr>
<td>PSA at diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1c</td>
<td>152</td>
<td></td>
</tr>
<tr>
<td>T2a</td>
<td>16</td>
<td>10%</td>
</tr>
<tr>
<td>Biopsy at diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 positive core</td>
<td>119</td>
<td>71%</td>
</tr>
<tr>
<td>2 positive cores</td>
<td>49</td>
<td>29%</td>
</tr>
</tbody>
</table>

Table II. MAX-PC total and subscales scores and distribution at T1 (N=168).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Observed score</th>
<th>Possible score</th>
<th>Clinical threshold</th>
<th>N (%) of patients above clinical threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAX-PC total score (T1)</td>
<td>13.34</td>
<td>9.28</td>
<td>12.00</td>
<td>0-39</td>
<td>0-45</td>
<td>22.5</td>
<td>27 (16%)</td>
</tr>
<tr>
<td>PCa anxiety (T1)</td>
<td>6.11</td>
<td>4.96</td>
<td>4.75</td>
<td>0-18.5</td>
<td>0-31.5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Fear of progression (T1)</td>
<td>4.04</td>
<td>2.96</td>
<td>3.50</td>
<td>0-13.5</td>
<td>0-13.5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PSA anxiety (T1)</td>
<td>3.23</td>
<td>2.49</td>
<td>3.00</td>
<td>0-9</td>
<td>0-9</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
descriptive scores for MAX-PC at T1. Twenty seven patients (16%) reported MAX-PC total score above the cut-off. The best model reported an overall p-value<0.0001, area under the curve (AUC)=0.85. Four factors resulted as potential predictors of high level of PCa-anxiety at T1: the Mini-MAC subscales helplessness/hopelessness and avoidance emerged as risk factors (odds ratio (OR)=1.99 and OR=1.92, respectively); emotional wellbeing (FACT-P) and mental health (SF-36) had a protective effect (OR=0.22 and OR=0.98, respectively). Discussion and Conclusion: Our findings showed that men who felt powerless and had negative expectations about oneself and their future for entrance in AS, thus adopting an avoidance attitude toward disease, were more likely to experience heightened PCa anxiety during AS. On the contrary, the presence of positive emotions, such as hope and satisfaction, as well as the absence of negative emotions toward the disease, such as fear and sadness and, also, an overall state of mental health at the beginning of AS, have been shown to protect patients from experiencing anxiety for their untreated cancer. These results suggest the importance of a routinely psychological assessment to detect risk factors for increased anxiety during AS, as well as the offer of tailored psychological interventions aimed at promoting interpersonal awareness and expression of emotions.

Acknowledgements to Foundation I. Monzino Onlus.


35
STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR OLIGOMETASTATIC PROSTATE CANCER PATIENTS: A SINGLE INSTITUTION EXPERIENCE

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Introduction/Aim: Recently, the detection of oligometastatic prostate cancer (PCa) recurrence is more common in clinical routine due to imaging innovations. In these patients (pts), the use of aggressive local treatments (surgery or radiotherapy) may be potentially justified rather than a systemic approach. The aim of the present study was to report our clinical experience on stereotactic body radiotherapy (SBRT) for isolated clinical recurrence (nodal, bone or visceral). Materials and Methods: From 2011 to September 2015, we treated 21 pts with clinical recurrence of prostate adenocarcinoma. Mean and median age was 69 and 70 years (range=56-81), respectively. All pts underwent radical prostatectomy at time of first diagnosis and 12 of them also received adjuvant radiotherapy (RT). Only 1 pt was submitted to salvage RT to prostatic bed after biochemical relapse. At staging, 16 pts had high-risk PCa, while the others had intermediate risk. Gleason Pattern Score (GPS) was less than 7 in 2 pts, equal to 7 in 9 and superior in 9. Median time to clinical relapse after primary treatment (surgery +/- RT) was 53.7 months (range=3-142). Thirteen pts received at least 1 hormonal therapy before being submitted to RT. Mean and median PSA before SBRT was 3.38 ng/ml and 3.14 ng/ml (range=0.36-14.9), respectively. All patients underwent restaging with 18F-Choline CT-PET before being submitted to SBRT to confirm the oligometastatic stage. SBRT was delivered due to nodal recurrence in 18 pts, while due to bone and brain metastases (MTS) respectively in 2 pts and in 1 pt. SBRT was delivered in association with androgen deprivation therapy (ADT) in 6 pts, while treatment was delivered alone in the other 14 pts. We analyzed outcomes in terms of local control (LC), progression-free survival (PFS) and overall survival (OS) using Kaplan-Meier method and log rank tests. Acute and late toxicity was also investigated to demonstrate feasibility and safety of SBRT. Results: At a median follow up of 11.3 months (range=2-35.3), all pts but 2 were still alive. Eighteen pts were treated with SBRT only to one site (14 to abdominal nodes, 3 bone lesions and 1 brain lesion), while 4 pts were treated to two different sites (all nodal). All pts were submitted to SBRT using Tomotherapy. For nodal metastasis, 7 pts received 30-32 Gy in 5 fractions (fx), 4 pts 36 Gy in 6 fx, 6 pts 35 Gy in 5 fx and, finally, 2 pts <25 Gy in 5 fx. For bone and brain MTS, 2 pts received 24 Gy in 3 fx. Mean and median PFS were, respectively, 14 and 11 (95% confidence interval (95% CI)=6-16) months, while mean OS was 31.2 (95% CI=23-35). One-year PFS and OS were 47.5%±13.5 and 93.8±6.0, respectively. Estimated 3-year OS was 83.3±11.2. Local control was 100%. Patients, tumor and treatment-related features were analyzed to find prognostic factors in terms of OS, PFS and LC. At univariate analysis,
association with ADT and hormone-sensitive PCa favorably influence OS with a statistical difference (p<0.01 and <0.03, respectively). Analyzing our population in terms of PFS, no prognostic factors were found as statistical significant: only hormone-sensitive PCa and site of MTS (node vs. bone/brain) seemed to have a positive impact on PFS showing a statistical trend (p<0.14 and <0.12) with a median PFS of 12.4 months in patients with nodal MTS only. At time of analysis, neither acute nor late toxicity was found after SBRT. Conclusion: SBRT seems to be a very promising feasible, very well-tolerated and non-invasive locoregional approach (1, 2, 3) for oligometastatic PCa pts producing an interesting median PFS of 11 months. Outcome is particularly favorable when nodal involvement is the only site of relapse.


36 PRIMARY ADENOCARCINOMA OF THE BLADDER TRIGON
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Introduction: Bladder adenocarcinoma is an uncommon malignancy (0.5-2 % of all bladder neoplasms) that may arise as a primary bladder tumor, as well as secondarily from a number of other organs. Differential diagnosis is often difficult. Materials and Methods: We have analyzed a case of a 75-year-old woman who underwent a bladder transurethral resection (TURB) for a 4.5 cm in diameter trigonal lesion. Clinical patient’s workup excluded any other adenocarcinoma onset location outside the bladder. The tumor was, therefore, defined as “primary” and the patient underwent a radical cystectomy (CRAD). Results: At TURB, histology demonstrated bladder adenocarcinoma of trigon with large areas of necrosis, while immunochemistry was positive for CDX2, CEA and negative for estrogens and progesterone cT2a. Pathology, following CRAD, confirmed the finding of a pTNM=pT2 pN0 tumor. At a 9-month follow-up, the patient is alive without evidence of tumor relapse. Discussion and Conclusion: Primary bladder adenocarcinoma is typical in patients over 50 and the most frequent localization is the dome. It exhibits several different growth patterns, including enteric, mucinous, signet-ring cell, not otherwise specified, and mixed patterns (1). Differential diagnosis should be done with urachal adenocarcinoma, which is typical in young patients, localized in the bladder dome, while secondary bladder adenocarcinomas may arise from the colorectum, prostate, endometrium, cervix and other sites. When primary, urachal adenocarcinoma has a more favourable prognosis than other onset locations. Immunohistochemical study is valuable in identifying the origin of secondary adenocarcinoma. It is imperative to identify each type of adenocarcinoma given that their origin does modify treatment (2). When bladder adenocarcinoma is primary, CRAD is mandatory; on the other hand, when it is secondary, tumour chemotherapy should be considered as front-line treatment.


37 DISCORDANT OUTCOMES TO ABIRATERONE ACETATE IN AN ELDERLY PATIENT WITH METASTATIC CASTRATION RESISTANT PROSTATE CANCER
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Introduction: Abiraterone acetate (AA) is an oral selective inhibitor of cytochrome P450c17 (CYP17). It is approved in
combination with low-dose of prednisone in patients affected by metastatic castration-resistant prostate cancer (mCRPC) in pre- and post-docetaxel settings (1, 2). Clinical practice shows that the assessment of response to treatments may be not easy in mCRPC and multiple parameters are recommended to evaluate patients for progression (3). Patients and Methods: We report the case of a 91-year-old man with mCRPC. At diagnosis, in August 2013, prostate-specific antigen (PSA) was 138 ng/ml and a bone scan revealed asymptomatic lesions involving spine and pelvic bones. In November 2013, he started total androgen blockade with leuprolerin 3.75 mg/ml plus bicalutamide 50 mg. After 3 months of treatment, a bone scan performed showed stable disease (SD) and PSA levels settled at 121 ng/ml. In September 2014, the patient showed biochemical progression (according to Prostate Cancer Working Group (PCWG2) criteria) when PSA increased to 183 ng/ml and antiandrogen treatment was suspended; no withdrawal response was observed with a further increase of PSA to 217 ng/ml. Computed tomography (CT) scan highlighted metastasis to mediastinal, paratracheal and obturator nodes, vertebral bones and a local invasion of bladder and left ureter. In November 2014, according to his good Performance Status, he started AA 1.000 mg/die plus prednisone 10 mg daily. Despite the biochemical response to AA (>50% decline from baseline PSA), a CT scan performed after 20 weeks of therapy showed bone progression. Considering both the patient’s good performance status and his clinically stable disease, we decided to continue AA. After 44 weeks of AA, PSA decreased to 12.74 ng/ml but CT revealed additional bone progression, leading to so palliative radiotherapy to prevent pathological fractures. After 64 weeks of treatment, PSA is 7.54 ng/ml and AA therapy still in progress with a good safety profile. Conclusion: We report a case of discordant outcomes to AA after 20 weeks of therapy. According to PCWG2-3 criteria, we decided to continue therapy with AA despite the radiographic disease progression, in respect of the durable and favorable biochemical response, patient’s good performance status, absence of symptomatic new lesions and treatment tolerance. This case focuses on the interesting question whether the adverse change in a single parameter, or discordant parameters, justifies changing treatment in mCRPC as this may support clinicians in their decision-making process.


38 SIURO-PRIAS-ITA, SIX-YEAR EXPERIENCE IN ACTIVE SURVEILLANCE

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Introduction/Aim: We here report on our 6-year experience in active surveillance (AS). Correlation between AS drop-out and patients’ characteristics at diagnosis was investigated to search for associations with disease reclassification after a period in AS. Survival analysis with active treatment free survival (ATFS) as an end-point was considered. Materials and Methods: In
December 2009, the SIUrO-PRIAS-ITA working group started including patients in PRIAS (Prostate cancer Research International: Active Surveillance). Eligibility criteria were: prostate-specific antigen (PSA) at diagnosis (iPSA) ≤10 ng/ml, Gleason Score (GPS)≤6, clinical stage T1c or T2a, PSA density≤0.2 ng/ml/cc, maximum 2 positive cores. Results: 837 patients were included in PRIAS between December 2009 and December 2015. Median age at inclusion was 66 years (range=42-81), median iPSA was 5.46 ng/ml (range=0.5-10). 243/837 (29%) patients had two positive cores at diagnostic biopsy. 793/837 (94.6%) patients were classified as T1c at digital rectal examination (DRE). 272/837 (32.5%) patients dropped out from AS, 181 due to upgrading and/or upsizing at re-biopsy (98/181 at first re-biopsy one year after inclusion) and 14 due to PSA doubling time. Median time in AS is 25 months (range=1-103). Biopsy-driven ATFS resulted to be correlated to body mass index (BMI) ($p=0.02$, stratified in three groups: ≤25, 25-30, >30, ATFS at 48 months: 84% vs. 71% vs. 65%, respectively), PSA density≤0.12 ng/ml/cc ($p<0.001$, ATFS at 48 months: 79% vs. 65%, respectively), prostate volume ($p<0.001$, stratified in three groups: ≤40 cc, 40-60 cc, >60cc, ATFS at 48 months: 60% vs. 76% vs. 84%, respectively), number of positive cores at diagnostic biopsy ($p<0.001$, ATFS at 48 months: 78% vs. 60%, 1 core vs. 2 cores, respectively) and number of total cores at diagnostic biopsy ($p=0.008$, ATFS at 48 months: 68% vs. 77%, ≤12 vs. >12 cores, respectively). No significant differences were found for iPSA, smoke, age and family history of prostate tumor. Results are shown in Figure 1. Best fit multivariable Cox model for biopsy-driven ATFS resulted in a 4-variable model (overall $p<0.0001$): BMI (continuous variable, hazard ratio (HR)=1.07), PSA density (continuous variable, HR=1.06), number of positive core (1 vs. 2, HR=1.86) and number of total cores (continuous variable, HR=0.96). Conclusion: Results suggest that BMI, PSA density, number of positive cores and number of total cores at diagnosis are associated with ATFS. Most drop-out events occur at first re-biopsy, which should probably be considered as a confirmatory biopsy. Largest prostate volumes could influence the chance of sampling positive cores at random biopsy and, consequently, result in a lower probability of biopsy-driven AS drop-out.

### COMPARISON OF TWO TEMPLATES OF LYMPHADENECTOMY IN PATIENTS AFFECTED BY HIGH RISK PROSTATE CANCER

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Department of Urology, Umberto I Hospital - ASL Salerno, Nocera Inferiore (SA), Italy

**Introduction/Aim:** High-risk prostate cancer treatment considers an extended lymphadenectomy. We compared two templates of pelvic lymphadenectomy in high-risk patients undergone an extraperitoneal or transperitoneal laparoscopic radical prostatectomy. **Materials and Methods:** Two consecutive series of patients affected by high-risk prostate cancer underwent laparoscopic radical prostatectomy. In group 1 (101 pts), the procedure was realized by a preperitoneal access with an extended lymphadenectomy, including external iliac and obturator nodes; in group 2 (25 pts), access was transperitoneal with a broader lymphadenectomy consisting of common iliac, external iliac, hypogastric and obturator nodes. We have compared perioperative outcomes in terms of number of nodes removed, positive nodes and complications in the two groups of patients. Statistical analysis has been realized using SPSS 16. **Results:** Data on 126 patients were analyzed. Baseline characteristics are reported in Table I. Pre-operative data were balanced between two groups of patients except for biopsy Gleason score. Post-operative outcomes are listed in Table II. Group 2 patients presented worse pathological stage, longer operative time, more nodes removed (mean 31.6 vs. 15.9, $p<0.001$) and more positive pathological nodes (28.0 vs. 1.9%, $p<0.001$). Moreover, a wider lymphadenectomy template was not associated to greater risk of complications or lymphoceles.

<table>
<thead>
<tr>
<th>Table I. Baseline characteristics.</th>
<th>All pts</th>
<th>Group 1</th>
<th>Group 2</th>
<th>$p$-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66.8±5.6</td>
<td>66.9±5.8</td>
<td>66.7±4.9</td>
<td>0.78</td>
</tr>
<tr>
<td>PSA (prostate specific antigen)</td>
<td>11.7±7.5</td>
<td>11.1±6.3</td>
<td>14.1±11.1</td>
<td>0.57</td>
</tr>
<tr>
<td>BMI (body mass index)</td>
<td>27.1±3.4</td>
<td>27.1±3.4</td>
<td>27.2±3.3</td>
<td>0.85</td>
</tr>
<tr>
<td>ASA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>2.9</td>
<td>2.5</td>
<td>5.1</td>
<td>NS</td>
</tr>
<tr>
<td>II</td>
<td>36.3</td>
<td>29.1</td>
<td>57.7</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>57.8</td>
<td>65.8</td>
<td>31.2</td>
<td></td>
</tr>
<tr>
<td>IV (%)</td>
<td>2.9</td>
<td>2.5</td>
<td>6.0</td>
<td></td>
</tr>
<tr>
<td>Clinical Stage (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>88.2</td>
<td>98.1</td>
<td>88.2</td>
<td>NS</td>
</tr>
<tr>
<td>T3</td>
<td>11.8</td>
<td>1.9</td>
<td>11.8</td>
<td></td>
</tr>
<tr>
<td>Bx Gleason (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤3</td>
<td>7.9</td>
<td>9.8</td>
<td>-</td>
<td>0.001</td>
</tr>
<tr>
<td>3±4</td>
<td>5.5</td>
<td>3.9</td>
<td>12.1</td>
<td></td>
</tr>
<tr>
<td>≥4</td>
<td>46.5</td>
<td>53.9</td>
<td>16.3</td>
<td></td>
</tr>
<tr>
<td>&gt;7</td>
<td>40.2</td>
<td>32.4</td>
<td>71.6</td>
<td></td>
</tr>
</tbody>
</table>
Table II. Post-operative outcomes.

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative time</td>
<td>249.4±60.2</td>
<td>246.1±64.2</td>
<td>271.0±51.8</td>
<td>0.005</td>
</tr>
<tr>
<td>Prostate volume</td>
<td>51.7±18.4</td>
<td>51.2±18.3</td>
<td>53.6±18.9</td>
<td>0.56</td>
</tr>
<tr>
<td>Path. Stage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pT2</td>
<td>65.1</td>
<td>67.5</td>
<td>56.2</td>
<td>0.01</td>
</tr>
<tr>
<td>pT3</td>
<td>33.4</td>
<td>31.5</td>
<td>39.7</td>
<td></td>
</tr>
<tr>
<td>pT4</td>
<td>1.6</td>
<td>1.0</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>Pathol. Gleason</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3+3</td>
<td>3.9</td>
<td>4.9</td>
<td>0</td>
<td>0.18</td>
</tr>
<tr>
<td>3+4</td>
<td>16.5</td>
<td>17.6</td>
<td>11.8</td>
<td></td>
</tr>
<tr>
<td>4+3</td>
<td>40.2</td>
<td>42.2</td>
<td>32.1</td>
<td></td>
</tr>
<tr>
<td>&gt;7</td>
<td>39.3</td>
<td>35.3</td>
<td>56.1</td>
<td></td>
</tr>
<tr>
<td>Positive surgical</td>
<td>22.0</td>
<td>19.6</td>
<td>32.2</td>
<td>0.15</td>
</tr>
<tr>
<td>margins</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complications</td>
<td>23.6</td>
<td>25.5</td>
<td>16.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Lymphocele</td>
<td>4.7</td>
<td>5.9</td>
<td>0</td>
<td>0.1</td>
</tr>
<tr>
<td>Number nodes</td>
<td>19.0±10.4</td>
<td>15.9±8.4 (2-38)</td>
<td>31.6±8.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>removed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive nodes</td>
<td>7.1</td>
<td>1.9</td>
<td>28.0</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: In our retrospective analysis, a transperitoneal laparoscopic radical prostatectomy with an extended lymphadenectomy template, including obturator, external iliac, common iliac and hypogastric nodes, allows to remove a greater number of nodes and obtain more positive nodes without increasing risk of complications.

40 EOSINOPHILIC RENAL NEOPLASMS:
A CASE REPORT

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Introduction: Eosinophilic renal neoplasms include a spectrum of solid and papillary kidney tumors ranging from indolent benign oncocytoma to highly aggressive malignancies. Materials and Methods: We present the case of a 69-year-old man with a right 5-cm renal mass in diameter who underwent robotic-assisted partial nephrectomy. The patient is alive and with no evidence of disease at a 9-month follow-up. Results: Macroscopic examination showed a brownish lesion with small cystic areas. The lesion was composed of cells with eosinophilic cytoplasm and many intracytoplasmic vacuoles. Immunohistochemistry showed of PAX8, CK 8-18, CK7 and parvalbumin expression. On the contrary, CK 20, S100A1, racemase and TTF1 were negative. Fumarase and succinate dehydrogenase (SDH) were present in neoplastic cells. The neoplasia was defined as “unclassifiable”, low-risk for its nuclear grade (G2) acc. ISUP. Discussion and Conclusion: The classification of eosinophilic renal neoplasms is sometimes difficult but essential for prognosis (1). Differential diagnosis among oncocytic renal cell neoplasm is between oncocytoma, chromophobe renal cell carcinoma (RCC), hybrid tumor, epithelioid angiomyolipoma and SDH deficient renal cell carcinoma. In the present case, the large number of intracytoplasmic vacuoles is not characteristic of RCC; the expression of CK7 excludes the diagnosis of oncocytoma; succinic dehydrogenase excludes SDH deficient renal cell carcinoma (2); negativity to HMB45 and Melan-A excludes epithelioid angiomyolipoma. Eosinophilic renal neoplasms include a large spectrum of diseases with different features; it is necessary to integrate histopathological, molecular and clinical data to better characterize each specific neoplasia.


41 CLAMPLESS LAPAROSCOPIC PARTIAL NEPHRECTOMY: PRELIMINARY EXPERIENCE

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**Introduction/Aim:** Nephron sparing surgery is now reference standard for many T1 renal tumors. Although hilar clamping creates bloodless operative field, it necessarily imposes kidney ischemic injury. “Zero ischemia” partial nephrectomy allows to eliminate ischemia during nephron sparing surgery. We report our preliminary experience of “zero ischemia” laparoscopic partial nephrectomy (LPN) realized by controlled hypotension.

**Materials and Methods:** Patients with a single, clinical T1 tumor were candidates for “zero ischemia” laparoscopic partial nephrectomy. High-risk patients with severe, preexisting, cardiopulmonary, cerebrovascular or hepatoenal dysfunction were not eligible. The pre-operative work-up comprised medical history, physical examination, routine laboratory tests and computed tomography (CT) scan or magnetic resonance imaging (MRI). A transperitoneal approach was performed in all patients; four or five laparoscopic ports were inserted. The hilar vessels were prepared in event that bulldog clamping could, subsequently, be needed. Intraoperative monitoring included electrocardiogram, central venous pressure (CVP), electroencephalographic bispectral (BIS) index (BIS monitor™), NICOM (non-invasive cardiac output monitoring), urinary Foley catheter. A controlled hypotension, to carefully lower the mean arterial pressure (MAP), while maintaining excellent systemic perfusion, was maintained at approximately 60 mmHg. To induce hypotension, the doses of inhalational isoflurane were increased. The renal lesion was excised using cold endoeshears. Upon completion of tumor excision, blood pressure was restored to pre-operative levels. Parenchyma was repaired with Vicryl™ sutures arrested with absorbable clips and Hem-O-lk™. Biologic hematic agents and Surgicel™ were applied to the resection bed.

**Results:** Forty-three patients affected by renal tumor underwent zero ischemia LPN. Mean age and mean BMI were 58.3±12.2 years and 28.2±5.4, respectively. The American society of anesthesiologists’ (ASA) score was 1, 2 and 3 in 1, 22 and 20 patients, respectively. Charlson comborbidty index was 3.1±1.5. Renal score was low (4-6) in 13pts, moderate (7-9) in 24 pts and high (10-12) in 6 pts. Mean tumor size was 42.8±16.6 mm. Operative time, blood loss, ΔHb were 138.0±53.4 min, 306.2±314.5 ml, 2.1±1.0 gr/dl, respectively. Hilar vessels were isolated in 44.2%. In all cases the procedure was performed without clamping. Resection and suture times were 7.1±3.6 and 12.2±9.4 minutes, respectively. Hospital stay was 6.3±2.2 days. Post-operative complications were: 3 fever (Clavien I), 1 fever (Clavien II), 1 urine leakage managed conservatively (Clavien IIIa). Histological evaluation revealed oncocytoma in 6 pts, acute myeloid leukemia in 2 pts, complex cyst in 1 pts, renal cell carcinoma in 34 pts (pT1a (17 pts), pT1b (12 pts), T2a (5 pts)). Pre-operative and post-operative serum creatinine was 0.8±0.24 and 0.9±0.22, respectively (Δ0.05±0.08; Δ% -6.2); Pre-operative and post-operative glomerular filtration rate was 96.43±33.03 and 88.03±26.35, respectively (Δ-8.41±12.97 Δ% -8.7).

**Conclusion:** Zero ischemia LPN represents a safe and reproducible technique that allows to sparing renal parenchyma and preserve renal function. However, long-term results are needed.

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**42**

**CONTEMPORARY PROSTATIC ENDOSCOPIC RESECTION AND 24-CORE SATURATION PROSTATE BIOPSY (TURP-sBX) IN PROSTATE CANCER DIAGNOSIS**

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**Introduction/Aim:** Despite the fact that prostatic biopsy is the gold standard in the diagnosis of prostate cancer, in selected cases combined transurethral resection of the prostate and saturation prostate biopsy have been proposed (TURP-sBX) (1). Indications for TURP-sBX may be incidental prostate cancer found at previous TURP or bladder outlet urinary obstruction in men with elevated prostate-specific antigen (PSA) and previous negative biopsy. The aim of the present report was to evaluate if transurethral resection of the prostate, combined with a contextual biopsy, can be useful in malignancy detection in selected patients.

**Patients and Methods:** We prospectively enrolled 74 patients submitted at our Institution, between December 2009 and October 2015, to TURP and 24-core saturation biopsy of the peripheral portion of the gland immediately after transurethral resection of the prostate (TURP-sBX). Patients were divided in 2 groups. Group A: patients with incidental diagnosis of prostate cancer after previous TURP; Group B: patients with previous negative biopsy, clinically suspects of prostate cancer and bladder outlet obstruction. Peri-operative and post-operative complications (acc. Clavien system modified) following TURP-sBX were collected and compared to our standard incidence after TURP alone in the same period of time.

**Results:** Group A included 48 patients with a mean age of 70 years (range=59-81), mean PSA 4.08 ng/ml (range=0.58-7.14) and mean gland volume 69.37 cc (range=30.15-105). Group B included 26 patients with a mean age of 65 years (range=53-80), mean PSA 9.29 ng/ml (range=1.16-19.86) and mean gland volume 84.44 cc (range=30-103). Among Group A patients, 6/48 (12.5%) had a histological diagnosis of prostate cancer both in prostate biopsy and in TURP; 14/48 (29.17%) had a positive biopsy and a negative TURP, in 2/48 (4.16 %) the resection resulted positive and the biopsy negative and in 26/48 (54.17%) no malignancies were found both in TURP and in the biopsy samples. It could be noticed that patients with
positive TURP and negative biopsy had a higher mean prostate volume (104 cc vs. 76.91 cc). Among Group B patients, 2/26 (7.14%) had both TURP and biopsy samples positive, 4/26 (15.29%) had a positive biopsy and a negative TURP, 2/26 (7.14%) were positive for prostate cancer only in the TURP samples, while in 18/26 (64.29%) prostate cancer was not found both at TURP and biopsy. TURP-sBX led to no increase in peri-operative and post-operative complications both in Group A and B patients. Discussion and Conclusion: Combination of endoscopic resection of the prostate and 24-core saturation biopsy (TURP-sBX) seems to be useless in prostate cancer diagnosis both in patients with incidental prostate cancer after TURP and in those with previous negative prostate biopsy, elevated PSA and bladder outlet obstruction.


43

IS BLADDER WASH CYTOLOGY AT THE TIME OF A NEGATIVE CYSTOSCOPY USELESS IN SBTCC FOLLOW-UP?

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Introduction/Aim: Occult urothelial cancer, transitional cell carcinoma (TCC), is the most frequent urinary tract tumor. Bladder wash cytology is a tool in diagnosis and follow-up of superficial transitional cell carcinoma of the bladder (SBTCC). It has been proposed that positive bladder wash cytology, in the absence of endoscopic evidence of a TCC, may identify occult urothelial cancer (1). Our aim was to identify the utility of bladder wash cytology at the time of a negative cystoscopy. Materials and Methods: From January 2015 to December 2015, 1,441 patients underwent cystoscopy for previous SBTCC follow-up. In 36 (2.4%) patients there was a negative cytoscopy with positive bladder wash cytology. All 36 patients underwent a secondary bladder mapping. Results: The 36 patients who underwent a secondary mapping were 32 male and 4 female with a mean age of 65.5 years (range=45-86). Only 8 out of 36 patients (22.2%) had a TCC at histology. When considering the general population of 1,441 patients submitted to cytoscopy for SBTTC follow-up, the incidence of TCC at secondary mapping was 0.55%. All patients with TCC at secondary mapping were high-risk and 2 of them brought spontaneous positive urine cytology before the procedure. Seven out of 8 had been recently treated with MMC or BCG intravesical therapy. After the bladder mapping with positive histology, 3 of them underwent cystectomy, 3 intravesical therapy and 2 had upper urinary tract TCC managed conservatively. Discussion and Conclusion: Bladder wash cytology is useless in low- and medium-risk SBTTC patients at cystoscopy. Bladder wash cytology may be useful only in high-risk patients recently treated with BCG or MMC topic therapy.


44

NO PROSTATE CANCER FOUND DURING ACTIVE SURVEILLANCE RE-BIOPSIES: ANALYSIS OF A SINGLE INSTITUTION POPULATION

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Introduction/Aim: A negative biopsy, which is absence of prostate cancer (PCa), during active surveillance (AS) follow-up, is likely a surrogate marker for extremely low-volume disease. For this reason we chose to examine a population of AS patients with negative biopsies and to evaluate possible differences between this selected subgroup and patients with positive re-biopsies. Materials and Methods: Patients enrolled in the Prostate cancer Research International: Active Surveillance (PRIAS) study and in the Institutional AS (SAINT) study were considered. Follow-up schedule combined prostate-specific antigen (PSA) and digital rectal examination (DRE) every 3 months for both protocols and re-biopsy following different time-schedules at 1, 4, 7, 10 years.
from diagnosis in PRIAS, while at 1 and 2 years and, then, every 2 years in SAINT. Association between negative biopsies during AS and diagnostic/clinical features was evaluated through Mann-Whitney and Chi-squared tests. A multivariable logistic model was developed to estimate the single patient probability of having negative biopsies after a PCa diagnosis. Results: Since March 2005, 725 patients were enrolled in AS; median and range values for clinical features were: age 65 years (42-80), iPSA 5.7 ng/ml (0.29-10), prostatic volume 46cc (13-201), PSA density (PSAD) 0.13 ng/ml/cc (0.01-0.88 ), 90% T1c, 64% patients had a single positive core at biopsy, percentage of maximum core involvement with PCa at diagnosis (maxperc) 10% (range=1-90). One thousand re-biopsies were performed in AS and 420/1000 (42%) were negative. We chose to focus on patients with at least 2 re-biopsies in AS (273 patients); 90/273 (32.97%) patients in this subgroup had a complete set of negative re-biopsies, i.e. no PCa found during AS, despite at least 2 biopic samplings. Median time and quartiles to last biopsy was 14.68 month (11.93-45.38), 48.3 for patients with all negative biopsy (38.1-51.75). The subgroup of patients with no PCa found during AS was characterized by lower PSAD (median=0.10 vs. 0.12 ng/ml/cc, p=0.03), larger prostate volumes (54 vs. 44 cc, p=0.002) and younger age (median=64 vs. 66 years, p=0.05). A trend towards less maxperc was also observed (5% vs. 10%, p=0.09), while iPSA, clinical stage and number of positive cores at diagnosis were not significantly different in the two groups. Distributions of significant variables are shown in Figure 1. Logistic multivariate model identified PSAD (odds ratio (OR)=0.95, p=0.06) and maxperc (OR=0.97, p=0.04) as the best predictors of having a complete set of negative re-biopsies, though with suboptimal discriminative power (area under the curve (AUC)=0.64). Conclusion: Analysis of a large cohort of patients highlighted that negative re-biopsies occur frequently in AS. The subgroup of patients with no PCa found during AS is characterized by low PSAD and low PCa involvement of diagnostic positive cores. These two variables can be considered as predictive of an extremely low-volume disease, though discrimination power is still not completely satisfying.
EARLY RECLASSIFICATION VS. LONG ACTIVE SURVEILLANCE: RESULTS FROM A SINGLE INSTITUTION POPULATION

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Aim: The aim of this analysis was to investigate differences in diagnostic/clinical characteristics between two groups of prostate cancer (PCa) patients enrolled in active surveillance (AS): patients experiencing an early PCa reclassification (defined as Gleason Pattern Score, GPS, upgrading ≤2 years from diagnosis) vs. the long AS patients (≥6 years in AS).

Materials and Methods: Patients enrolled in the Prostate cancer Research International: Active Surveillance (PRIAS) study and in the Institutional AS (SAINT) study were considered. Inclusion criteria for PRIAS are: iPSA≤10 ng/ml, prostate-specific antigen (PSA) density (PSAD)<0.2 ng/ml/cc, clinical stage (digital rectal examination (DRE)) T1c/T2a, GPS=6, maximum 2

Figure 1. Differences between early PCa reclassification and Long AS patients for PSA density (a), age (b), maximum percentage of PCa in positive bioptic cores (c) and prostate volume.
biopsy cores invaded with PCa. SAINT differs from PRIAS in: T1a and T1b can be included, % positive biopsy cores≤25%, maximum core length containing PCa (maxpos)≤50%, no cut-off in PSAD. Follow-up schedule combines PSA and DRE every 3 months for both protocols and re-biopsy following different time-schedules: at 1, 4, 7, 10 years from diagnosis in PRIAS, while at 1, 2 years from diagnosis and every 2 years in SAINT. Differences in patients’ characteristics between the two groups (early reclassification vs. long AS) were evaluated through Mann-Whitney and Chi-squared tests. A multivariate logistic model was proposed to estimate the probability of still being in AS, thus treatment-free, 6 years after PCa diagnosis.

**Results:** Between March 2005 and September 2015, 725 patients were enrolled in AS. 116 (16%) patients dropped out due to upgrading (GPS>6 at re-biopsy) within the first two years, while 60 patients (8.3%) were classified as long AS. The two populations were significantly different with respect to: median age (68 years vs. 63.5, p<0.001), PSAD (0.13 vs. 0.10 ng/ml/cc, range=0.02-0.3 vs. 0.03-0.2 ng/ml/cc, p<0.001), maxpos (10% vs. 5%, range=2%-60% vs. 2%-15%; p<0.001) and prostate volume (40cc vs. 51cc, range=18-85 vs. 14-120cc; p<0.001). The number of positive cores at diagnosis was statistically different in the two groups (p=0.03). Clinical stage and iPSA did not result in significant differences. Figure 1 shows the distribution of patients’ characteristics stratified in the two groups considered for this analysis. The multivariate model identified patients with low-PSAD (odds ratio (OR)=0.92, continuous variable), younger-age (OR=0.89, continuous variable), low percentage of PCa in positive bioptic cores (OR=0.93, continuous variable) and large prostate volume (OR=2.2, cut-off=50 cc) as having a high probability of still being in AS after 6 years, with an area under the curve (AUC)=0.82. **Conclusion:** Analysis of a large cohort of AS patients with long follow-up allowed identification of a set of diagnostic/clinical features that “protect” patients from an early reclassification. Specifically, younger patients, with low PSA density, high prostate volume and low involvement of their positive cores have a high probability of remaining in AS for a long time. This seems to confirm AS as a remarkably appropriate option for this subgroup of patients.

**Moderate Hypofractionated 3DCRT-IG vs. VMAT-IG for Localized Prostate Cancer: Comparison of Toxicity Outcome**

Alessandro Magli1, Caterina Fontanella2, Fabrizio Tonetto3, Giuseppe Parisi1, Margherita Crespi4, Eugenia Moretti4, Claudio Foti4, Paola Ermacora2, Cosimo Tamislao Sacco3, Gioacchino De Giorgi3, Barbara Grossetti5 and Gianluca Giannarini5

**Introduction/Aim:** The escalation dose in the treatment of prostate cancer with external beam radiation therapy has proved the winning way in the biochemical control of the tumor (1-3). However, the dose escalation to the whole prostate gland, which is considered as clinical target volume in external beam radiotherapy, is limited by the tolerance of the surrounding tissue. We have compared the toxicity profiles between patients treated with moderate hypofractionated 3-dimensional conformal radiotherapy (3D-CRT) collated with volumetric-modulated arc therapy (VMAT), both with image-guided radiotherapy (IGRT) by implanted fiducial markers in prostate gland (FM4). **Materials and Methods:** Between 2009 and 2011, 41 patients with prostate cancer were treated with 3DCRT-IG to a dose of 70 Gy, 2.5 Gy/fr, with daily online correction of the target position based on MV/MV. This group of patients was compared to a similar cohort of 39 patients who were treated between 2012 and 2014 with VMAT-IG to the same prescription dose with daily online correction of the target position based on MV/KV imaging. The clinical characteristics of these two patient populations are shown in Table I. The Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer late morbidity (RTOG/EORTC) scores were used for acute and late effects. The median follow-up time was 3 years (range=1-6). The rectal and bladder dose parameters were also included in the statistical analysis. **Results:** The rectal acute and late toxicity was low for both treatment groups and no significant reduction was observed for VMAT-IG patients compared with the 3DCRT-IG patients (p=0.33). The likelihood of acute genitourinary toxicity for the VMAT-IG and 3DCRT-IG cohorts was 14.5% and 18.0%, respectively (p=0.61). Only for grade ≥2 acute genitourinary toxicity, the analyses showed a better, but non-significant, trend on behalf of VMAT-IG (p=0.09). Finally, no significant correlation was observed between the dose parameters and genitourinary and rectal late toxicity. The prostate-specific antigen (PSA) relapse-free survival in accordance to Phoenix criteria (nadir plus 2 ng/ml) for 3DCRT and VMAT were similar (98% vs. 96%; p=0.34). **Conclusion:** Moderate hypofractionated IGRT is associated with a lower rate of genitourinary and rectal toxicity for both treatment 3D-CRT and VMAT. These data suggest that the placement of fiducial markers and daily online correction of target positioning may represent the preferred mode of external-beam radiotherapy delivery for patients treated by definitive radiotherapy.


Table I. Patients’ characteristics.

<table>
<thead>
<tr>
<th>Patient demographics</th>
<th>3DCRT-IG</th>
<th>IMRT-IG</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Pretreatment PSA (ng/mL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>32 (82)</td>
<td>30 (73)</td>
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<td>10-20</td>
<td>4 (10)</td>
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<td>&gt;10</td>
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<td>0</td>
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<tr>
<td>Total Gleason Score</td>
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<td></td>
</tr>
<tr>
<td>&lt;7</td>
<td>11 (28)</td>
<td>13 (31)</td>
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<tr>
<td>7</td>
<td>54 (49)</td>
<td>69 (69)</td>
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<tr>
<td>&gt;7</td>
<td>18 (18)</td>
<td>0</td>
</tr>
<tr>
<td>T stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1c-T2a</td>
<td>25 (64)</td>
<td>28 (68)</td>
</tr>
<tr>
<td>T2b</td>
<td>10 (26)</td>
<td>17 (17)</td>
</tr>
<tr>
<td>&gt;T2b</td>
<td>10 (10)</td>
<td>15 (15)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70</td>
<td>11 (28)</td>
<td>37 (37)</td>
</tr>
<tr>
<td>&gt;70</td>
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<td>28 (62)</td>
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<td>NCCN risk</td>
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<td>Low</td>
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<td>0</td>
</tr>
<tr>
<td>Intermediate</td>
<td>56 (56)</td>
<td>100 (100)</td>
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<tr>
<td>High</td>
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<td>0</td>
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<tr>
<td>Neoadjuvant ADT</td>
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</tr>
<tr>
<td>Yes</td>
<td>82 (82)</td>
<td>90 (90)</td>
</tr>
<tr>
<td>No</td>
<td>18 (18)</td>
<td>10 (10)</td>
</tr>
</tbody>
</table>

ADT, androgen deprivation therapy; NCCN, National Comprehensive Cancer Network; PSA, prostate-specific antigen.

Introduction: Prostate biopsy is a fundamental tool for monitoring prostate cancer during active surveillance (AS), with biopsy findings (upgrading and upsizing) being the major cause of AS drop-out. There is a shared awareness that repeated biopsies could lead to increase in occurrence of biopsy-driven complications. This is why search for non-invasive AS follow-up tools (i.e. biomarkers or magnetic resonance imaging (MRI)) is one on the main open issues, with the final aim of limiting the number of repeated biopsies. Therefore, the aim of this study was to objectively describe the presence and nature of biopsy-driven complications as assessed by a patient reported (PRO) questionnaire.

Materials and Methods: Patients were enrolled in two different AS protocols: the international PRIAS study and the institutional SAINT study. PRIAS patients underwent re-biopsy after 1, 4 and 7 years from the diagnostic one, while SAINT patients after 1, 2, 4 and 6 years from diagnosis. AS patients completed a patient reported (PRO) questionnaire on biopsy-driven complications. Morbidities considered were: infection (body temperature>38°C), rectal bleeding, haematuria, haemospermia, pain and urinary retention. For all these possible events, a severity grade was registered: mild (i.e. requiring administration of drugs), moderate (needing specific procedure) and severe (hospitalization). Patients’ features associated with no/mild complications (NOTOX) and with moderate/severe complications (TOX) were evaluated through Mann-Whitney and Chi-squared tests.

Results: Between Oct 2014 and Nov 2015, 125 patients completed the PRO questionnaire after their re-biopsy. 11/125 patients (9%) reported no morbidity, while mild, moderate and severe complication were registered in 12 (9.6%), 7 (5.6%) and 4 patients (3%), respectively. Severe morbidity was related to infection (2 patients), rectal bleeding+haematuria+haemospermia (1 patient) and prostatitis (1 patient). Figure 1.
shows the distributions of reported biopsy-driven complications. 28% of patients reported one single complication, 30%, 21% and 12% described 2, 3 and 4 concomitant morbidities, respectively. Median age was higher in the TOX group (65 vs. 68 years, \( p = 0.04 \)) as shown in Figure 2. Although not statistically significant, Charlson Index showed a trend towards higher values in TOX patients (mean values 1.5 vs. 1.9, \( p = 0.13 \)). BMI, number of total core and number of previous biopsies were not significantly different in TOX and NOTOX groups. Conclusion: PRO questionnaire allowed prospective, not biased registration of mild to severe complications. Severe biopsy-driven complication occurred in a low percentage of patients; nevertheless, due to the high number of re-biopsies, which are performed in AS programs, search for tools of non-invasive follow-up seems to be highly justified. Repeated biopsies might have a more prominent negative impact on the older population and in patients with multiple comorbidities. This subgroup of patients might benefit from a more precautionary policy for use of biopsies during AS follow-up.

51
THREE-DIMENSIONAL ULTRASOUND-BASED IMAGE-GUIDED HYPOFRACTIONATED RADIOThERAPy IN PROSTATE CANCER PATIENTS

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Introduction/Aim: External beam radiotherapy (EBRT) is a mainstay therapeutic option for prostate cancer. Given the lower \( \alpha/\beta \) ratio of prostate cancer compared to surrounding normal tissues, hypofractionated schedules were proposed as a suitable approach. Recent technological advances allowed for a safe delivery of high dose hypofractionated EBRT. Image guidance procedures are strongly needed to provide ballistic precision, minimize geometric uncertainties and further diminishing unintended normal tissue irradiation. The Clarity Platform allows for the acquisition of three-dimensional ultrasound scans (3D-US) of the pelvic region to perform image-guided radiotherapy. Materials and Methods: Patients affected with organ-confined prostate cancer were included. All patients should have a reliable ultrasound visualization of the prostate gland within the Clarity Platform. All patients received 62.1 Gy/23 fractions to the prostate gland and seminal vesicles; a subsequent boost of 8.1 Gy in 3 fractions was delivered sequentially to the only prostate gland up to a total dose of 70.2 Gy/26 fractions. The Clarity system is made of two separate platforms, in the computed tomography (CT) and treatment room. After CT scan, a free hand axial sweep is acquired. During each treatment session, a free-hand axial sweep is acquired and the treatment positioning reference volume (PRV) is aligned with the reference PRV. When the alignment is ideal, the system takes into account any final target displacements. The whole procedure takes only few minutes. Results: A total of 186 prostate cancer patients were treated between January 2009 and June 2015 with a hypofractionated schedule (70.2 Gy/26 fractions) under 3D-US guidance with the Clarity Platform. Median follow-up was 32 months. Patients had a mean age of 71.5 years and a prostate-specific antigen (PSA) mean level of 9 ng/ml, with a Gleason Score of 7 in 101 patients. Nine patients experienced biochemical failure. Among them, six patients also went into distant spread with bone lesions. Only two patients died of disease, while other five died of other
causes. Cancer-specific and overall survival were 99.05% (confidence interval (CI)=98.1-100%) and 95.2% (CI=88.7-97.8%), respectively. Maximum detected acute genitourinary (GU) toxicity was G0 in 23.8% of patients, G1 in 47.6%, G2 in 23.5%, G3 in 3.4%, G4 in 0.7%. Maximum detected acute gastrointestinal (GI) toxicity was G0 in 59.4% of patients, G1 in 30.8%, G2 in 13%, G3 in 1%. The actuarial rates of ≥G2 late toxicities were 4% for GU and 5.4% for GI. Conclusion: Three-dimensional ultrasound-based image-guided hypofractionated radiotherapy resulted in being robust and reliable providing excellent imaging of prostate gland. EBRT delivered, employing a hypofractionated schedule under 3D-US-based image guidance, is a safe and effective treatment with optimal biochemical control and a good toxicity profile. Nowadays we are working with Autoscan probe to also evaluate intra-fraction motion for severe hypofractionation.

53 EVALUATION OF FUNCTIONAL OUTCOMES AFTER LAPAROSCOPIC PARTIAL NEPHRECTOMY: THE ROLE OF RENAL SCANNING IN THE COMPARISON BETWEEN CLAMPLESS TECHNIQUE AND CLAMPING OF RENAL ARTERY

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Introduction/Aim: The ischemic damage produced by clamping the renal artery during partial nephrectomy can influence the post-operative renal function. Aim of this study was to evaluate post-operative renal function by renal scanning, considering laparoscopic partial nephrectomies performed with clampless technique (cl-LPN) and with standard renal artery clamping (st-NPL). Moreover, we attempted to identify which factors could be predictive for worse post-operative functional outcomes without the influence of ischemia. Patients and Methods: Between November 2011 and December 2014, all patients with a renal mass suitable for LPN were enrolled in this study. A pre-operative evaluation of renal function by serum creatinine (SCr), estimated glomerular filtration rate (eGFR) and renal scanning parameters (split renal function (SRF) and estimated renal plasma flow (ERPF)) was performed. All patients with solitary kidney or abnormal baseline renal function were excluded. The population study was then divided in two groups according to the type of procedure performed: patients who underwent st-LPN and cl-LPN were enrolled in Group A and Group B, respectively. For each cohort, demographic, perioperative and pathological variables were evaluated. The functional variables (SCr and eGFR) were completed with the determination of split renal function (SRF) and effective renal plasma flow (ERPF) 3 months after surgery to better quantify the functional loss of the treated kidney. A multivariate analysis on the Group B was then performed to evaluate which factors, except for the ischemia-induced damage, could influence the post-operative functional outcomes. Results: 172 patients were enrolled in the present study: 86 of them were included in Group A and the other 86 in the Group B. No differences were found between the groups in terms of demographic, perioperative and pathological variables except for warm ischemia time (WIT) (19.6±7.3 min in the Group A and 0 min in the Group B, p=0.001) and estimated blood losses (214.7±221.7 and 252.3±224.3 ml in Group A and B respectively, p=0.01). No differences were found in terms of loss of renal function in the operated kidney between the two groups, with reductions of 6.4±1.1% and 9.2±1.3% for the SRF (p=0.236) and of 11.3±22.6% and 21.4±17.6% for the ERPF (p=0.081), in group B and A, respectively. The multivariate analysis in the group B highlighted that poorer pre-operative SRF and ERPF are related with worse post-operative functional results. Conclusion: This analysis demonstrates that the management of renal pedicle during LPN (clampless vs. renal artery clamping technique) does not influence the post-operative renal function, especially with ischemia times <25 min. The factors that play a role in the worsening of post-operative functional outcomes, excluding the WIT, seem to be related with a baseline poor renal function. This should be taken in consideration pre-operatively for the choice of the most appropriate surgical management.

54 LAPAROSCOPIC PARTIAL NEPHRECTOMY FOR T1 RENAL MASSES: RESULTS OF MORE THAN 500 CASES IN A TERTIARY LAPAROSCOPIC CENTER

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Introduction/Aim: In the last twenty years, partial nephrectomy has become the gold standard treatment in the management of T1 renal tumors. Aim of this study was to evaluate perioperative, pathological and early functional outcomes of patients treated with laparoscopic partial nephrectomy (LPN) for T1 renal tumors. Materials and Methods: All patients who underwent LPN between 06/2000 and 03/2015 were enrolled
in this study and analyzed retrospectively. All surgical procedures were performed by the same surgeon. Demographics’ variables, such as gender, age, body mass index (BMI) and comorbidity (classified by Charlson Comorbidity Index (CCI)) were evaluated; pre-operative variables, such as side, size and surgical complexity of the lesion (classified by PADUA score), perioperative variables like blood losses, intra- and post-operative complications (classified by Clavien-Dindo system) and hospital stay were considered. Concerning pathological variables, histology and positive surgical margins’ rate were analyzed. Functional outcomes like serum creatinine (SCr) and estimated glomerular filtration rate (eGFR) were evaluated preoperatively and at discharge. 

**Results:** 502 patients were included in the present study: 340 of them (67.7%) were males with a mean age of 61±12.7 years, mean BMI of 26.3±5.1 and mean CCI of 0.8±1.3. Lesions were right-sided in 51.4% (258/502), with a mean size of 36.2±18.6 mm and a mean PADUA score of 7.8±0.6. Twenty-six patients (5.2%) had solitary kidney. Concerning perioperative variables, mean operative time was 115.6±40.1 min, with mean blood losses of 202.1±224.6 ml. Mean ischemia time was 21.9±12.0 min. and 30.6% (154/502) of the procedures were performed without clamping of renal artery. Intraoperative complications rate was 1.8% (9/502). The rate of post-operative complications was 9.3% (47/502), with Clavien >3 in 9 patients only. Mean hospital stay was 6±4 days. Concerning pathological findings, 94 lesions (18.7%) were benign, while 408 malignant (81.3%, with 106 papillary and with 245 clear cells carcinoma). Positive surgical margin rate was 2.7% (14/502). No differences were found in terms of SCr and eGFR between pre-operative and post-operative (at discharge) evaluation (SCr: 0.97±0.2 vs. 1.07±0.4; GFR: 86.5±20.8 vs. 80.0±21.9 respectively).

**Conclusion:** The present study highlights that LPN, if performed by experienced hands, could be the best approach in nephron-sparing surgery management. Indeed, the laparoscopic approach guarantees great post-operative and functional outcomes with short ischemia times (<25 min), minimal impairment of renal function, low complications rate and good oncological outcomes.

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**55**

**ONE YEAR FOLLOW-UP AFTER RADICAL PROSTATECTOMY IN AN HIGH-RISK PROSTATE CANCER POPULATION: A FIRST REPORT OF [-2]proPSA **VERSUS** ULTRASENSITIVE PSA FLUCTUATIONS OVER TIME**

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**Aim:** To investigate the fluctuations over time for [-2]proPSA vs. ultrasensitive prostate-specific antigen (PSA) (uPSA) and their possible clinical/pathological determinants, in the first year from radical prostatectomy (RP). 

**Patients and Methods:** A prospective cohort of 106 consecutive patients, undergone RP for high-risk prostate cancer (pT3/pT4 and/or positive margins), was enrolled. No patient received pre-operative or post-operative androgen deprivation therapy or immediate adjuvant radiotherapy (RT); the latter for patient choice. [-2]proPSA and uPSA were measured at 1, 3, 6, 9 and 12 months after surgery. The trends over time and their modifications by clinical and pathological covariates were estimated by the mixed-effects linear model. The uPSA relapse was defined as 3 rising uPSA values after nadir and by two consecutive uPSA >0.2 ng/ml after RP. 

**Results:** The rate of biochemical recurrence (BCR) at one year from RP was either 38.6% (using BCR definition of three rising uPSA values) or 34.9% (using BCR definition of uPSA >0.2 ng/ml after nadir). The main risk factors for uPSA fluctuations were PSA at diagnosis (p=0.014), pT (p=0.038) and pN staging (p=0.001); [-2]proPSA time trend was modified by PSA pre-RP (p=0.012) and pN (p<0.001). In 39 patients, uPSA decreased from month 1 to 3, while [-2]proPSA increased in even 90% of them; in further follow-up, both uPSA and [-2]proPSA increased in almost all cases. The [-2]proPSA time trend was independent from BCR status in the whole cohort, as well in the 39 men subgroup. 

**Conclusion:** Both uPSA and [-2]proPSA showed clear fluctuations over time, with an independent pattern. PSA at diagnosis and pathological staging significantly modified both these trends. Since BCR was not confirmed as a modifier of [-2]proPSA time trend, the use of [-2]proPSA as marker of an early biochemical relapse may not be actually recommended among high-risk prostate cancer patients.

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**57**

**PROSTATE CANCER DETECTION WITH A RIGID SYSTEM FOR MRI/TRUS SOFTWARE-BASED TARGETED BIOPSY: OUR EXPERIENCE**

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2580
Introduction/Aim: A more accurate and safe diagnosis and reliable staging of prostate cancer (PCa) are essential to carry out the best treatment for each patient. With development of targeted biopsies, urologists have achieved encouraging results in the diagnosis of clinically significant (CS) PCa. Fusion biopsy (FB), with a software capable to co-record magnetic resonance imaging (MRI) and transrectal ultrasound (TRUS), is emerging as a fast, effective and safe way to perform targeted biopsies. Aim of our study was to report our initial experience on rigid MRI/TRUS fusion software-based targeted biopsy.

Patients and Methods: Patients with suspicion of PCa and the presence of one or more suspicious areas on MRI were enrolled in this prospective study (05/2014 to 09/2015). With MRI that consisted of T2-weighted, diffusion-weighted and dynamic contrast-enhanced imaging, all lesions were classified according to PIRADS system. All patients were subjected to FB using the Biojet® system, performing at least 3 samples for suspected lesion. Naïve patients were also subjected to a transrectal standard mapping (SM) with 12 cores. All radiologic and pathologic data and complications were recorded. PCa was considered CS according to START consortium definition (for FB) and Epstein criteria (for SM).

Results: The study population consisted of 316 patients. Mean age was 64.2±7.5 years; mean PSA was 8.3±5.6 ng/ml. Transrectal and transperineal approach was carried out in 67.2% and 32.8%, respectively. 194 (61.4%) patients were previously submitted to prostate biopsy. PCa diagnosis was obtained in 58.1% of patients, of which 71.6% had a CS PCa. Biopsy Gleason Score (GS) was: GS 6 in 16.4%, GS 7 (3+4) in 52.3%, GS 7 (4+3) in 29.1%, GS>8 in 2.2% of cases. Evaluating the results of only FB, PCa detection rate was equal to 56.9%, of which 74.8% CS PCa, while the detection rate for lesions classified on MRI as PIRADS≥3 was 75.1%. Among naïve patients, in 5 patients (1.6%) PCa was detected by SM only (all insignificant PCa). Finally, 107 patients who were diagnosed with PCa by FB (33.8%) underwent radical prostatectomy. The concordance between biopsy and pathological GS in these patients was 97.2%. Regarding complications, we registered a rate of 11.7% of mild hematuria and two cases (0.6%, both underwent FB+SM) of febrile urinary tract infection (UTI) that required hospitalization.

Conclusion: In our series, which were similarly represented, both naïve patients and those undergone previous biopsies and using both approaches (transrectal and transperineal) seem to justify the use of FB as a result of the high detection rate, especially in CS PCa. SM does not add information to the diagnosis of PCa, according to the most recent literature. FB seems to guarantee a high detection rate of CS PCa with a reasonable rate of complications. Furthermore, it allows obtaining biopsy samples representative of GS pathology.

58 HIGH/VERY HIGH-RISK AND OLIGOMETASTATIC PROSTATE CANCER PATIENTS TREATED BY TOMOTHERAPY AND ANDROGEN DEPRIVATION: LONG TERM RESULTS

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Introduction: Pelvic irradiation and irradiation of oligometastases in prostate cancer patients is a controversial topic and, to date, there are not conclusive data. Modern imaging, as multiparametric- magnetic resonance (MRI) and choline-positron emission tomography (PET) can allow a better staging of disease and allow guiding the radiotherapy treatment. Patients and Methods: Between October 2010 and October 2014, 108 patients staged as high/very high-risk prostate cancer, were treated using a moderate hypofractionation scheme by an intensity-modulated simultaneous integrated boost and image-guided (IMRT-SIB-IGRT) technique with Tomotherapy Hi-Art and HD Systems. Patients were staged by MRI, bone scan and PET in suspected nodal metastases. 23 patients had nodal metastases (21%) showed by PET, 6 of which in lumbar-aortic site. 7 patients had also a single bone metastasis (6%). Considering a mean α/β ratio of 3 for prostate cancer, the prescribed doses were: 75.2 Gy in 32 fractions of 2.35 Gy per fraction (equivalent dose (EQD2)=80.5 Gy) on the prostate gland; between 67.2 Gy and 75.2 Gy in 32 fraction of 2.1 (EQD2=70 Gy) or 2.35 Gy (EQD2=80.5 Gy) on the seminal vesicles; between 60 and 70.4 Gy in 32 fractions of 2-2.2 Gy on the positive nodes; 54.4 Gy in 32 fractions of 1.7 Gy (EQD2=51.2 Gy) on the prophyllactic pelvic and lumbar-aortic volumes (when required); 54.4 Gy/32 fractions of 1.7 Gy (EQD2=51.2 Gy) on single bone metastasis when present. In 101 patients, a long-term androgen deprivation therapy (ADT) was applied with anti-androgen for 1 month and a luteinizing hormone-releasing hormone (LHRH) analogue (in neoadjuvant, concomitant and adjuvant way).
Results: Ninety-eight patients were evaluated for late toxicity and outcome. Eighty patients were lost at follow-up. With an average follow-up of 37.5 months (range=12-60), the severe late toxicity (≥G3) was: genitourinary 1.2% (1 patient), gastrointestinal 3% (3 patients). At last follow-up, 27 patients were still receiving ADT. Ten percent of patients (10) had progression disease in nodes or bone sites. One patient died due to progression disease. Two patients had a second primary tumor (in the lung). 87% of patients (85) were alive without evidence of disease. Conclusion: Radiotherapy performed by Tomotherapy, on extensive volumes, as pelvic and lumbar-aortic sites, is safe in our experience and allows an escalated dose without severe late toxicity and with a satisfactory outcome. Our experience is consolidated by a sufficiently long follow-up and the long-term result can be considered as excellent. This paper is supported by the 5%1000 2008 Ministero della Salute-FPRC Onlus and 5 per Mille 2009 Ministero della Salute-FPRC Onlus.

59 PROSTATE CANCER DETECTION WITH MULTIPARAMETRIC MRI: IS THERE A DIFFERENCE BETWEEN THE 32-CHANNEL "PHASED-ARRAY" AND THE "DUAL-COIL" MRI?

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Introduction/Aim: The prostatic multiparametric-magnetic resonance imaging (mp-MRI) has grown rapidly and is increasingly used in clinical practice for the diagnosis of prostate cancer (PCa). Currently, concerning 1.5T MRI scans, the most effective method for diagnosis involves the use of a double coil (abdominal and endorectal), with a technique called "dual coil" allowing a better spatial and contrast resolution. Recently, the use of a MRI scan with a surface coil with 32-channel digital technology allowed a study of the pelvis with high spatial and contrast resolution, with the advantage of not using an endorectal coil, thus reducing discomfort for the patient. The aim of the study was to report the preliminary results of the comparison between 32-channel phased-array mp-MRI (PA-MRI) and 4+1-channel dual coil mp-MRI (DC-MRI) in terms of PCa detection and local stadiation. Patients and Methods: After Ethics Committee approval, 29 patients with biopsy diagnosis of PCa were enrolled in a prospective observational cohort study. All patients underwent, prior to radical prostatectomy, two 1.5T mp-MRI scans (PA-MRI and DC-MRI) at two different radiology departments, performed by experienced uro-radiologists blinded to each other’s results. The MRI consisted of T2-weighted, diffusion-weighted and dynamic contrast-enhanced imaging. The results of the PA-MRI and DC-MRI studies were compared using whole-mount histological sections after prostatectomy, performed by an experienced pathologist, as the reference standard. The comparison was performed using the McNemar test, while the Kappa Cohen coefficient was calculated both for PCa detection and local staging. Results: 29 consecutive patients were included in the study. Median age was 69 (46-74) years. 15 patients had confined PCa: 2 patients had stage T2a (6.9%) and 13 T2c (44.8%) PCa. 14 patients had extraprostatic disease: 12 had stage T3a (41.4%) and 2 stage T3b (6.9%) PCa. Overall, 44 lesions were detected in whole-mount histological sections. 34 lesions were detected with PA-MRI and 33 lesions with DC-MRI. Both approaches did not diagnose 8 lesions, all of them with a volume <1% and a Gleason Score of 6. The positive predictive value and sensitivity for PCa detection were, respectively, 87.2% and 77.2% for PA-MRI and 86.8% and 75.0% for DC-MRI. Concerning PCa detection, the correlation between the two methods was significant with a Cohen’s Kappa coefficient of 0.38 (confidence interval (CI)=0.10-0.65). The accuracy, sensitivity and specificity for PCa local staging were the same for the two methods: 82.7%, 92.8% and 73.3%, respectively. Concerning PCa local staging, the correlation between the different methods was very high with a Cohen’s Kappa coefficient of 0.85 (CI=0.66-1.00). A limitation of this preliminary study was certainly represented by the small number of the sample. Conclusion: Our preliminary results suggested that both PA-MRI and DC-MRI seem accurate in terms of PCa diagnosis and local stadiation. Further investigations in a larger series are needed.

60 CYBERKNIFE STEREOTACTIC RADIOTHERAPY FOR ISOLATED RECURRENCE IN THE PROSTATIC BED

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Introduction/Aim: Radiotherapy is the mainstay of locoregional treatment in limited sites of relapse and
usually performed with the use of stereotactic radiotherapy (SRT) (1). In fact, this technique allows the delivery of high tumor ablative doses to small target lesions, with low toxicity (2). Stereotactic body radiation therapy (SBRT) can be performed using many different technologies. We aim to report a clinical experience of SBRT with CyberKnife for isolated recurrence in the prostatic bed from prostate cancer. 

Materials and Methods: Between November 2011 and November 2013, 16 patients were treated with SBRT for a macroscopic isolated recurrence of prostate cancer in the prostatic bed. The mean age at primary diagnosis was 64.9 years (range=52-78). All patients were initially treated with radical prostatectomy and half of them also received radiotherapy. Only five patients received an adjuvant hormonal therapy. Mean prostate-specific antigen (PSA) at relapse was 4.1 ng/ml (range=0.5-11.09). Two schedules of SBRT were used: 30 Gy in 5 fractions in previously irradiated patients, 35 Gy in 5 fractions in radiotherapy-naïve patients. After treatment, complete response (CR) was defined as no visible gross tumor, partial response (PR) as at least a 30 % decrease, progressive disease (PD) as at least a 20 % increase and stable disease (SD) as neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, according to RECIST. Local control was evaluated on computed tomography/magnetic resonance (CT/MR) imaging at 3 months after treatment and every 3 months afterward. Acute and late toxicities were evaluated according to NCI Common Terminology Criteria for Adverse Events (CTCAE version 4.0). 

Results: At a median follow-up of 10 months (range=2-21), a significant biochemical response was found in all but one patient; ten patients (62.5%) had an almost negativized PSA nadir. At the imaging evaluation, no local progression was noted: 10 patients showed PR, while six SD. Nine patients performed also a [11C]-choline positron emission tomography (PET), which showed a complete metabolic response in all cases. At the moment of analysis, all 16 patients were alive. Seven of them developed distant relapse (median time to distant relapse=9.3 months), while nine maintained biochemical control, without further therapy. The treatment was well-tolerated: one patient experienced G2 acute genitourinary and gastrointestinal toxicity. Late toxicity was evaluated in patients with more than 3 months of follow-up and no late toxicity was reported. 

Conclusion: Our experience shows that SBRT is an appealing non-surgical salvage treatment for selected patients with prostate cancer, experiencing isolated macroscopic relapse in the prostatic bed, with potential for long-term disease remission. More data, possibly coming from larger series, are necessary, while the optimal combination of this local therapy with systemic treatments is still lacking.

61 STEREOTACTIC RADIOTHERAPY FOR ISOLATED NODAL RECURRENCE OF PROSTATE CANCER

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Aim: To report a clinical experience in stereotactic body radiation therapy (SBRT) for isolated nodal metastases from prostate cancer. 

Materials and Methods: Between November 2011 and December 2013, 30 patients (39 lesions) were treated with SBRT, delivered using CyberKnife, for recurrent prostate cancer with isolated nodal metastases. Prescribed doses and schedules of fractionation varied, ranging from 24 Gy in 1 fraction to 36 Gy in 3 fractions. Most commonly used schedules were 30 Gy in 3 fractions and 36 in Gy in 3 fractions on alternate days. Biochemical response, acute and late toxicity were analyzed. 

Results: At a median follow-up of 12 months (range=2-24.9), a significant reduction of prostate-specific antigen (PSA) was observed in 24 cases, while PSA was stable in 1 case and augmented in 9 cases. At the time of analysis, among the 30 patients treated, two were dead from systemic disease; 12 patients experienced a relapse of disease in other sites. Sixteen patients were still free of disease. In 24 cases, imaging evaluation 3 months after treatment was available. No in-field recurrence was detected. SBRT was well-tolerated: One patient experienced G2 acute genitourinary toxicity. Late toxicity was evaluated in patients with more than 6 months of follow-up and only one complained G1 proctitis. We did not observe any acute or late severe toxicity (≥G3). 

Conclusion: Our experience shows that SBRT for isolated nodal relapse from prostate cancer is a safe treatment, with promising results in terms of efficacy.

62 STANDARD PROSTATE BIOPSY VS. NEW DIAGNOSTIC PATH WITH MRI AND FUSION BIOPSY: PRELIMINARY RESULTS OF A PROSPECTIVE RANDOMIZED STUDY
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Divisions of 1Urology, 2Pathology and 4Radiology San Luigi Gonzaga Hospital (University of Turin), Orbassano (TO), Italy; 3Division of Radiology, Candiolo Cancer Institute, Candiolo (TO), Italy; 5Division of Radiology, Mauriziano Hospital, Torino, Italy

Introduction/Aim: Nowadays, in the suspicion of prostate cancer (PCa), the patient undergoes a prostate biopsy with multiple samples using a standardized template (standard biopsy (SB)). Many of these samples are unnecessary and reveal "indolent" tumors. With the introduction of novel approaches, prostatic multiparametric magnetic resonance imaging (mp-MRI) can be performed on targeted biopsies with a software capable of co-record MRI and transrectal ultrasound (TRUS) (fusion biopsy (FB)), with the aim of reducing the number of biopsy samples and increasing performance. The primary objective of this randomized, prospective, two-arm study was to evaluate the efficacy of a new diagnostic path based on MRI and FB, compared to diagnostic standard.

Patients and Methods: After approval of the local Ethics Committee, all naive patients suspected for prostate cancer (prostate-specific antigen (PSA) <15 ng/ml and negative digital rectal examination (DRE)) were randomized into 2 groups using a computer-generated random allocation in a 1:1 ratio: Arm A (undergoing MRI) and arm B (not undergoing MRI). With the MRI study that consisted of T2-weighted, diffusion-weighted and dynamic contrast-enhanced imaging, all lesions were classified according to PIRADS system. The patients were then biopsied as follows: Arm A with positive mp-MRI (PIRADS score≥3): MRI/TRUS fusion software-based targeted biopsy using the Biojet® system, performing at least 3 samples for suspected lesion; Arm A with negative mp-MRI or lesion of low suspicion (PIRADS score <3) and arm B: transrectal TRUS-guided SB with 12 samples. PCa was considered clinically significant (CS) according to START consortium definition (for FB) and Epstein criteria (for SB). Results: As summarized in Table I, during the period 11/2014 to 09/2015, 122 patients were enrolled. Median age was 64 (49-75) years and mean PSA was 6.9 (±3.6) ng/ml. The demographic characteristics of patients in both arms and in the subgroups in arm A were comparable. Table I shows the preliminary results. Conclusion: In our study, the detection rate of FB was significantly higher than SB with a significantly lower mean number of samples. These results are even more significant considering CS PCa. In patients in Arm A submitted to SB, the probability of finding a PCa was minimal and none CS PCa was revealed. Although it is necessary to extend the series, this new diagnostic path, based on MRI and FB technique, seems to be safer and more effective than the standard one.

### Table I. Patients’ characteristics and results archived in the two arms of the study.

<table>
<thead>
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<th>Patients</th>
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<th>PCa</th>
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<th>Proportion of positive cores</th>
<th>CS PCa</th>
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<td>N°(%); cores % mean (SD)</td>
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63 LINAC-BASED EXTREME HYPOFRACTIONATION FOR LOCALIZED PROSTATE CANCER WITH VOLUMETRIC MODULATED RADIATION THERAPY: PRELIMINARY REPORT OF A PHASE II STUDY

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Introduction/Aim: Extreme hypofractionation, also called stereotactic body radiation therapy (SBRT), in prostate cancer (PC) is a promising radiation treatment that delivers highly conformal dose in few fractions, typically 4 to 5 fractions. The aim of the present preliminary analysis of a phase-II prospective study was to evaluate the feasibility and preliminary side effects of SBRT in a cohort of localized PC...
patients. Patients and Methods. The study, approved by the Ethical Committee, started on January 2014. Inclusion criteria were: age inferior or equal to 80 years, World Health Organization performance status inferior or equal to 2, histologically proven prostate adenocarcinoma, low-/intermediate-risk according to D'Amico criteria, no distant metastases, no previous surgery other than transurethral resection of the prostate (TURP), no other malignant tumor in the previous 5 years, a pre-SBRT International Prostate Symptoms Score (IPSS) ranging between 0 and 7. The SBRT schedule was 35 Gy for low risk and 37.5 Gy for intermediate-risk PC in 5 fractions, delivered in consecutive days. SBRT was delivered with volumetric-modulated radiation therapy (VMAT). Toxicity assessment was performed according to CTCAE v4.0 scale. Neoadjuvant/concomitant hormonal therapy was prescribed according to risk classification. Results: At the time of analysis, forty-two patients were recruited in the protocol and treated. Median age was 74 years (63-80) and median follow-up was 16 months (range=4-24). According to risk-category, 31/42 patients were low-risk and 11/42 were intermediate-risk. Median initial prostate-specific antigen (PSA) was 6.1 ng/ml (range=3.4-12.8 ng/ml). Median Gleason score was 6 (6-7). IPSS pre-SBRT was registered for all patients, with a median value of 4 (range=0-10). All patients completed the treatment as planned. Acute genitourinary (GU) toxicity was: G0 29/42, G1 7/42, G2 6/42. Acute gastrointestinal (GI) toxicity was: G0 36/42, G1 4/42, G2 2/42. No acute toxicities superior or equal to G3 were recorded. Late GU and GI toxicities were mild without severe events: GU-G0 39/42, GU-G1 2/42, GU-G2 1/42; GI-G0 40/42, GI-G1 2/42. At one-year of follow-up, IPSS was recorded in 25/42 patients with a median value of 4.5 (range=0-18). At the time of analysis, biochemical control was 100%. Conclusion: Preliminary analysis of this SBRT phase-II prospective study for low-/intermediate-risk PC proved to be feasible and tolerable. Longer follow-up is needed to assess late toxicity profiles and clinical outcomes.

**Validation of PIRADS Classification System Through MRI/TRUS Fusion Software-Based Targeted Biopsy**

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**Introduction/Aim:** A more accurate and safe diagnosis and reliable staging of prostate cancer (PCas) are essential to carry out the best treatment for each patient. Multiparametric magnetic resonance imaging (mp-MRI) of the prostate is a non-invasive diagnostic tool with high sensitivity and specificity for prostate cancer. MRI/transrectal ultrasound (TRUS) fusion biopsies (FB) can enhance the detection of significant disease. Aim of this study is to correlate the level of suspicion on MRI with pathologic findings after FB. **Patients and Methods:** Patients with suspicion of PCa and the presence of one or more suspicious areas on MRI were enrolled in this prospective study (05/2014 to 09/2015). MRI consisted of T2-weighted, diffusion-weighted and dynamic contrast-enhanced imaging and all lesions were classified according to PIRADS system. All patients were subjected to FB using the Biojet® system, performing at least 3 samples for suspected lesion. Naïve patients were also subjected to a transrectal standard mapping (SM) with 12 cores. All radiologic and pathologic data, as well as complications were recorded. PCas were considered clinically significant (CS) according to START consortium definition (for FB) and Epstein criteria (for SM). **Results:** The study population consisted of 316 patients. Mean age was 64.2±7.5 years; mean PSA was 8.3±5.6 ng/ml. Transrectal and transperineal approach was carried out in 67.2% and 32.8% of patients, respectively. 194 (61.4%) patients were previously submitted to prostate biopsy. Detection rate split for PIRADS and prostatic area was reported in Table I. There were no differences between groups, considering lesion size (p>0.05). A statistical difference between PIRADS 3 lesions in comparison to PIRADS 4 and 5 (p=0.007 and <0.0001, respectively) was highlighted. Subdividing PIRADS 3 lesions for anatomical area, there were no statistical differences between peripheral PIRADS 3 with PIRADS 4 or 5 (p>0.05) in contrast to central PIRADS 3 (p=0.001 and <0.0001, respectively). **Conclusion:** The preliminary results of this study confirm the high diagnostic accuracy of MRI and FB technique. Besides, lesions classified by radiologists as PIRADS 4 and 5 were very frequently tumors and should, therefore, be subject to biopsy. Lesions with a PIRADS score of 1 or 2 should not be considered for FB. Lesions with score 3 remain an open question. In our limited experience, peripheral lesions classified as PIRADS 3 must be considered as more suspicious than those in central area and have to be subjected to FB. Probably, version 2 of PIRADS, which assigns different weights to the sequences of MRI based on the location of the lesion, can address this question and allow a superior FB detection rate.
HIGH PCA3 SCORES CORRELATE WITH ELEVATED PROSTATE IMAGING REPORTING AND DATA SYSTEM (PI-RADS) GRADE AND BIOPSY GLEASON SCORE AT MRI/US FUSION SOFTWARE-BASED TARGETED PROSTATE BIOPSY AFTER A PREVIOUS NEGATIVE STANDARD BIOPSY

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Aim: To determine the relationship between PCA3 score and prostate cancer as assessed by the Prostate Imaging Reporting and Data System (PI-RADS) and Gleason Score (GS) in a cohort of patients with elevated prostate-specific antigen (PSA), undergoing repeat magnetic resonance imaging/ ultrasound (MRI/US) fusion software-based targeted prostate biopsy (TBx).

Patients and Methods: 282 patients who have undergone TBx after previous negative randomized “standard” biopsy (SBx) and PCA3 urine assay were enrolled. The associations PCA3 score/PI-RADS and PCA3 score/GS were investigated by the Fisher’s exact test. The diagnostic performance of PCA3 score in predicting a positive TBx result was assessed by a receiver operating characteristic (ROC) analysis.

Results: PCA3 score difference for negative versus positive TBx cohort was statistically significant. One unit of increase in PCA3 score was associated to a 2.4% increased risk to have a positive TBx result. The association between PCA3 score and PI-RADS was highly significant (its median value for PI-RADS groups 3-4-5 was 58-104-146, respectively; \( p=0.006 \)). A similar pattern was detected for the relationship between PCA3 score and GS; an increasing PCA3 score was clearly associated to a worse GS (median PCA3 score equal to 62-105-132-153-322 for GS 3+4, 4+3, 4+4, 4+5, 5+4, 5+5, respectively; \( p<0.001 \)). The ideal PCA3 score cut-off was 80.

Conclusion: TBx improves PCA3 score diagnostic and prognostic performance, being directly associated both with PI-RADS and biopsy GS, respectively. We suggest that PCA3 cut-off of 35 should be raised, mostly in a prognostic context.

DOES A LEARNING CURVE EXIST FOR ROBOTIC EXTENDED LYMPHADENECTOMY AT THE TIME OF RADICAL PROSTATECTOMY?


68 A CASE OF XP11-TRANSLOCATION RENAL CARCINOMA WITH UNUSUAL MORPHOLOGIC FEATURES

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Introduction: Xp11-translocation renal carcinoma (Xp11-tRCC) and t(6;11)-tRCC are members of the microphthalmia-associated transcription factor (MiTF) t-RCCs (1-4). tRCC usually arises in young patients having typical microscopic features; Xp11 and t(6;11)-tRCC seem to be as indolent tumors with good prognosis (4). tRCC, microscopically, shows papillary structures, calcifications, pseudorosettes and eosinophilic hyaline globules, whereas its morphological features may also be indistinguishable from ordinary clear cell or oncocytic RCC. Conversely, Xp11-tRCC occurrence in adult patients is extremely rare, has a more aggressive behavior and oncocytic RCC. Conversely, Xp11-tRCC occurrence in adult patients is extremely rare, has a more aggressive behavior and oncologic risk.

Conclusion: Use of TFE3, TFEB, Ksp-cadherin and Melan-A can easily identify the specific sub-type (4).
HIGH-RISK PROSTATE CANCER AND RADIOTHERAPY: IEO EXPERIENCE AND BENCHMARK FOR AIRC IG 2013-N14300

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Introduction/Aim: Prostate cancer (Pca) is the second most common male cancer. D’Amico risk stratification defines high-risk Pca as clinical stage ≥T2c or prostate-specific antigen (PSA)>20 ng/ml or Gleason-score (GS)≥8. The prognosis for this category of patients is poor. No consensus exists on the most effective treatment (from surgery to radiotherapy (RT), combined treatments and the debate use/duration of the androgen deprivation therapy). External beam radiation therapy (EBRT) has been used over the last 15 years with a 5-year biochemical control probability after conventional photon irradiation reported of 47% (1). In the last decade, hadrontherapy with carbon ions has been considered a suitable strategy for high-risk Pca, in terms of the dose deposition with a resulting better sparing of organs at risk, based on the promising Japanese results and first Italian data (CNAO) (2). The aim of this retrospective study was to identify the biochemical progression-free survival (BFS) and the toxicity profile of localized high-risk Pca treated with definitive photon EBRT. Results of this study will constitute a benchmark for a prospective “mixed beam” trial: a boost with carbon ions followed by a pelvic photon intensity modulated radiotherapy (IMRT) to be performed within the AIRC project (IG 2013-N14300), where the first step is to analyze the outcome in the high-risk Pca after photon EBRT and then compare it with “mixed beam” RT. Patients and Methods: We retrospectively reviewed the data of patients treated at IEO with photon EBRT according to the inclusion criteria of the future AIRC “mixed beam” trial: cT3a and/or PSA>20 ng/ml and/or GS of 8-10, cN0 cM0. BFS was measured from the beginning of RT to PSA relapse defined according to ASTRO criteria (nadir + 2 ng/ml) and confirmed by one measurement. Toxicity was evaluated using RTOG/EORTC criteria. Results: Between 05/2010 and 12/2014, 76 patients presenting the AIRC study inclusion criteria were treated. Median age, initial PSA and GS were 74.9 years, 26.4 ng/ml and 8, respectively. EBRT, using IMRT technique, consisted in the irradiation of prostate-vesicles or prostate/pelvis for 46 and 30 patients, respectively. Moderate hypofractionation was employed (Fox Chase regimen), median dose was 70.2 Gy (2.7 Gy for 26 fractions). In 61 (80.3%) patients, androgen deprivation (ADT) was added. The median follow-up was 28.7 months (range=6.4-54.2). No grade ≥2 acute and late toxicity, including urinary and rectal complications, were reported. Biochemical progression during follow-up was observed in 20 patients after a median time of 20.2 months (range=5-58.1) from the end of EBRT. Fourteen patients had clinical progression, in all the cases preceded by biochemical progression. At January 2016, 53 (69.7%) patients are alive with no evidence of disease, 20 (26.3%) are alive with clinically evident disease, 3 died (1 for Pca). Conclusion: Our results, showing biochemical progression in 26.3% of patients at 20 months after photon EBRT+ADT, suggest that a more aggressive treatment is necessary. Local treatment intensification based on the “mixed beam” combining carbon ions boost (with its known radiobiological advantages (3)) and pelvic photon IMRT might really represent a promising strategy in the high-risk Pca and should be investigated with a future prospective study like our AIRC trial.

The study was partially supported by the research grants from AIRC (Italian Association for cancer research): IG-13218 and IG-14300.


STEREOTACTIC RADIOTHERAPY IN PATIENTS WITH LYMPH NODE METASTASES FROM PROSTATE CARCINOMA

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1Division of Radiotherapy, Sant Anna Hospital San Fermo Della Battaglia, Como (CO), Italy;
2Medical Physics, Sant Anna Hospital San Fermo Della Battaglia, Como, Italy

Introduction: Isolated nodal recurrent prostate is treated in most patients with hormone therapy. Androgen deprivation, however, is burdened with side effects that can affect the quality of life
of patients. Stereotactic radiotherapy may be proposed in selected patients as an alternative to hormone therapy in order to delay the onset of complications. Materials and Methods: From October 2012 to December 2015, 9 patients for a total of 10 lesions have been treated. One patient was in low-risk class of disease, 2 patients in the intermediate-risk category and 6 patients in the high-risk one. Seven patients have undergone surgery for primary disease. Three of these were, subsequently, subjected to adjuvant radiotherapy and 3 to salvage radiotherapy. Seven patients had never performed hormonal therapy, 2 patients had undergone neoadjuvant and adjuvant hormonal therapy. The clinical recurrence was documented in all patients with choline positron emission tomography (PET). Six lymph node lesions were external iliac lymph nodes, one was an internal iliac, one was common lymph node and one was an obturator lymph node. Computed tomography (CT) simulation was performed for all patients with contrast medium. Patients were treated with LINAC accelerator with Rapid Arc technique or VERO accelerator with dynamic arcs. The total dose of treatment was 35 Gy in 7-5 fractions for 6 patients and 30 Gy in 3 fractions for 1 patient. Patients at the end of treatment were sent to a half-yearly follow-up with quarterly monitoring of prostate-specific antigen (PSA) and choline PET six months after the end of radiotherapy. Toxicity was registered following RTOG scale. Results: The complete response to treatment occurred in 60% of patients treated. The relapse-free survival at one year was 60%. No patient relapsed in the treatment field. The patients relapsed were staged for the primary disease in high-risk class, except one patient in low-risk class. Clinical toxicity was registered. Conclusion: The delivered treatments are characterized by a low toxicity profile and a good local control. Further studies are needed to identify patients who may benefit from this method and define the correct combination and timing of a local treatment with androgen deprivation.

71 OPEN VERSUS ROBOT-ASSISTED SALVAGE RADICAL PROSTATECTOMY: ARE THERE ANY DIFFERENCES IN ONCOLOGICAL OUTCOMES?

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1Department of Urology, San Giovanni Battista Hospital, Città Della Salute E Della Scienza, Turin, Italy; 2Department of Statistics, University of Turin, Turin, Italy; 3Department of Radiotherapy, Pasini Hospital, Aosta, Italy; 4Department of Urology, Institut Mutualiste Montsouris, Paris, France; 5Urology Centre, Guy’s Hospital, London, U.K.; 6Department of Urology, North Bristol NHS Foundation Trust, Bristol, U.K.; 7Department of Urology, Leuven University Hospitals, Leuven, Belgium; 8Department of Urology, Clinique Saint Augustin, Bordeaux, France; 9Department of Urology, CHU Mondor, Créteil, France; 10Department of Urology, Pitié Salpêtrière Hospital University Paris 6, Paris, France; 11Department of Urology, Martini Klinik, Hamburg, Germany; 12Department of Urology, Fundació Puigvert, Barcelona, Spain; 13Department of Urology, OLV Clinic, Aalst, Belgium; 14Roland Van Velthoven Department of Urology, Jules Bordet Institute, Bruxelles, Belgium

Introduction/Aim: Salvage radical prostatectomy (sRP) is a valid treatment option in men with biochemical recurrence (BCR) seeking curative treatment. Robotic (R) and open (O) approaches have never been compared concerning oncological outcomes in large contemporary series. Our aim was to report and compare oncological outcomes of R and OsRP procedures. Materials and Methods: Two hundred and nine men having BCR after radiotherapy (n=178), high intensity focused ultrasound (HIFU) (n=8), cryotherapy (n=9) or other treatments (n=14) underwent sRP at 10 European tertiary referral institutions between 1991 and 2015. Retrospectively collected data included age, prostate-specific antigen (PSA), clinical and pathological TNM, primary and pre-sRP biopsy and sRP gleason score (GS), surgical margins, imaging type and positive sites, number of nodes (removed and positive) and ASA and ECOG performance status. Presence or absence of hormonal treatment (HT) before sRP was also required for the study inclusion. Men with missing data at baseline or at BCR or after sRP were excluded. After testing, normal distribution for continuous variables group comparisons were performed with Wilcoxon-Mann-Whitney test; Chi-square or Fisher’s exact tests were used for categorical variables. Amongst oncological outcomes, cancer-specific survival (CSS) was calculated by excluding deaths from other causes. Results: Final analysis was performed in 126 men (n=64 OsRP; n=62 RsRP) followed up for a median of 37.6 months (interquartile range (IQ) range=19.8-72.7) in the OsRP and for 25.1 months (IQ range=11.2-35.8) in the
RsRP group \( (p<0.01) \). No pre-sRP extra-nodal metastases were present. The only baseline feature yielding significant differences amongst groups was the number of pathologically positive nodes, being higher in the OsRP group \( (mean=1.5\pm3.8) \) versus RsRP \( (mean=0.51\pm1.6), \ p=0.04 \). Surgical margins were focally or extensively positive in 10.2\% \((n=6)\) and 32.2\% \((n=19)\) of the OsRP group versus 27.4\% \((n=17)\) and 12.9\% \((n=8)\) of the RsRP group \( (p<0.01) \). No statistically significant differences were present in BCR \( (50.8\% \text{ of OsRP (n=30) and 40\% of RsRP (n=24) patients}; \ p=0.23) \). However, 31.4\% \((n=16)\) of OsRP versus 6.9\% \((n=4)\) of RsRP developed castration-resistant prostate cancer (CRPC) \( (p<0.01) \) and overall survival (OS) was 88.71\% \((n=57)\) for OsRP versus 100\% \((n=62)\) for RsRP \( (p<0.01) \). Conclusion: Salvage radical prostatectomy yields promising oncological outcomes. Despite similar BCR rates compared to the open approach, the robot-assisted procedure favours lower rates of extensively positive surgical margins and higher OS. Longer follow-ups and higher number of patients are needed to validate the present findings.

### Table I. Patients’ characteristics and outcome.

<table>
<thead>
<tr>
<th></th>
<th>PL (40 patients)</th>
<th>DL (40 patients)</th>
<th>(p)-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, median (range)</strong></td>
<td>66 (51-78)</td>
<td>66.5 (57-74)</td>
<td>ns</td>
</tr>
<tr>
<td><strong>BMI, median (range)</strong></td>
<td>26 (17-36)</td>
<td>25.9 (21-30)</td>
<td>ns</td>
</tr>
<tr>
<td><strong>iPSA, median (range)</strong></td>
<td>8.23 (4.1-18.51)</td>
<td>5.51 (3.0-8.56)</td>
<td>ns</td>
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<tr>
<td><strong>ASA score, No. (%)</strong></td>
<td></td>
<td></td>
<td>ns</td>
</tr>
<tr>
<td>1</td>
<td>4 (10.0%)</td>
<td>3 (7.5%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>34 (85.0%)</td>
<td>33 (82.5%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2 (5.0%)</td>
<td>4 (10.0%)</td>
<td></td>
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<tr>
<td><strong>Biopsy GS, No. (%)</strong></td>
<td></td>
<td></td>
<td>ns</td>
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<tr>
<td>6</td>
<td>18 (45.0%)</td>
<td>26 (65%)</td>
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<tr>
<td>7</td>
<td>14 (35.0%)</td>
<td>12 (30.0%)</td>
<td></td>
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<tr>
<td>8</td>
<td>4 (10%)</td>
<td>1 (2.5%)</td>
<td></td>
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<tr>
<td>9</td>
<td>4 (10%)</td>
<td>1 (2.5%)</td>
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<tr>
<td><strong>Clinical stage, No. (%)</strong></td>
<td></td>
<td></td>
<td>ns</td>
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<tr>
<td>T1</td>
<td>26 (65.0%)</td>
<td>24 (60.0%)</td>
<td></td>
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<tr>
<td>T2</td>
<td>12 (30.0%)</td>
<td>15 (37.5%)</td>
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<tr>
<td>T3</td>
<td>2 (5.0%)</td>
<td>1 (2.5%)</td>
<td></td>
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<tr>
<td><strong>Blood loss (ml), median (range)</strong></td>
<td>0 (0-500)</td>
<td>25 (0-500)</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Preoperative Hb (g/dl), median (range)</strong></td>
<td>14.6 (13.1-15.7)</td>
<td>13.75 (10.8-16.1)</td>
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</tr>
<tr>
<td><strong>Postoperative Hb (g/dl), median (range)</strong></td>
<td>13.1 (10.9-15.7)</td>
<td>12.4 (10.0-15.4)</td>
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<tr>
<td><strong>Complication (Clavien-Dindo classification), No. (%)</strong></td>
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<td></td>
<td>ns</td>
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<td>1</td>
<td>2 (5.0%)</td>
<td>1 (2.5%)</td>
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<td>1 (2.5%)</td>
<td>2 (5.0%)</td>
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<td>3</td>
<td>0 (0%)</td>
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<tr>
<td>4</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
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<tr>
<td><strong>Pathological stage, No. (%)</strong></td>
<td></td>
<td></td>
<td>ns</td>
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<tr>
<td>pT2</td>
<td>25 (62.5%)</td>
<td>26 (65.0%)</td>
<td></td>
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<tr>
<td>pT3</td>
<td>15 (37.5%)</td>
<td>14 (35.0%)</td>
<td></td>
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<tr>
<td>pNx</td>
<td>22 (55.0%)</td>
<td>20 (50.0%)</td>
<td></td>
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<tr>
<td>pN0</td>
<td>18 (45.0%)</td>
<td>19 (47.5%)</td>
<td></td>
</tr>
<tr>
<td>pN1</td>
<td>0 (0%)</td>
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<td><strong>Pathological GS, No. (%)</strong></td>
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<td>ns</td>
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<td>6</td>
<td>21 (52.5%)</td>
<td>22 (55%)</td>
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<td>7</td>
<td>13 (32.5%)</td>
<td>14 (35.0%)</td>
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<tr>
<td>9</td>
<td>4 (10.0%)</td>
<td>2 (5.0%)</td>
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<tr>
<td>not classified</td>
<td>2 (5.0%)</td>
<td>2 (5.0%)</td>
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<tr>
<td><strong>PSM, No. (%)</strong></td>
<td></td>
<td></td>
<td>ns</td>
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<tr>
<td>positive apex</td>
<td>8 (20.0%)</td>
<td>10 (25.0%)</td>
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<tr>
<td>1-month PSA, median (range)</td>
<td>0.01 (0.01-0.05)</td>
<td>0.01 (0.01-0.08)</td>
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<td>1-month continence, No. (%)</td>
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<td>0 pad</td>
<td>12 (30.0%)</td>
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<td>1 security pad</td>
<td>14 (35.0%)</td>
<td>13 (32.5%)</td>
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<tr>
<td>≥1 pad</td>
<td>14 (35.0%)</td>
<td>13 (32.5%)</td>
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</table>
**PATHOGENESIS, FEATURES AND PROGNOSIS OF RENAL RELAPSE AFTER PARTIAL NEPHRECTOMY**

Alessandro Antonelli, Mario Sodano, Maria Furlan, Regina Tardanica, Simona Fisogni, Francesca Carobbio, Alberto Cozzoli, Tiziano Zanotelli and Claudio Simeone

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**Introduction/Aim:** Partial nephrectomy (PN) is the gold standard for all T1 renal cell carcinoma (RCC), whenever technically feasible. With respect to radical nephrectomy, PN has the specific risk of local recurrence that is rare and poorly investigated. This study presents the results of the pathological review of a series of second surgeries for a renal neoplasm relapsed after PN, in order to elucidate the pathogenesis of this event. **Patients and Methods:** The records and specimens of 15 patients (out of 710 consecutive PNs performed between 1983 and 2015, prevalence 3%) who were submitted to a salvage surgery for a renal relapse after PN for a non-familiar and non-hereditary RCC were fully reviewed. In all cases, RCC was localized at the time of first surgery; patients were systematically followed according to an institutional schedule; no other relapses were found at a whole-body re-staging before second surgery. **Results:** The average latency of the relapse was 42 months (minimum 3, maximum 132 months). Second surgery was a radical nephrectomy in all cases. Histological subtype was concordant in 14/15 cases; an upstaging was found in 7/15 cases (47%), an upgrading in 4/15 (26%). In 8/15 cases (53 %), the topographic position of the relapsing and primary tumors was the same, i.e. there was a minimal margin of resection at the first PN (median margin=1.6 mm, range=0-3 mm) and the cellularity of the relapsing tumor was strictly mixed with the granulomatous reaction due to the sutures of the first operation. In 7/15 cases, the position of the first and second neoplasm were different and the site of the first tumor showed multiple granulomas without tumoral cellularity: in 4 cases, the first tumor showed a microvascular embolization in the rim of healthy parenchyma removed and in the peritumoral fat, while the relapses were multifocal with a diffuse microvascular embolisation; in 2 cases, the histology was consistent with a papillary RCC and the relapse was multifocal; in 1 case, the histotype of primary and relapsing tumor were different. At a median follow-up time of 42 months from the second surgery, 7 patients died from RCC, while 4 are alive with metastasis; the 2 patients with multifocal papillary RCC and the one with different histologies are alive without evidence of disease. **Conclusion:** Renal relapse after PN can be due to an incomplete resection, a newborn tumor from a primary one showing a pattern of aggressiveness or a true multifocality. In the case of an incomplete resection or primary tumor with aggressive features, the event of the relapse leads to an adverse prognosis, in spite of a prompt salvage surgery. Follow-up of patients with suspected incomplete resection of aggressive tumor should be more intensive.
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Introduction/Aim: The surface-intermediate-base (SIB) margin score is a novel system proposed by Minervini et al. to standardized resection technique (RT) in partial nephrectomy (PN). The score depends on the thickness of healthy parenchyma around the intrarenal side of the surgical specimen. This score is visually assigned by the surgeon analyzing the minimal margin (score specific area (SSA)) of superficial, intermediate and deep area of the tumor (surface-intermediate-base margins). Outcome of each surgical approach (resection, enucleoresection and enucleation) is defined by adding the three values of the SSA. The aim of this study was to validate SIB score by comparing the surgeon’s values of SSA with the histopathological measure of the surgical margins. Materials and Methods: From November 2014 to September 2015, data from patients who underwent PN were prospectively collected. One surgeon performed the SIB score in all cases. Three different colors of inks were used to indicate the surface (green), intermediate (blue) and base (black) SSA. Surgical specimens were evaluated by one pathologist who reported maximum, minimum and most represented thickness of healthy renal margins. To evaluate any significant differences between the SIB score and the histopathological data the t-test was used. Results: We collected data of 57 consecutive patients who underwent open (33 patients) or robot-assisted (24 patients) PN in our center. In Table I, the SIB score and the surgical technique assigned in each case are reported. At the histopathological evaluation, maximum, minimum and most represented thickness of healthy renal margin among SSA grade S 0 vs. 1 was 0.16/0.39/0.48 mm vs. 1.03/1.60/1.24 mm, for I or B 0 vs. 1 vs. 2 was 0.3/0.42/0.35 mm vs. 0.93/1.33/0.97 mm vs. 1.52/2.10/2.13 mm. We found significant differences in all comparisons. Conclusion: It is reasonable to think that there are different perioperative, oncological and long-term outcomes in each PN surgical approach. We need a standard reporting system to improve comparisons between different RT and surgical series. The surgeon’s visual assignment of healthy parenchyma thickness around the tumor significantly correlates with the pathological measures than the SIB score can correctly classify the RT during PN.

Table I. SIB scores and consequent RT assigned.

<table>
<thead>
<tr>
<th>S</th>
<th>I</th>
<th>B</th>
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75

FUNCTIONAL OUTCOMES AND COMPLICATIONS OF SALVAGE RADICAL PROSTATECTOMY: OPEN VERSUS ROBOTIC APPROACHES

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AIM: To report and compare open (O) versus robotic (R) salvage radical prostatectomy (sRP) functional outcomes and complications in a large multi-institutional cohort. Materials and Methods: We retrospectively collected data of 209 men undergoing sRP between 1991 and 2015 at 10 European institutions. Baseline characteristics included oncological, clinical and pathological features, acute and late gastrointestinal or urinary tract toxicity following primary treatment, primary treatment type, number of nodes removed, ECOG, ASA and Charlson Comorbidity Index (CCI). Operating time (OT), blood loss (BL) and hospital stay (HS) were recorded. Complications were graded using the Clavien-Dindo score. Erectile function (EF) and urinary continence (UCon) were assessed pre-sRP at 6 and at 12 months with International index of erectile function (IIEF) before and according to the type of therapy needed to obtain erections after sRP and with number of pads/day used respectively. Men with insufficient follow-up data were excluded. After testing normal distribution for continuous variables, Wilcoxon-Mann-Whitney test was used for group comparisons; Chi-square or Fisher’s exact tests were used for categorical variables. Continence trends were evaluated with analysis of variance for repeated measures. Results: Sixty four OsRP and 62 RsRP were included. No significant baseline differences were present amongst groups except for the mean number of nodes removed (OsRP=13.8±13, RsRP=6±6.1; p<0.01) and CCI (OsRP=1.65±1.9, RsRP=1.46±1.55; p=0.02). Mean OT was 220.3±137.6 and 201.49±107.9 min for OsRP and RsRP, respectively (p=0.71), whilst mean BL was 675.87±612.58 in the OsRP and 260±202.92 ml in the RsRP group (p<0.01). Ten OsRP patients (15.6%) required transfusions versus 4 RsRP (6.5%) (p=0.1). Ten OsRP patients (15.6%) required transfusions versus 4 RsRP (6.5%) (p=0.1). Mean days of HS were 10.2±6.4 for OsRP and 3.7±2.3 for RsRP (p<0.01). In the OsRP group, 26 men (40.6%) developed ≥1 complications versus 17 (27.4%) in the RsRP group (p=0.12); 30.0% of OsRP (n=19) had at least one Clavien-Dindo ≥3 versus 8.0% (n=5) of RsRP (p<0.01). The most frequent complications were anastomotic stricture, occurring in 14.06% (n=9) and 3.23% (n=2) of OsRP and RsRP, respectively (p=0.03), and rectal injury, 10.9% (n=7) in the OsRP and 0% in the RsRP group (p<0.01). Pre-operatively, no difference in EF was present between groups (p=0.6). One bilateral nerve sparing (NS) OsRP compared to 5 and 16 uni- and bilateral NS RsRP were performed (p<0.01). At 1 year, 4 (11.1%) OsRP and 6 (10.9%) RsRP had spontaneous or phosphodiesterase type-5 (PDE-5)-assisted erections. No significant differences in UCon were present amongst groups at baseline and during follow up (p=0.15). At 12 months, 18 OsRP (51.5%) and 30 RsRP (77%) patients were continent, whereas 17 (48.5%) and 9 (23%) had severe incontinence (≥3 pads/day).

Conclusion: RsRP yields shorter hospital stay, lower blood loss and lower rates of high grade complications compared to OsRP. However, no advantages are detectable in terms of continence and erectile function.

76 PROSTATE BIOPSY BEFORE SALVAGE RADICAL PROSTATECTOMY: DETECTION RATE AND PATHOLOGICAL CONCORDANCE

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11Department of Urology, Pitié Salpêtrière Hospital University Paris VI, Paris, France;
12Department of Urology, Martini Klinik, Hamburg, Germany;
Introduction/Aim: Current guidelines consider a positive prostate biopsy (Bx) result as an important requirement in men seeking to undergo salvage radical prostatectomy (sRP) after biochemical recurrence (BCR). However, results of confirmatory pre-sRP biopsy (cBx) have never been reported in large contemporary cohorts. Our aim was to evaluate the detection rate of pre-sRP prostate Bx; to establish the Gleason score (GS) concordance (Conc) of cBx and first diagnostic biopsy (fBx) with the final sRP specimen GS, respectively; to analyse the GS Conc between the fBx and cBx GS. Materials and Methods: We retrospectively collected data of 209 men who underwent sRP after BCR at 10 European high-volume centres between 1991 and 2015. Clinical and pathological features, including age, prostate-specific antigen (PSA), TNM, imaging and previous treatments were recorded. FBx, cBx and sRP GS sums were categorised in ≤6, 7, 8, 9 and 10. Men without appropriate information or undergoing sRP without an available cBx result were excluded. Cohen’s Kappa coefficient was used for Conc to consider inter-rater agreement. Detection rate and Conc, upgrading (UpGr) and downgrading (DownGr) are reported as number of events and percentages. Results: One hundred and sixty six men were included. Mean age, initial and pre-sRP PSA were 64.8±6.1 years, 19.6 and 8.7 ng/ml, respectively. Pathological stage of the sRP specimen was pT2 in 43.7% and pT3 in 54.4%. Two cases were pT0 and no pT4 were present. All had negative imaging for extra-nodal metastasis. Sixty percent of the patients had hormone therapy before sRP. CBx Detection rate was 89.8% (n=149) with the remaining 10.24% (n=17) having no prostate cancer diagnosis due to radiation injury or absence of tumour being detected. Conc, UpGr and DownGr between cBx and sRP specimens were 61.1% (n=88, k=0.208), 28.5% (n=41) and 10.4% (n=15). Five sRP specimens were not evaluable due to radiation injury or had no tumour. Conc, UpGr and DownGr between FBx and cBx were 48.9 (n=45, k=0.284), 43.8 (n=40) and 7.61 (n=7) (fBx missing n=57). Conc, UpGr and DownGr between fBx and sRP specimens were 36.7% (n=32, k=0.105), 55.1% (n=48) and 8.0% (n=7), respectively. Conclusion: Pre-sRP confirmatory biopsy has an appropriate ability of confirming the presence of tumour. However, it underestimates GS in a significant proportion of men, having a higher GS at the final histology of the sRP specimen. The original diagnostic biopsy is not a reliable source of GS information when planning second-line treatment after BCR as it is upgraded in more than half of the cases.

Discussion and Conclusion: Pre-sRP confirmatory biopsy has an appropriate ability of confirming the presence of tumour. However, it underestimates GS in a significant proportion of men, having a higher GS at the final histology of the sRP specimen. The original diagnostic biopsy is not a reliable source of GS information when planning second-line treatment after BCR as it is upgraded in more than half of the cases.
Figure 1. Schematic view of surgical anatomy (left picture) and critical sites of lymph node dissection (right picture) for upper tract urothelial carcinoma. A, aorta; IVC, inferior vena cava; GV, gonadal vein; GA, gonadal artery; AB, aortic bifurcation; VCB, vena cava bifurcation; CIA, common iliac artery; EIA, external iliac artery; IIA, internal iliac artery; CIAB, common iliac artery bifurcation; RH, renal hilum; SMI, superior mesenteric artery; IMA, inferior mesenteric artery; Ki, kidney; Ad, adrenal; UB, urinary bladder.

Figure 2. A: Anatomical templates of lymph node dissection (LND) according to laterality and location of the primary tumor based on a critical analysis of the current literature: LND templates for tumors of the renal pelvis and upper third of the ureter. RP, renal pelvis; UU, upper third of the ureter; MU, middle third of the ureter; LU, lower third of the ureter; LN, lymph node.
Figure 2. B: Anatomical templates of lymph node dissection (LND) according to laterality and location of the primary tumor based on a critical analysis of the current literature: LND templates for tumors of the middle third of the ureter. RP, renal pelvis; UU, upper third of the ureter; MU, middle third of the ureter; LU, lower third of the ureter; LN, lymph node. C: Anatomical templates of lymph node dissection (LND) according to laterality and location of the primary tumor based on a critical analysis of the current literature: LND templates for tumors of the lower third of the ureter. RP, renal pelvis; UU, upper third of the ureter; MU, middle third of the ureter; LU, lower third of the ureter; LN, lymph node.
PREDICTIVE FACTORS OF RESECTION TECHNIQUES DURING PARTIAL NEPHRECTOMY IN A COHORT OF “ENUCLEATIVE” CENTERS: INSIGHTS FROM THE SURFACE-INTERMEDIATE-BASE (SIB) MARGIN SCORE INTERNATIONAL CONSORTIUM

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Abstracts of the 26th Annual Meeting of the Italian Society of Uro-Oncology (SIUrO), 9-11 June, 2016, Florence, Italy

Introduction/Aim: Detailed reporting of resection strategies (RS) and resection techniques (RT) for tumor excision during partial nephrectomy (PN) is lacking in the current literature. The aim of the study was to evaluate (i) possible correlations between patients’ and/or tumors’ characteristics and RT performed and (ii) whether the type of RT does influence perioperative outcomes after PN, harnessing the newly proposed Surface-Intermediate-Base (SIB) margin score as a standardized reporting system. Materials and Methods: After Institutional Review Board’s approval, data were prospectively collected from a cohort of 507 patients undergoing nephron-sparing surgery (NSS) at 16 high-volume Centers across the U.S. and Europe over a 6-month enrollment period. RT was classified according to the SIB score. RS was classified as “enucleative”, “enucleoresective” or “resective” according to the most prevalent RT performed in each centre’s cohort. Descriptive and comparative analyses were performed in the nine enucleative RS centres (EC). Results: Overall, 507 patients were finally enrolled in the study. The RT was classified as pure or hybrid enucleation (E, SIB 0-2), pure or hybrid enucleoresection (ER, SIB 3-4) and resection (R, SIB 5) in 266 (52.5%), 150 (29.6%) and 91 (17.9%) patients, respectively, in the overall cohort, while in 207 (74.7%), 56 (20.2%) and 14 (5.1%) patients in the EC cohort. Demographic data, comorbidity scores, surgical indication and approach did not significantly differ between the E, ER and R groups in the EC. Median PADUA score was 8 (interquartile range (IQR)=7-9), 9 (7-10) and 9 (8-10) (p=0.03); a PADUA score ≥10 was recorded in 19.3%, 37.5% and 28.6% (p=0.02) in the E, ER and R groups, respectively. A clampless strategy was used in 79/204 (38.7%), 6/55 (10.9%) and 5/14 (35.7%) patients in the E, ER and R groups (p<0.001). Median warm ischemia time (WIT) was 17 (12-23), 18 (14-22) and 18 (16-20) minutes (p>0.05). Surgical post-operative complications were recorded in 6.8%, 12.5% and 14.2% of patients (p>0.05). Positive surgical margin rate was recorded in 2.4%, 7.1% and 0% of patients, respectively (p>0.05). Trifecta outcome was achieved in 74.8%, 65.0% and 80.0% of patients for the E, ER and R groups (p>0.05). Discussion and Conclusion: This is the first study evaluating pre-operative predictive factors of RTs performed during PN and whether the type of RT significantly impacts on NSS outcomes using a standardized instrument of reporting. Overall, in EC, E represents nearly 75% of all procedures and is associated with a significantly higher rate of clampless procedures compared to ER. However, ER and R are preferred in highly complex cases. Concerning surgical outcomes, E was associated with a lower rate of post-operative surgical complications compared to ER and R and lower positive margin rates and higher Trifecta achievement compared to ER, although these differences were not statistically significant.
CLINICAL FEATURES AND THERAPEUTIC HINTS IN INCIDENTAL PROSTATE CANCER

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Introduction/Aim: Incidental prostate cancer (iPCa) is found in about 5% patients with lower urinary tract symptoms (LUTS). However, to establish how to manage this pathological condition could be an interesting therapeutic hint to emphasize (1). The aim was to evaluate clinical features in patients with iPCa who underwent surgical or endoscopic treatment. Subsequently, we describe therapeutic strategies implemented in our population.

Materials and Methods: We retrospectively analyzed 1,002 patients affected by LUTS who underwent surgical or endoscopic treatment between April 2010 and December 2015. When iPCa was found, we collected cTNM stages (T1a or T1b), clinical, pathological and biochemical patients’ data, as well as those regarding treatment, overall survival and disease-free survival. We used t-test (p<0.05) and Fisher’s test for statistical analysis.

Results: In 1,002 patients with LUTS, we performed 227 prostatic adenomectomies and 775 transurethral resections of prostate (TURP). Sixty patients (6%) were found with iPCa of whom 30 were cT1a and in the other 30 cT1b. These two groups, as compared by the characteristics regarding age, prostate volume (determined by transrectal ultrasound), prostate-specific antigen (PSA) density, weight of prostatic adenoma removed and operative time, did not show statistically significant differences. PSA was significantly higher in cT1b patients (p=0.03). Four patients were lost at follow-up; in the other 56 patients, the mean time of follow-up was 45 months. In 27 patients, the clinical iPCa stage was T1a; 20 underwent the Watchful Waiting approach and 7 were treated by active surveillance (AS) strategy. Of the 29 patients with cT1b, 15 (51.7%) underwent conservative treatment (Watchful Waiting or AS strategies), 4 patients (13.7%) radical prostatectomy, 6 (20.6%) radiotherapy, 4 (13.7%) androgen deprivation, mainly according to comorbidities and clinical conditions. Biochemical failure occurred in 4 patients (7%), of these 2 belonged to cT1a group and 2 to cT1b. Only one patient died from other causes.

Discussion: iPCa is still a clinical and pathological condition whose characteristics are not yet fully defined. TNM classification seems to have a role in stratifying patients as for their management (2, 3). This study has confirmed that the value of PSA is the only statistically significant variable, like in the two groups of patients examined. The therapeutic strategies regarding the two groups of patients (cT1a and cT1b) were different: conservative in cT1a group or conservative vs. curative in T1b group, depending on the stratification of clinical and pathological characteristics of patients. A longer follow-up could give us more information about “oncological end-points” and, in particular, concerning disease-free survival and overall survival. Conclusion: In our experience, Watchful Waiting and AS strategies represent the choice in cT1a iPCa, while cT1b iPCa deserves to be treated or strictly followed-up.


ADIPONECTIN, LEPTIN AND MMP-3 PLASMATIC LEVELS CANNOT IDENTIFY HIGH-RISK PROSTATE CANCER IN PATIENTS UNDERGOING BIOPSY

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Introduction/Aim: To reduce the diagnosis of indolent prostate cancer (PCa) and to prevent progression of aggressive tumors are two important targets in urological oncology. Prostate-specific antigen (PSA) demonstrates low accuracy in the early detection of high risk tumors. There is some evidence in literature that obese patients and/or patients affected by metabolic syndrome (MS) might be at higher risk for biologically aggressive PCa characterized by Gleason patterns 4 or 5. The aim of our study was to investigate the correlation between the body mass index (BMI) class, serum levels of adiponectin, leptin and metalloproteinase 3 (MMP-3) that are biomarkers related to MS and the detection at biopsy of Gleason patterns 4 and 5. Materials and Methods: Consecutive patients undergoing prostate biopsy for PSA levels ≥4 ng/ml and/or positive digital rectal examination were included.
Patients were classified in relation to BMI. Blood samples for the evaluation of adiponectin, leptin and MMP-3 were collected. A 12-core transrectal prostate biopsy was performed. Serum adiponectin, leptin and MMP-3 were measured using “Human Leptin Instant ELISA”, “Human Adiponectin ELISA”, “Human MMP-3 ELISA” kits, respectively. Statistical analysis was performed to relate the plasmatic levels of the above-mentioned biomarkers to the presence of Gleason patterns 4 and 5 at biopsy. Results: Fifty-six patients were enrolled. Median serum levels of leptin, adiponectin and MMP-3 were 0.829 ng/ml, 1.72 ng/ml and 1.767 ng/ml, respectively. In relation to BMI class, the plasmatic levels of leptin and MMP-3 were higher in obese ($p=0.02$) and in normal-weight patients ($p=0.02$), respectively. No statistically significant difference was detected in serum levels of leptin ($p=0.18$), adiponectin ($p=0.68$) and MMP-3 ($p=0.49$) between the 24 patients (42.8%) with diagnosis of PCa and the 30 patients (53.7%) with a negative biopsy. Comparing the levels of biomarkers in 11/24 patients (45.8%) with Gleason 6 (3+3) and in 13/24 (54.2%) showing Gleason patterns 4 and 5 at biopsy, again, no statistically significant difference in leptin ($p=0.4$), adiponectin ($p=0.6$) and MMP-3 ($p=0.5$) levels was found. Conclusion: In our preliminary study, we found increased plasmatic levels of leptin and MMP-3 in obese and normal-weight patients undergoing prostate biopsy, respectively. The significance of this finding, in patients with an elevated PSA, is uncertain. On the other hand, no other statistical difference was found between BMI, plasmatic levels of leptin, adiponectin, MMP-3 and detection of an aggressive Gleason pattern at biopsy.

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Introduction/Aim: Tumor excision is a fundamental step during partial nephrectomy (PN), yet resection technique (RT) is rarely reported in current nephron-sparing surgery (NSS) literature. We recently proposed the Surface-Intermediate-Base (SIB) margin score as a new classification model for standardized reporting of RT during NSS. The aim of the study was to validate the SIB model from a histopathological perspective. Materials and Methods: Data were prospectively collected from a cohort of 40 patients undergoing NSS, between June and September 2014, at a single Institution. The SIB score was assigned in the operating room by the surgeon. The score-specific areas (SSA) were outlined on a digital picture as anatomic landmarks for histopathological analysis. Two dedicated uropathologists inked the landmark areas and measured, in a blinded fashion, the maximum, minimum and mean thickness of healthy renal margin (HRM) within the SSAs (360 overall histologic measures, Figure 1). The Mann-Whitney U-test was used to assess the correlation between the SIB visual definitions of RTs and the thickness of HRM at histopathological analysis. Results: The overall RT was classified as pure enucleation, hybrid enucleation and pure enucleoresection in 28 (70%), 7 (17%) and 3 (7%) patients, respectively, while as hybrid enucleoresection and resection in 1 (3%) patient each. At histopathological analysis, the maximum, minimum and mean thickness of healthy renal margin (HRM) within the SSAs (360 overall histologic measures, Figure 1). The Mann-Whitney U-test was used to assess the correlation between the SIB visual definitions of RTs and the thickness of HRM at histopathological analysis. Results: The overall RT was classified as pure enucleation, hybrid enucleation and pure enucleoresection in 28 (70%), 7 (17%) and 3 (7%) patients, respectively, while as hybrid enucleoresection and resection in 1 (3%) patient each. At histopathological analysis, the maximum, minimum and mean thickness of HRM was significantly different between both the SSA-grades S=0 and S=1 (p<0.001) and the SSA-grades I or B=0, I or B=1 and I or B=2 (p<0.001), for all histological measures (maximum, minimum and mean values). S, surface; I, intermediate; B, base.

Figure 2. Box-plots showing the minimum (Min), mean and maximum (Max) thickness of healthy renal margin (HRM) for the score-specific area (SSA) – grades Surface=0 (S=0), Surface=1 (S=1), Intermediate or Base=0 (I or B=0), Intermediate or Base=1 (I or B=1) and Intermediate or Base=2 (I or B=2). Median values and interquartile ranges (white boxes) are shown. Thickness of HRM was significantly different between both the SSA-grades S=0 and S= 1 (p<0.001) and the SSA-grades I or B=0, I or B=1 and I or B=2 (p<0.001), for all histological measures (maximum, minimum and mean values). S, surface; I, intermediate; B, base.
(Figure 2) (p<0.001). Conclusion: The SIB margin score is the first standardized reporting system to communicate RT during NSS. Our study proved the applicability of the model in a real-world clinical setting and provided robust histopathological validation of its utility.

A WHOLE TOMATO-BASED DIETARY SUPPLEMENT TO COMPLEMENT THE OUTCOMES OF THE WCRF/AICR RECOMMENDATIONS

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Introduction: Despite differences in outcomes, due to heterogeneity in study designs, a wealth of clinical and experimental evidences underscore the beneficial effects of the consumption of lycopene-rich tomatoes on prostate functions (1). Such effect, which is maximally reached using cooked tomatoes, has been shown to be dose-dependent (2).

Thus, development of tomato-processing methods aimed at optimally preserving the health-promoting activity of this fruit is of major translational relevance. Materials and Methods: Using the transgenic adenocarcinoma of the mouse prostate (TRAMP) model, the effect of a diet enriched with processed whole tomato on animal survival, tumorigenesis and progression was investigated. Results: Tomato-enriched diet significantly increased overall survival, delayed progression from prostatic intraepithelial neoplasia to adenocarcinoma and decreased the incidence of poorly differentiated carcinoma. This was paralleled by an increase of plasma antioxidant capacity and a reduction of circulating pro-inflammatory and pro-angiogenic cytokines of known relevance in human prostate carcinogenesis. Based on these preclinical data, we have developed a dietary supplement containing a blend of ad-hoc processed whole tomato and olive vegetable water for human use, called Lycoprozen® (Italian Health Ministry, code 68843) (3).

Conclusion: This new dietary supplement may help to maintain prostate health and can contribute to the beneficial effect of adherence to the WCRF/AICR recommendations, especially when proper life styles are adopted.

LIMITS OF TRANSURETHRAL RESECTION IN DETECTING RARE HISTOLOGICAL VARIANTS WITHIN LARGE UROTHELIAL BLADDER TUMORS

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Introduction/Aim: Rare histotypes represent almost 10% of bladder tumors, although more often represented as small foci within large and invasive transitional cell tumors of the bladder (TCCB). It might be clinically relevant that rare histological variants remain unrecognized at transurethral resection (TURBT), since they could indicate more aggressive tumors, less responsive to systemic chemotherapy and unfit for “organ-sparing” management. We investigated the accuracy of TURBT to detect rare histological variants in patients-candidates to cystectomy for bladder cancer with clinical and radiological features of invasiveness.

Materials and Methods: The clinical and pathologic data of 340 patients submitted to TURBT and/or cystectomy for bladder cancer, between January 2010 and July 2015, were reviewed. The presence of uncommon histotypes within urothelial bladder carcinoma has been assessed. The diagnosis of rare variants of bladder cancer was made according to WHO criteria. Standard hematoxilyn-eosin stain was adopted and further immunohistochemistry was performed as follows: Micro-papillary carcinoma, MUC1, EMA, CK7, CK20; Squamous cell carcinoma, CK5/6, CK5/14; Adenocarcinoma, CK7, CK20, CEA, EMA; Small cell carcinoma, EMA, CAM5.2, synaptophysin, vimentin, chromogranin, neuro-specific enolase (NSE), CK7, c-kit and TTF1; Mesenchymal...
tumors, keratin, EMA, vimentin and CEA and, sometimes, hCG. Additional immunohistochemistry was adopted when required to improve the pathological diagnosis. Candidate patients to cystectomy, for reason other than large bladder tumor with radiologic imaging suggestive of bladder wall infiltration, i.e. Tis, multiple and/or recurrent non muscle invasive and patients submitted to TURBT at other centers, were excluded. Inferential statistical analysis was performed. **Results:** Out of 340 patients, 35 (10.3%) showed rare histotypes of bladder cancer, i.e. in 30 cases (32%) out of 94 radical cystectomies and in 5 (2%) out of 246 TURBTs. The rare histotypes were distributed as follows: squamous carcinoma 11 (31%), sarcomatoid 8 (23%), undifferentiated 6 (17%), neuroendocrine 3 (9%), micropapillary 2 (6%), adenocarcinoma 1 (3%), mixed 4 (11%). TCCB with histological rare variants showed at cystectomy considerable size (average diameter=7.7x6.7 cm; range=4.5x5-11x9 cm), while 13 (43%) were pT4 category. In 13 patients (37%), the uncommon histotype was detected at the pre-operative TURBT, while, in 22 (63%), it was recognized only in the cystectomy specimen. Regarding the correlation between TURBT and re-TUR, rare histotypes were not identified at the first TURBT in 9 patients (26%) but found at re-TURBT in 4 patients (44%) and at cystectomy in 5 patients (56%) (Figure 1). Conversely, an atypical component diagnosed at first TURBT was not confirmed by a subsequent re-TUR in only 1 patient (3%). **Discussion:** Although the important prognostic role of rare histologic variants of bladder cancer is well-recognized, TURBT is not standardized in relation to tumor size. Unrecognized rare histotypes might have important therapeutic implications since they are probably less responsive to neoadjuvant chemotherapy or bladder-sparing approaches, thus benefiting early cystectomy. The inaccuracy of TUR in everyday clinical practice in detecting uncommon variants could be explained by the inadequacy of sampling of large tumors. The “pre-cystectomy” TUR is often considered a limited biopsy to confirm the tumor and to demonstrate the infiltration of the muscular layer. As a matter of fact, pathologists often do not analyze a sufficient amount of tissue to identify different histological components. Standardization of the TURBT strategy, including sampling of different areas of bulky tumors, could be of clinical value.

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**Figure 1. Flow chart showing the correlation between TURBT, re-TUR and cystectomy.**

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**84 PREDICTIVE FACTORS OF RESECTION TECHNIQUES DURING PARTIAL NEPHRECTOMY IN A COHORT OF “ENUCLEORESCTIVE” CENTERS: INSIGHTS FROM THE SURFACE-INTERMEDIATE-BASE (SIB) MARGIN SCORE INTERNATIONAL CONSORTIUM**

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Introduction: Detailed reporting of resection strategies (RS) and resection techniques (RT) for tumor excision during partial nephrectomy (PN) is lacking in the current literature. The aim of the study was to evaluate (i) possible correlations between patients’ and/or tumors’ characteristics and RT performed and (ii) whether the type of RT does influence perioperative outcomes after PN, harnessing the newly proposed Surface-Intermediate-Base (SIB) margin score as a standardized reporting system. Materials and Methods: After Institutional Review Board’s approval, data were prospectively collected from a cohort of 507 patients undergoing NSS at 16 high-volume Centers across the U.S. and Europe over a 6-month enrollment period. RT was classified according to the SIB score. RS was classified as "enucleative", "enucleoresective" or "resective" according to the most prevalent RT performed in each centre’s cohort. Descriptive and comparative analyses were performed in the six enucleoresective RS centres (ERC).

Results: Overall, 507 patients were finally enrolled in the study. The RT was classified as pure or hybrid enucleation (E, SIB 0-2), pure or hybrid enucleoresection (ER, SIB 3-4) and resection (R, SIB 5) in 266 (52.5%), 150 (29.6%) and 91(17.9%) patients, respectively, in the overall cohort, while in 53 (33.1%), 83 (51.9%) and 24 (15.0%) patients in the ERC. Demographic data, comorbidity scores, surgical indication and approach and PADUA score did not significantly differ between the E, ER and R groups in the ERC. Tumors >4.0 cm were 21 (40.4%), 41 (49.4%) and 4 (16.7%) in the E, ER and R groups (p=0.02), respectively. A clampless strategy was used in 19.2%, 13.2% and 8.3% of patients (p<0.05). Median warm ischemia time (WIT) was 19 (15-24), 17 (14-23) and 17 (15-21) minutes in the E, ER and R groups (p<0.05). Positive surgical margin rate was 7.0%, 13.4% and 0% of patients (p=0.02). Surgical post-operative complications were recorded in 7.5%, 13.2% and 4.2% of patients (p=0.05). Positive surgical margin rate was 7.0%, 13.4% and 0% of patients, respectively (p<0.05). Trifecta outcome was achieved in 67.2%, 71.6% and 73.7% of patients for the E, ER and R groups (p<0.05). Discussion and Conclusions: This is the first study evaluating pre-operative predictive factors of RTs performed during PN and whether the type of RT significantly impacts on NSS outcomes using a standardized instrument of reporting. Overall, in ERC, ER represents less than 52%. ER and E are performed in a significantly higher proportion of tumors >4 cm compared to R. Relating to surgical outcomes, ER was associated with a significantly higher rate of post-operative surgical complication compared to E and R. However, Trifecta achievement was comparable among the three techniques.

RESECTION TECHNIQUES FOR NEPHRON SPARING SURGERY VARY: INSIGHTS FROM A PROSPECTIVELY COLLECTED MULTI-INSTITUTIONAL COHORT HARNESSING THE SURFACE-INTERMEDIATE-BASE (SIB) MARGIN SCORE (SIB INTERNATIONAL CONSORTIUM)

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Introduction/Aim: Resection methodology is rarely reported in current nephron-sparing surgery (NSS) literature. Yet, a...
relationship between resection technique (RT) and complication rates, preserved parenchymal volume, surgical margins and oncologic outcomes likely exists. The aim of the study was to evaluate the newly proposed Surface-Intermediate-Base (SIB) margin score as a standardized reporting system of RT in a cohort of patients undergoing NSS at 16 high-volume Centers across the U.S. and Europe. 

Materials and Methods: After Institutional Review Board’s approval, data were prospectively collected over a 6-month enrollment period. Results: A total of 507 patients were finally enrolled in the study. The mean number of patients included per center was 32 (range=11-90). A mix of open (150, 29.4%), laparoscopic (67, 13.2%) and robotic (290, 57%) approaches were harnessed for NSS. The median interquartile range (IQR) of pre-operative tumor size for the entire cohort was 3.10 cm (2.50-4.30). Based on the PADUA score, 195 (38.5%), 188 (37.1%) and 114 (22.5%) tumors were classified as low (PADUA 6-7), moderate (PADUA 8-9) and high (PADUA 10-13) complexity tumors, respectively. At pathological analysis, 30 (5.9%) positive surgical margins were recorded. Overall, the Trifecta outcomes (defined as absence of perioperative complications, negative surgical margins and warm ischemia time (WIT)<25 min) were achieved in 370 (73%) of patients. A snapshot of RTs performed in the entire cohort according to the SIB margin score is presented in Figure 1. The overall RT was classified as pure enucleation (SIB 0-1), hybrid enucleation (SIB 2), pure enucleoresection (SIB 3), hybrid enucleoresection (SIB 4) and resection (SIB 5) in 174 (34.3%), 92 (18.1%), 106 (20.9%), 44 (8.7%) and 91 (17.9%) patients, respectively. Conclusion: Standardized reporting of resection technique is lacking in the current NSS literature. We recently introduced a standardized scoring system, the SIB margin score, which quantitates the salient aspects of resection approaches after PN through a visual analysis of the intrarenal portion of the specimen immediately after surgery. Harnessing this systematic characterization of renal mass RTs, in an international multi-institutional cohort, we -for the first time- demonstrated that resection approaches vary and renal tumor

Figure 1. Snapshot of RTs performed in the entire cohort according to the SIB margin score is presented.
enucleation is employed quite frequently even at institutions that do not support its ubiquitous use. These data lay the groundwork for determining whether RT is a modifiable variable for functional and oncologic outcomes in patients who undergo NSS.

86
ENDOSCOPIC ROBOT-ASSISTED SIMPLE ENucleATION (ERASE) VS. OPEN SIMPLE ENucleATION (OSE) FOR THE TREATMENT OF CLINICAL T1 RENAL MASSES: ANALYSIS OF PREDICTORS OF TRIFECTA OUTCOME
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Aim: The aim of this study was to analyse the intra- and post-operative complications, as well as the predictive factors of Trifecta outcome in patients submitted to endoscopic robot-assisted simple enucleation (ERASE) and open simple enucleation (OSE) for clinical T1 renal masses. Materials and Methods: Overall, 634 cases treated with OSE (n=290) and ERASE (n=344) were prospectively recorded in our Department between 2006 and 2014. Trifecta was defined as simultaneous ischemia time <25 min, no surgical complication and negative surgical margin. A univariate analysis and multivariate logistic regression were performed for Trifecta. Results: The two groups were comparable for body mass index (BMI), comorbidity, tumor side, clinical T score, tumor diameter, surgical indication, pre-operative renal function, pre-operative hemoglobin and hematocrit. A significant difference was found between the OSE and the ERASE groups in operative time (115 (96-130) vs. 86 (70-110) minutes, p<0.0001), pedicle clamping (93.8% vs. 86.2%, p<0.0001), estimated blood loss (EBL) (150 (100-200) vs. 100 (100-143) cc, p<0.0001) and intraoperative complications (3.4% vs. 1.7%, p=0.02). The two groups were comparable for warm ischemia time (WIT) ≥25 min. A significant difference was found between OSE and ERASE in overall (16.6% vs. 5.5%, p<0.0001), Clavien 2 (11.7% vs. 4.4%, p=0.02) and Clavien 3 (3.1% vs. 1.7%, p=0.04) post-operative surgical complications, length of stay (6.0 (5.0-7.0) vs. 5.0 (4.0-6.0) days, p<0.0001), pre-operative 1st day delta creatinine (0.3 (0.2-0.4) vs. 0.15 (0.1-0.2) mg/dl, p<0.0001), positive surgical margins (2.1% vs. 1.5%, p=0.04), and Trifecta achievement (73.8% vs. 85.5%, p<0.0001). At univariate analysis, a higher median clinical diameter, a higher mean age, a higher median Charlson comorbidity index (CCI), endophytic tumor growth pattern, renal sinus and calyceal dislocation of the tumor, a higher median PADUA score and OSE were predictive factors of Trifecta achievement. At multivariate analysis, CCI lost significance (p=0.26), while age (odds ratio (OR)=1.02, 95% confidence interval (CI)=1.00-1.04, p=0.001), clinical diameter (OR=1.22, CI=1.05-1.42, p=0.008), PADUA score (OR=1.23, CI=1.07-1.41, p=0.004) and OSE (OR=1.74, CI=1.13-2.68, p=0.01) were confirmed predictive factors for Trifecta failure. Conclusion: The ERASE is a feasible and safe technique, which shows a comparable WIT, together with a significantly lower EBL, surgical complications rate, length of stay and a significantly higher Trifecta achievement compared to OSE. Age, comorbidity, tumor diameter and PADUA score, in association with surgical approach, represent significant predictive factors of Trifecta failure.

87
PROSPECTIVE ANALYSIS OF COMPLICATIONS AND THEIR PREDICTIVE FACTORS AFTER PARTIAL NEPHRECTOMY IN A MULTICENTER COMPARATIVE ITALIAN STUDY (RECORD1)
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Introduction/Aim: Absence of surgical complications represents an important perioperative goal of partial nephrectomy (PN). The aim of this study was to analyse intra and post-operative complications related to nephron-sparing surgery (NSS) in clinical T1 renal tumors in a wide Italian multicentre dataset and search for possible predictive factors. Materials and Methods: Overall, 1,075 patients treated with NSS for clinical renal tumors, between January 2009 and December 2012, were prospectively recorded. Overall, 13% of patients, post-operative surgical complications were recorded (7.6% surgical Clavien 2 and 3.8% surgical Clavien 3). Overall, 6.4% of patients had post-operative medical complications (3.2% were respiratory, 1.9% cardiacologic, 0.2% thromboembolisms and 1.1% for other causes). At multivariate analysis, ECOG score ≥1 (odds ratio (OR)=1.9, 95% confidence interval (CI)=1.21-3.10, p=0.01), clinical diameter (OR=1.42, CI=0.107-1.90, p 0.02), open approach (OR=3.2, CI=1.11-9.30, p 0.03) and estimated blood loss (EBL) (OR=1.01, CI=1.00-1.01, p 0.01) were significant predictive factor of surgical post-operative complications. Intra-operative complications, at univariate analysis, were predictive factors for surgical post-operative complications (p=0.0001); however, they did not achieve significance at multivariate analysis (OR=2.08, CI=0.94-4.59, p=0.07). Conclusion: In this study, comorbidity status (ECOG score) and clinical diameter of the tumor were the only pre-operative significant predictive factors of surgical complications, along with higher EBL and the open approach.

DEFINITIVE RADIOThERAPY IN THE TREATMENT OF BLADDER CANCER IN ≥80-YEAR-OLD PATIENTS: ANALYSIS OF TOXICITY AND OUTCOMES

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Aim: The aim of this study was to evaluate toxicities and survival rates of exclusive radiation therapy (RT) in the treatment of elderly patients with bladder cancer. Material and Methods: Between May 2011 and January 2016, 20 patients with bladder cancer previously submitted to transurethral resection (TURB) with diagnosis of high-grade transitional cell carcinoma, were treated with exclusive RT. Age ranged from 80 to 87 years (median=81). Five patients (25%) presented stage II disease, 10 (50%) stage II and 5 (25%) stage IV (M0). A 3-dimensional conformal treatment (3D-CRT) with a four-field box technique was planned delivering to the pelvis 45 Gy in 25 fractions with a sequential boost of 22 Gy in 11 fractions to the bladder and positive nodes for a total dose of 67 Gy. Acute and late toxicities were evaluated according to RTOG scale. Results: The median follow-up was 10 months (range=3-44). Acute genitourinrian (GU) toxicity rates were 75%: grade 1/2 and grade 3 were, respectively, 70% and 5%. Grade 1-2 gastrointestinal (GI) toxicity rate was 25%. Grade 1/2 GI late toxicity rates was 10%. No grade ≥2 toxicity was recorded. Grade 1 and grade 2 GU late toxicity rate was 35% and 10%, respectively. No grade ≥3 toxicity was recorded. Overall survival (OS) was 100% at 2 years and 56% at 3 years. Four patients died because of systemic disease progression. Five patients died from intercurrent disease without evidence of bladder cancer. The actuarial 1-year and 2-year disease-free survival (DFS) were 59.8% and 33.7%, respectively. Conclusion: This study demonstrated that in ≥80-year-old patients, not candidate to surgery or to concomitant radiochemotherapy for age and general conditions, exclusive definitive radiotherapy represents a valid alternative, after TURB, with acceptable toxicity profile.
Introduction/Aim: Nephron-sparing surgery (NSS) has become the standard of care for the surgical management of small (<4 cm) and clinically localized renal tumors. Currently, the conservative management of clinically localized renal tumors is increasing over time. The aim of this study was to report a snapshot of the clinical, perioperative and oncological results after NSS for renal tumors in Italy. Materials and Methods: We evaluated all patients who underwent conservative surgical treatment for renal tumors, between January 2009 and December 2012, at 19 urological Italian Centers (RECORd project). Preoperative, radiological, intraoperative, postoperative and histopathological data were recorded. Surgical eras (2009 vs. 2012 and year periods 2009-2010 vs. 2011-2012) were compared. Results: Globally, 983 patients were evaluated for the final analyses. In the most recent years, patients undergoing NSS were found to be significantly younger (p=0.05) than those surgically treated in the first study period, with a significantly higher rate of NSS with relative and imperative indication (p<0.001). A higher percentage of procedures for cT1b or cT2 renal tumors was observed in the most recent era (p=0.02). Overall, enucleoresection was the most widely adopted technique over time. The open approach (OPN) constantly decreases during years, while the laparoscopic approach (LPN) remains approximately constant and the robot-assisted approach (RAPN) increases. In 2012, LPN and RAPN together represented 61.9% of all interventions for cT1b tumors. Overall, 36.3% of patients underwent clampless NSS and its rate constantly increases from 33% in 2009 to 42.4% in 2012. The use of at least one haemostatic agent was recorded in 91.3% of procedures, with a significantly higher utilization in the most recent surgical era (p<0.001). Globally, no statistically significant differences among the surgical periods were found in terms of tumor nature and surgical margin status. Conclusion: The utilization rate of NSS in Italy is increasing over time, even in elective and more complex cases. RAPN is expanding and OPN constantly decreases. A higher awareness of Italian surgeons towards functional results is witnessed in RECORD1 study, confirmed by the increasing use of clampless procedures. This study confirms the expanding use of haemostatics.
lesion (OR=2.9, CI=1.56-5.35, p=0.01) and pathologic extracapsular lesion (OR=2.9, CI=1.05-7.90, p=0.04) were confirmed as significant predictive factors of positive surgical margins. **Conclusion:** Tumor renal site represents an important nephrometric pre-operative characteristic predictive of PSM. Extracapsular lesions are also correlated with a higher risk of PSM. Mini-invasive approach seems to present lower PSM rate for optical magnification; however, these data should be revised assessing similar pre-operative conditions in both approaches.

91

**IMPACT OF GENDER IN NEPHRON-SAVING SURGERY: COMPARISON OF PERIOPERATIVE AND PATHOLOGICAL OUTCOMES FROM THE DEFINITIVE RESULTS OF RECORD1 PROJECT**

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**Aim:** The aim of this study was to analyze gender differences in terms of perioperative and pathological features in a multicentre Italian dataset of patients (RECORd Project) undergoing nephron-sparing surgery (NSS).

**Materials and Methods:** Overall, 1,055 patients treated with NSS, between January 2009 and December 2012, were evaluated. An evaluation of gender differences of pre-, intra- and postoperative, as well as pathological variables was performed.

**Results:** Overall, 630 males and 346 females were analyzed. No significant difference was found between males and females in age at operation (analyzed as continuous and nominal (<75 years and ≥75 years) variable), ECOG score, clinical symptoms at diagnosis, tumor side, tumor growth pattern and localization and, also, number of lesions at radiological evaluation. A significant difference was found between males and females in body mass index (BMI) (26.3 (24.7-28.4) vs. 25.3 (22.5-27.5), p<0.001), surgical indication (relative 14.9% vs. 11.9%; absolute 8.8% vs. 3.2%, respectively; p=0.001), pre-operative hemoglobin (14.5±1.3 vs. 13.3±1.1, p<0.001) and creatinine (1.0±0.5 vs. 0.8±0.2, p<0.001). In intra-operative variables, no significant difference was found between the two groups regarding surgical approach (open vs. minimally invasive), technique (standard partial nephrectomy vs. simple enucleation), pedicle clamping and ischemia time. A significant difference was found between

| Table I. PSM, compared to negative surgical margins (NSM), by mean age, lesion site, approach and pathologic T. |
|---------------------------------|------------------|------------------|------------------|
| Pre-operative data              | NSM              | PSM              | P               |
| Age Mean (SD)                   | 61.8             | 12.7             | 65.5            | 9.9 | 0.02 | -    | -    | -    |
| Indication, n. (%)              | Elective         | 748              | 80.3%           | 27              | 61.4% | 0.002 | -    | -    | -    |
|                                | Rel/Abs          | 184              | 19.7%           | 17              | 38.6% |         | -    | -    | -    |
| Lesion site, n. %               | Other site       | 676              | 72.5%           | 20              | 45.5% | 0.01  | 2.89 | 1.56-5.35 | 0.001 |
|                                | Polar superior   | 256              | 27.5%           | 24              | 54.5% |         | -    | -    | -    |
| Approach, n. (%)                | Open             | 525              | 56.3%           | 33              | 86.8% | 0.01  | 2.11 | 1.05-4.27 | 0.04  |
|                                | Mini-invasive    | 407              | 43.7%           | 5               | 13.2% |         | -    | -    | -    |
| Pathologic T, n. %              | Intracapsular    | 894              | 95.9%           | 39              | 88.6% | 0.02  | 2.89 | 1.05-7.90 | 0.04  |
|                                | Extracapsular    | 38               | 4.1%            | 5               | 11.4% |         | -    | -    | -    |
males and females in operative time (200 (100-300) vs. 150 (100-250) min, respectively, p=0.03) and estimated blood loss (EBL) (135 (105-180) vs. 125 (105-160) cc, respectively, p=0.01). A slight difference between the two groups was found in intraoperative complication (5.8% vs. 3.2%, respectively, p=0.07). No difference between the two groups was found regarding overall medical, overall surgical, surgical Clavien 2 and 3 complications. A significant difference was found between the two groups in preoperative-1st and preoperative-3rd day delta estimated glomerular filtration rate (eGFR) (10.1 (0.0-23.0) vs. 12.7 (0.0-30.2), respectively, p=0.01 and 8.5 (0.0-23.0) vs. 18.9 (0.0-30.2), respectively, p=0.01). Regarding pathological data, a significant difference was found between males and females relating to malignant/benign histotype (84.1%/15.9% vs. 71.4%/28.6%, respectively, p=0.001). Males present a 58.3% of clear cells renal cell carcinoma (RCC) vs. 54.6% of females with a slightly higher 3rd-4th Fuhrman grade (19.6% vs. 15.0%, respectively, p=0.15). Conclusion: NSS in males presented a higher intra-operative difficulty in terms of time, bleeding and complications. Females present a higher rate of benign tumors, as described in literature. Males present a slightly higher clear cell RCC rate with higher Fuhrman grade.

92 ROLE OF SBRT WITH VMAT TECHNIQUE AND FFF BEAMS FOR LYMPH NODE METASTASES IN OLIGOMETASTATIC PATIENTS FROM GENITOURINARY MALIGNANCIES

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Introduction/Aim: Stereotactic body radiotherapy (SBRT) is considered a safe and effective approach for several sites of metastatic disease but few published data exist on local control rates in the context of isolated or limited lymph node metastases. We analyzed the outcome of oligometastatic patients suffering from genitourinary primary neoplasms and treated with SBRT on isolated lymph node metastases. Materials and Methods: Patients with a maximum of 5 lymph-nodal metastases (with a diameter of less than 5 cm) were included in this analysis. Radiotherapy was delivered with Volumetric Modulated Arc Therapy Rapid-Arc (VMAT-RA) and flattening filter-free (FFF) beams; median prescribed dose was 45 Gy in 6 fractions. We analyzed dosimetric data and correlated them with acute toxicity (CTCAE 3.0), local control of disease, progression-free survival and overall survival.

Results: From September 2007 to May 2015, 52 patients with 74 lymph node metastases were submitted to SBRT. Primary malignancies were prostate (56.7%), kidney (22.9%), bladder (19.2%), ureters (5.4%) and testicle (1.3%). At the post-treatment re-evaluation, a complete response was achieved in 39 lesions (52.7%) and a partial response in 25 lesions (33.7%). A stable disease was observed in 7 (9.4%) cases, while 3 (4%) lesions showed a disease progression. The overall clinical benefit rate was 95.8% (71/74 lesions). Acute toxicity was mild, 18 (34.6%) patients having experienced a G1 nausea and fatigue; no heavier toxicities were reported. At a median follow-up of 21.8 months (range=4.2-95.6), in-field progression of disease was observed in 12 sites (16.2%) after a median time of 6.8 months. Out-field lymph node progression was observed in 19 (36.5%) cases, while distant metastases occurred in 15 (28.8%) cases. Local control and overall survival at 1 year were 83% and 93%, respectively. Conclusion: Our results prove that SBRT with VMAT-RA and FFF beams can be considered a safe and effective approach for oligometastatic patients with isolated lymph node metastases from genitourinary tumors. Although this can be considered an initial experience, it suggests that SBRT may be an interesting strategy to preserve patients’ quality of life and delay further systemic treatments.

93 BLADDER PARAGANGLIOMA MISDIAGNOSED AS MUSCLE-INVASIVE UROTHELIAL CARCINOMA. AN ERROR THAT COULD BE AVOIDED

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Introduction: Extra-adrenal paragangliomas are most commonly found in superior para-aortic area (45%), followed by inferior para-aortic (30%) and urinary bladder (10%), accounting for less than 0.5% of all bladder neoplasms (1). Previous reports show a female predominance with an age range of 32-79 years (mean=53) and a relatively good prognosis (1, 2). There is a documented tendency for paraganglioma of the urinary bladder to be misinterpreted as urothelial carcinoma (1-3). We report a case of bladder paraganglioma incidentally discovered in a female patient and diagnosed as muscle-invasive urothelial carcinoma. Patients and Methods: A 76-year-old woman was admitted to our hospital after recurrent episodes of vomiting for a hiatal hernia. A polypoid lesion of the bladder measuring 1 cm in diameter was incidentally found by computed tomography scanning. During surgery for hiatal hernia, she
underwent cystoscopy with trans-urethral resection of the bladder lesion. The specimen was submitted to histopathology examination and the diagnosis of “high-grade urothelial carcinoma, infiltrating the superficial muscular tissue” was rendered by a senior pathologist and a resident. After that report, the head of urology Department advised radical cystectomy; however, the patient denied asking for a second opinion. The original and additional slides were submitted to another centre and, on the basis of histological features, cromogranin A positivity and GATA-3 negativity, a diagnosis of paraganglioma, was proposed. Cystoscopy was repeated 3 and 6 months later in a third centre, with no significant endoscopic or histological finding. Sixteen months after the first observation, the patient is alive and well. Results: Retrospective examination of this case allowed us to establish that the error in the first diagnosis could be avoided, because pitfalls in distinction between paraganglioma and urothelial carcinoma are well-described in the literature. Appropriate immunostains could be of help in this task. Although significant cautery artefact involved most of the specimen, nested, zellballen pattern was recognizable. Large polygonal cells with eosinophilic cytoplasm had round nuclei with inconspicuous nucleoli. Mitoses were absent, as well as tumor necrosis. Muscular tissue was not observed after careful search. Neoplastic cells were diffusely immunoreactive for chromogranin A, whereas S100 strongly highlighted sustentacular cells. GATA-3 (not available in our laboratory) had been documented as negative in consultation. Discussion and Conclusion: As paragangliomas typically arise deep in the wall and are naturally permeative of muscularis propria, the pathologist may be led to diagnose muscle-invasive carcinoma (1). In a well-preserved specimen removed by partial cystectomy, the features of paragangliomas are easily appreciated, but most tumors are first encountered in transurethral resection material, where the typical histology is not always well-displayed because of fragmentation and cautery artifacts (1). The distinction between paraganglioma and muscle-invasive urothelial cancer is critical because of the extremely different therapeutic options (1-2). Localized paragangliomas are treated by transurethral resection, wedge resection or partial cystectomy. There is no need to follow patients with multifocal disease and there are no histologic criteria predictive of distant spread. Muscle-invasive urothelial carcinoma is treated by radical cystectomy and patients need to be followed for life for multifocal disease, with chemotherapy also used in advanced stages. Immunohistochemistry provides definitive answers, as paragangliomas are always positive for neuroendocrine markers, negative for cytokeratins, with S100-positive sustentacular cells (1, 2). GATA-3, a well-known marker of urothelial carcinoma, is often positive in paraganglioma (3) but, in the present case, gave negative results, definitely excluding urothelial carcinoma. In summary, the first diagnostic error could be avoided paying attention to routine histology, usually leading to correct diagnosis or raising the suspicion of paraganglioma and prompting immunohistochemical investigation. Furthermore, the urologist should have doubted the first diagnosis because it did not match the cystoscopic findings of an incidental lesion.


94 MULTIVARIABLE MODELS FOR URINARY SYMPTOMS AT 6-24 MONTHS AFTER RADICAL RADIOTHERAPY FOR PROSTATE CANCER

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Aim: To assess clinical and dose factors affecting the incidence of urinary symptoms between 6 and 24 months after therapy completion in patients treated with radical radiotherapy for prostate cancer. Materials and Methods: This study examined the dataset of a prospective study with patients treated with conventional (74-80 Gy at 1.8-2 Gy/fr) or moderately hypofractionated radiotherapy (RT) (65-75.2 Gy at 2.2-2.7 Gy/fr) in 5 fractions per week. Clinical factors were collected for each patient: comorbidities, drugs, hormone therapies, previous surgeries, smoking, alcohol, age, and body mass index. Bladder dose-volume histograms (DVHs) were corrected in the frame of the linear-quadratic model with alfa/beta=3Gy. Urinary symptoms were evaluated through the International Prostate Symptom Score (IPSS) and International Consultation on Incontinence Modular Questionnaire short form (ICIQ) questionnaires filled in by the patients at start/end of radiotherapy and every 6 months until 5 years of follow-up. We considered the sum of the 7 IPSS questions and the sum of questions 3-4 of ICIQ for the two end-points: (i) IPSS≥15 and (ii) ICIQ34≥4 at least once between 6 and 24 months after RT. The best predictors to be included in the logistic regression model were identified through backward feature selections on 1,000 bootstrap re-samplings: the reported normalized area (NArea) identifies the weighted occurrences of the variables at the leading positions. Then, multivariate regressions on 1,000 bootstrap re-samplings were employed to compute the odds ratio (OR) distributions of the selected variables and to have non-parametric calculations of the coefficients to be included in the model. Results: 539 patients were enrolled. Dose parameters and toxicity data at baseline and between 6-24 months were available for 195 (IPSS) and 197 (ICIQ) patients. 158/195 (81%) and 150/158 (95%) patients did not show toxicity at baseline (IPSS≤12 and ICIQ3=0, respectively). At 6-24 months, the incidence of IPSS≥15 was 42/158 (27%) and of ICIQ34≥4 was 34/150 (23%). A 6-variable model (area under the curve (AUC)=0.86) was considered for IPSS (details in Table I): baseline IPSS (NArea=0.72, OR=1.51) and the change of IPSS at radiotherapy end (deltaIPSS) (NArea=0.74, OR=1.16) were the leading risk factors. Bladder volume receiving >62Gy (V62Gy) was also a risk factor (NArea=0.36, OR=1.04), while the analogues and antiandrogens in hormone therapies were found protective (NArea=0.34, OR=0.38) and risk parameters (NArea=0.29, OR=2.57), respectively. The Figure shows toxicity probability as a function of V62Gy and baseline IPSS. For ICIQ, a backward feature selection was employed: antiaggregants (OR=2.16, p=0.11), antiandrogens (OR=2.03, p=0.08) and age (OR=1.09, p=0.04) were found as risk factors, whereas none dose parameter was found correlated with toxicity. Conclusion: The analysis showed an important correlation of urinary toxicities at 6-24 months with the patients’ urinary condition at baseline and, also, with the acute worsening of symptoms. Urinary symptoms were also found to be associated to the bladder volume receiving medium-high doses (around 60 Gy). Interestingly, hormone therapies with analogues (protective) and antiandrogens (risk) showed an opposite behaviour for late toxicities. The absence of correlation of incontinence with dose might be due to the very low number of severe toxicities registered.
Table I. Details of the 6-variable logistic model for prediction of International Prostate Symptom Score (IPSS) ≥15 in the first two years after the end of radiotherapy.

<table>
<thead>
<tr>
<th></th>
<th>Coefficient</th>
<th>Median OR</th>
<th>NArea for logistic regression (5˚perc-regression 95˚perc)</th>
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<tbody>
<tr>
<td>IPSS≥15 (baseline IPSS&lt;12)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delta IPSS</td>
<td>0.15</td>
<td>1.16 (1.09-1.25)</td>
<td>0.74</td>
</tr>
<tr>
<td>Baseline IPSS</td>
<td>0.41</td>
<td>1.51 (1.32-1.8)</td>
<td>0.72</td>
</tr>
<tr>
<td>Lymph node irradiation</td>
<td>1.15</td>
<td>3.17 (1.38-6.9)</td>
<td>0.58</td>
</tr>
<tr>
<td>Volume receiving &gt;62 Gy (%)</td>
<td>0.04</td>
<td>1.04 (1.01-1.07)</td>
<td>0.36</td>
</tr>
<tr>
<td>Hormone therapy with analogues</td>
<td>-0.97</td>
<td>0.38 (0.14-0.8)</td>
<td>0.34</td>
</tr>
<tr>
<td>Hormone therapy with androgens</td>
<td>0.94</td>
<td>2.57 (1.23-6.02)</td>
<td>0.29</td>
</tr>
<tr>
<td>Constant</td>
<td>-6.05</td>
<td></td>
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95

**RELATIONSHIP BETWEEN PATIENTS’ PERCEIVED IMPAIRMENT OF URINARY QOL AND URINARY SYMPTOMS AFTER PROSTATE CANCER RADIOTHERAPY**

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**Introduction/Aim:** DUE01 is a large multi-center prospective observational study, devoted to evaluation and modelling of urinary symptoms after prostate cancer radiotherapy. Patients who report urinary symptoms are recorded before radiotherapy and at different follow-up times after treatment. The aim of the current analysis was to determine which urinary symptom has the greater impact on impairment of urinary quality-of-life (QoL) as perceived by the patient. **Materials and Methods:** Patients were treated in 9 institutes with radical three-dimensional conformal radiotherapy /intensity-modulated radiation therapy (3DCRT/IMRT) for localized prostate cancer with conventional or moderate hypo-fractionation (2.35-2.7 GY/fr) filled in International Prostate Symptom Score (IPSS) and (International Consultation on Incontinence Questionnaire (ICIQ) before radiotherapy, at the end of treatment, at 3 and 6 months follow-up and thereafter every 6 months up to 5 years. Current analysis focused on IPSS question devoted to patients’ perceived urinary QoL. Operating characteristic (ROC) curves were used to analyze association between a severe impairment of perceived urinary QoL (binary end-point defined here above) and different urinary symptoms as measured by IPSS items 1 to 7 and ICIQ (continuous scores). The area under the curve (AUC) was calculated for each symptom and each follow-up measurement. **Results:** Severe impairment of patients’ perceived urinary QoL was reported in 50/499, 126/449, 25/412, 24/361, 23/339, 28/304 and 21/238 patients before radiotherapy, at treatment end and at 3-, 6-, 12-, 18-, 24-month follow-up, respectively. When considering total IPSS, AUC was quite constant over time, ranging from 0.84 to 0.90 without any significant differences. Interestingly, when considering single IPSS items (i.e. single urinary symptoms), AUC dramatically changed over time, with little difference among symptoms before radiotherapy (0.71-0.76) but, then, exhibiting very different pattern during follow-up. Urinary frequency (item#2), urgency (item#4) and nocturia (item#7) were highly associated with severe impairment of QoL at end of treatment and at 3-month follow-up (acute phase, AUC=0.77-0.87). In the mid-term (24 months), weak stream (item#5) was mainly associated to urinary QoL (AUC=0.87). Interestingly, the AUC for ICIQ continuously increases during follow-up from 0.62-0.63 at end of treatment up to 0.82 at 24 months. In Figure 1a and1b, ROC curves are shown for the different follow-up times for overall IPSS and ICIQ; AUC changes over follow-up are shown in Figure 1c. **Conclusion:** The analysis of a prospectively-followed cohort of patients with evaluation of patients reporting urinary symptoms, coupled to patients’ perceived urinary QoL, allowed evaluation of the symptoms that are significantly associated to severe impairment of QoL. IPSS shows a general good correlation with QoL. Some specific urinary symptoms (frequency, urgency, nocturia) have the strongest impact on QoL in the acute phase, while weak stream plays an important role at mid-term follow-up.
months). Urinary incontinence (ICIQ) has low impact on QoL before radiotherapy and in the acute phase, while its role was enhanced with increasing follow-up time.

**96**

**CYCLIN D1 SILENCING SUPPRESSES TUMORIGENICITY AND RADIOSENSITIZES ANDROGEN-INDEPENDENT PROSTATE**

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Figure 1. a) and b) ROC curves for the different follow-up times for overall IPSS and ICIQ. c) AUC changes over follow-up.
Introduction: Patients with hormone-resistant prostate cancer (PCa) have higher biochemical failure rates following radiation therapy (RT). Cyclin D1 deregulated expression in PCa is associated with a more aggressive disease; however, its role in radioresistance has not been determined. Materials and Methods: Cyclin D1 levels in the androgen-independent PC3 and 22Rv1 PCa cells were stably inhibited by infecting with cyclin D1-shRNA. Tumorigenicity and radiosensitivity were investigated using in vitro and in vivo experimental assays. Results: Cyclin D1 silencing interfered with PCa oncogenic phenotype by inducing growth arrest in the G1 phase of cell cycle and reducing soft agar colony formation, migration, invasion in vitro and tumor formation and neo-angiogenesis in vivo. Depletion of cyclin D1 significantly radiosensitizes PCa cells by increasing the RT-induced DNA damages by affecting the non-homologous end-joining (NHEJ) and homologous recombination (HR) pathways responsible of the DNA double-strand break repair. Following treatment of cells with RT, the abundance of a biomarker of DNA damage, γ-H2AX, was dramatically increased in sh-cyclin D1-treated cells compared to shRNA control. Concordant with these observations, DNA-PKcs-activation and RAD51-accumulation, part of the DNA double-strand break repair machinery, were reduced in shRNA-cyclin D1-treated cells compared to shRNA control. We further demonstrate the physical interaction between CCND1 with activated-ATM,-DNA-PKcs and RAD51, which is enhanced by RT. Finally, siRNA-mediated silencing experiments indicated DNA-PKcs and RAD51 are downstream targets of CCND1-siRNA-mediated silencing experiments. Following treatment of cells with RT, the abundance of a biomarker of DNA damage, γ-H2AX, was dramatically increased in sh-cyclin D1-treated cells compared to shRNA control. Concordant with these observations, DNA-PKcs-activation and RAD51-accumulation, part of the DNA double-strand break repair machinery, were reduced in shRNA-cyclin D1-treated cells compared to shRNA control. We further demonstrate the physical interaction between CCND1 with activated-ATM,-DNA-PKcs and RAD51, which is enhanced by RT. Finally, siRNA-mediated silencing experiments indicated DNA-PKcs and RAD51 are downstream targets of CCND1-mediated PCa cells' radioresistance. Conclusion: These observations suggest that CCND1 is a key mediator of PCa radioresistance and could represent a potential target for radioresistant hormone-resistant PCa.

Introduction/Aim: Radiobiological findings suggest an improvement in the therapeutic ratio for prostate cancer (PCa) treated with hypofractionation compared with conventional fractionation. On this basis, in 2012, we activated a prospective study on extreme hypofractionated image-guided intensity modulated radiation therapy (IG-IMRT) in organ-confined PCa. The aim of this study was to assess the feasibility of the proposed protocol “Give me five” in terms of acute and late toxicity and biochemical efficacy. Materials and Methods: The study was performed within the Institutional Ethics Committee notification regarding hypofractionated IGRT for PCa. Inclusion criteria were: low-to intermediate-risk (according to NCCN risk categories) histologically confirmed PCa; personalized indication for high-risk patients; prostate volume <100 cm³; N0 and cM0; age >18 years; specific informed consent. In 10% of patients, multiparametric magnetic resonance imaging (mp-MRI) was used for an improved definition of the patients’ anatomy, in addition to computed tomography (CT) imaging. The nominal prescription dose was 32.5 or 35 Gy scheduled in 5 fractions on alternate days (consequently, the name of protocol “Give me five”), namely 6.5-7 Gy/fraction, respectively, corresponding to a normalized total dose delivered at 2-Gy/fraction of 74.3 or 85 Gy, respectively, estimating an α/β ratio of 1.5 Gy. Dose delivery was performed with VERO®-BrainLab-Mitsubishi or RapidArc®-Varian. No fiducial markers were implanted and set-up verification was performed daily through cone beam computed tomography (CBCT) imaging. Toxicity was evaluated according to RTOG/EORTC scales. The study was founded by Associazione Italiana per la Ricerca sul Cancro - AIRC, grant no. 13218. Results: Between April 2012 and May 2015, 166 patients were eligible. All patients completed the treatment. Median follow-up was 12.5
months (range=6-32.7). Fifty-eight, 83, 24 and 1 patients out of 166 were at low-, intermediate-, high- and unknown risk, respectively. Median age was 74.3 years, median Gleason score was 6. Considering acute toxicity, 89.8%, 7.8%, 2.4% of patients had gastrointestinal G0, G1, G2 toxicity, respectively; 54.2%, 35.5%, 9.6%, 0.6% of patients had genitourinary G0, G1, G2, G4 toxicity, respectively. Late toxicity and outcome were assessed in 129 patients (6-month minimum follow-up). Considering late toxicity, 3.1% and 0.8% of patients had gastrointestinal G1 and G2 toxicity; 12.4%, 6.2% and 0.8% of patients had genitourinary G1, G2, G3 toxicity, respectively. Clinical and biochemical progression prostate disease was observed in 2/129 of patients; currently, there is no evidence of prostate disease in 127/129 patients. 

Conclusion: Longer time is needed to corroborate our encouraging early results in terms of toxicity, biochemical control rates, disease-free survival and overall survival. Our report showed that extremely hypofractionated IG-IMRT in localized PCa is feasible, safe and well-tolerated with good prostate-specific antigen response and minimal toxicity.

98
ABIRATERONE ACETATE: PROSPECTIVE EVALUATION OF THE CARDIOVASCULAR SAFETY PROFILE IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER PATIENTS

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Introduction/Aim: Abiraterone acetate (AA) is a potent inhibitor of CYP17, a crucial enzyme in testosterone and estrogen synthesis. The most common adverse events are associated with increased concentrations of mineralocorticoids and include hypokalaemia, fluid retention and hypertension, which are mitigated by concomitant administration of prednisone. The aim of this study was to evaluate the cardiotoxicity of AA in metastatic castration-resistant prostate cancer (mCRPC) patients (pts) with cardiovascular comorbidities or coronary artery disease (CAD) risk factors. Patients and Methods: We prospectively analyzed pts receiving AA for mCRPC who had experienced disease progression after docetaxel chemotherapy or after androgen-deprivation therapy. At baseline, we recorded for all pts CAD risk factors (hypertension, heart disease (HD), dyslipidemia, diabetes, tobacco smoke, obesity) and cardiovascular comorbidities (HD, rhythm disturbances, valvular disease and heart failure); we performed electrocardiogram (ECG) and echocardiography with evaluation of left ventricular ejection fraction (LVEF) and diastolic function at baseline, every 6 months and at the end of treatment. Cardiotoxicity has been defined as a median ≥10% LVEF reduction compared to baseline value or absolute LVEF value <50%. All clinical and instrumental variables and toxicity data were analyzed by descriptive statistics. We searched correlations between cardiotoxicity onset and CAD risk factors or cardiovascular comorbidities; results were assessed with paired Student’s t-test and Chi-square test. Results: Between November 2011 and December 2015, 87 consecutive pts, median age 66 years (range=50-81) were treated with 1,000 mg AA orally once daily and 5 mg prednisone twice daily. The median duration treatment was 9 months (1-44). Fifty-eight pts (66.7%) had received previous chemotherapy. At baseline, 84 pts (96%) had one or more CAD risk factors: 70 pts (80.5%) hypertension, 13 (15%) diabetes, 37 (42.5%) obesity, 31 (35.5%) dyslipidemia, 34 (39.1) tobacco smoke. Preexisting cardiovascular comorbidities included heart failure (9.2%), rhythm disturbances (16%) and valvular disease (13%). On AA therapy, 26 pts (30%) worsened the preexisting HD and 4 pts (4.6%) developed HD, which was controlled with adequate medical treatment according to American Heart Association guidelines, without determining treatment discontinuation. Two pts (2.3%) developed atrial fibrillation during AA treatment. Median LVEF at baseline was 64% and 63% after AA treatment. LVEF reduction and diastolic function changes were not statistically significant (p<0.005). Conclusion: AA appears to be safe and well-tolerated even in pts with cardiovascular comorbidities or CAD risk factors. A cardiovascular monitoring during AA treatment is recommended to optimize the clinical management of these pts.

99
ANDROGEN DEPRIVATION DYNAMICALLY MODULATES THE EXPRESSION OF GENES INVOLVED IN PROSTATE CANCER PROGRESSION

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Aim: To analyze in vivo and in vitro the dynamic modulation of gene expression profile along prostate cancer progression determined by androgen-deprivation therapy (ADT).

Materials and Methods: ERG:TMPRSS2, WNT-11, SPINK-1, CgA, AR and PDEF gene expression was analyzed by means of real-time polymerase chain reaction (PCR) in a series of 78 surgical samples of prostate carcinomas, including 47 cases pre-operatively treated with androgen deprivation (ADT+) and 31 untreated cases (ADT-) and, also, in 43 corresponding biopsies. The same genes were analyzed in androgen-deprived and control LNCaP cells. Results: Three genes were significantly up-modulated (WNT-11 and AR) or down-modulated (PDEF) in ADT+ vs. ADT- cases, as well as in androgen deprived LNCaP cells. The effect of ADT on CgA gene up-modulation was almost exclusively detected in cases positive for the TMPRSS2:ERG fusion. The correlation between biopsy and surgical samples was poor for all genes tested. Gene expression analysis of separate tumor areas from the same patient showed an extremely heterogeneous profile in all 6 untreated cases tested. Discussion and Conclusion: Our results demonstrate that ADT induces relevant transcriptional modifications, potentially associated to the onset of a more aggressive phenotype. However, intra-tumoral heterogeneity limits the use of this gene as a potential prognostic or predictive biomarker in patients treated with ADT.

100
ACTIVE SURVEILLANCE OR RADICAL TREATMENT FOR LOW-RISK PROSTATE CANCER PATIENTS: THE START PROJECT

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Introduction/Aim: An active surveillance (AS) strategy is recommended as an appropriate management for men with low-risk localized prostate cancer (PC); however, its diffusion, at least in the Oncology Regional Network of Piedmont and Valle d’Aosta, is still very limited. The central hypothesis of the START project is to evaluate the acceptability, safety and cost-effectiveness of a population-based program of AS, whose implementation into routine practice will be encouraged within the setting of a research framework. Specific objectives are to (i) encourage the diffusion of AS at a regional level, in the context of a research project based on standardized and settled criteria for patients’ selection and management; (ii) supply to all newly diagnosed low-risk PC patients standardized information about the benefits and risks of the available treatments, including AS, to allow an informed choice; (iii) involve patients and citizens in the project design and management; (iv) compare, at a population level, the clinical outcomes, quality of life and costs associated to different treatment choices. Materials and Methods: Comparative effectiveness research project. All newly diagnosed PC patients fulfilling the low-risk definition, residents in Piedmont or in Valle D’Aosta, will be invited to participate to this observational prospective study. All enrolled patients will receive full and clear information about their prognosis together with a balanced synthesis of the benefits and risks of the available treatments. For all participating patients, independently from the treatment chosen, baseline clinical, histological and psychological data, any treatment received and follow-up data (including clinical and quality-of-life (QoL) outcomes) will be collected through an electronic case report form (eCRF). Patients accepting AS will be offered a structured follow up program. Clinical, QoL and costs outcomes will be compared according to the different treatment choices. We plan to enrol about 3,000 patients. Results: The START protocol has been designed by a multidisciplinary panel of specialists of the Regional Oncology Network, including urologists, radiotherapists, epidemiologists, pathologists, oncologists and patients’ representatives. All the regional Hospital units of Urology and Radiotherapy have been involved (36-center
ASSOCIATION BETWEEN STEROID HORMONES’ LEVELS AND ABIRATERONE ACTIVITY IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER PATIENTS

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Introduction/Aim: Abiraterone acetate (AA) is an inhibitor of CYP450 that impairs androgen signaling by depleting adrenal and intratumoral androgens. It is approved for treatment of patients (pts) with castration-resistant prostate cancer (mCRPC). The aim of this study was to describe changes in hormonal levels determined by AA and explore the association between levels (both baseline and changes) of hormones implied in steroid biosynthesis or changes induced by AA and treatment activity.

Methods: After local ethical committee approval and after failure with docetaxel, patients with mCRPC were prospectively enrolled in this mono-institutional study between June 2010 and December 2010. AA 1000 mg daily + prednisone 5 mg twice daily was administered until disease progression or unacceptable toxicity. Serum levels of progesterone, 17OH-progesterone, cortisol, dehydroepiandrosterone (DHEA) sulphate, androstenedione, testosterone, sex hormone binding globulin, aldosterone, plasma renin activity, adrenocorticotropic hormone (ACTH) and cholesterol were determined at baseline and every 12 weeks, until progression. Hormonal levels at baseline vs. subsequent samples were compared by Wilcoxon matched-pairs test. Association between hormones and treatment activity (≥50% prostate-specific antigen –PSA- reduction) was tested for comparing (i) baseline levels of responders vs. non-responders; (ii) progression-free survival (PFS) of pts with baseline low vs. high values of each hormone; (iii) levels after 12 weeks of responders vs. non-responders, adjusted by baseline levels. Results: Forty-nine pts were included in the analysis (median age=70, ECOG PS 0/1/2 61%, 33% and 6%, respectively, median baseline PSA=116.95%). Eighty-two percent were metastatic to bone. PSA reduction was obtained in 26 pts (53.1%). Median PFS was 10.2 months. Baseline levels of all hormones were not statistically different between responders and non-responders. For all hormones, difference in PFS of pts with low baseline values vs. pts with high baseline values was not statistically significant. Several hormones showed significant and sustained changes vs. baseline, but all significant changes were similar between responders and non-responders. Conclusion: Although limited by low statistical power, our exploratory analysis does not suggest a significant association between baseline levels of hormones implied in steroid biosynthesis or changes induced by AA and treatment activity.

NEUROENDOCRINE DIFFERENTIATION OF CWR22R CELLS GROWN IN NUDE MICE IN PRESENCE OF BONE MARROW STROMAL CELLS AND ANDROGEN DEPRIVATION CONDITIONS

Giovanni Luca Gravina, Andrea Mancini, Alessandro Colapietro, Antonella Vetuschi, Roberta Sferra, Patrizia Sanità, Simona Pompili, Francesco Marampon, Simona Delle Monache, and Claudio Festuccia

Introduction: Prostate cancer (PCa) is usually characterized by an excellent prognosis, largely due to little biological aggressiveness and the power of hormonal deprivation therapy. In spite of these favorable characteristics, however, a significant quota of patients does not respond to androgen deprivation therapy (ADT) and develop a progressive disease until to castration-resistant stage (CRPC). PCs that has metastasized to bone undergoes critical interactions with bone marrow stromal
cells, ultimately promoting tumor survival. Previous studies have shown that bone marrow stromal cells (BMSCs) secrete factors that promote early tumor cell apoptosis and a late tumor survival and growth. This new growth is associated both to cancer stem cell proliferation and neuroendocrine (NE) differentiation. Materials and Methods: We injected a mixture (1:100) of 22rv1 PCa cells and murine bone stromal cells in the flank of intact or castrated male nude mice and analyzed the growth of tumors obtained with this mixture in comparison with tumors obtained from the 22rv1 alone. PC3, PCb2, VCaP and C4-2B (bone derived PCa) or 22rv1 and DU145 (primary and brain derived PCa) were tested for apoptosis and NE differentiation in vitro in co-cultures with BMSCs or in presence of conditioned media from BMSCs. Western blots, Elisa determinations for TGF-β1 levels and SMAD phosphorylation status, during apoptosis or NE differentiation, were tested. Results: The inoculation of BMSCs alone was not able to grow in subcutaneous engraftment. Although 22rv1 cells are a model for primary non-bone metastatic CRPC, these cells maintain sensibility to androgens. We observed that tumors originated from 22rv1/BMSC mixture are larger than tumors originated from 22rv1 alone. This difference was higher when compared to tumors grown in castrated nude mice. Because of the significance of TGF-β family cytokines in cytostasis and bone metastasis, the role of TGF-β1 was investigated in the context of PCa-BMSC interactions. 22rv1 cells basally express neuron-specific enolase (NSE) and chromogranin A. The expression of these neuroendocrine markers was, however, increased in tumor grown in castrated nude mice. The presence of BMSCs increases angiogenesis, mesenchymal recruitment and favors the growth in absence of androgens. In vitro, we showed that neuroendocrine phenotype, acquired in co-culture conditions between 22rv1 and BMSCs and culturing 22rv1 cells with exogenous TGF-β1, was associated to increased pro-inflammatory cytokine expression and THP-1 monocyte/macrophage recruitment. However, PC3, PCb2, VCaP and C4-2B showed a reduced NE differentiation in presence of BMSCs or TGF-β1. Moreover, PC3 cells, grown in the bone marrow of tibia (intratibial engraftment), showed, instead, an increased expression of cancer stem cell markers (CD44 or CD133). We believe that NE differentiation represents an alternative mechanism to evade PCa apoptosis in the bone, which might overcome androgen pressure through increased expression of androgen insensitive tumor cancer stem cell population born in the highly hypoxic bone marrow niche. Conclusion: The use of drug targeting cancer stem cell development (TGF-β1 blocking antibodies or TGFBRI inhibitor) or the growth of neuroendocrine PCa cells by somatostatin antagonists might be used for the treatment of bone metastatic PCa.
cytokeratin 8). The induction of pro-MMP9 and uPA was also associated to matrigel invasion. PC3 and22rv1 cells induce the expression of arginase-1 and reduce eNOS, supporting a role in the M2 polarization.

**104 NEPHRON-SPARING SURGERY FOR RENAL MASSES >4 CM (CTIB-T2) IN PATIENTS WITH CHRONIC RENAL FAILURE**

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**Aim:** The aim of this study was to evaluate functional and oncological outcomes in nephron-sparing surgery (NSS) in large renal masses (T1b/2) in patients with chronic renal failure (1). **Patients and Methods:** In our Urology Department, 70 patients underwent NSS (enucleo-resection) (2). Among these cases, 24 patients underwent conservative surgery for tumours >4 cm: 18 cT1b and 6 with cT2; median diameter was 6.4 cm (4.2-12) and median RENAL score was 7.5 (4-10); Renal score grouping was 7 pts (29%) with score 4-6, 15 (62.5%) 7-9 and 2 (8.3%) with score 10. Chronic renal failure (CRF) was staged according to pre-operative estimated glomerular filtration rate (eGFR) measurement: stage I in 10/24 (41.7%) patients, stage II in 7/24 (29.2%), stage III in 5/24 (20.7%), stage IV in 1 (4.2%), stage V in 1 (4.2%). Only 1 patient had a single kidney unit. **Results:** We performed open flank incision and retroperitoneal approach. Warm ischemia (WI) was used in 10/24 (42%) cases and no clamping in 14/24 cases (58%) with controlled hypotension. WI time (WIT) was 19 s (12-26). Any intra- or post-operative nephrectomy was performed. To verify intraoperative urine leakage, we used saline flushing from the ureteral catheter in 13/24 cases. Mean blood loss was 337.5 ml (0-700): 2/24 (8.3%) required blood transfusion (1 unit). Renal function worsened in 3 pts (12.5%) belonging to stage II and III, with 1 stage decline. The 5-day post-operative eGFR was assessed as stage I in 10 (41.7%), stage II in 6 (25%), stage III in 5 (20.7%), stage IV in 2 (8.4%), stage V in 1 (4.2%). All patients underwent at least abdominal computed tomography/magnetic resonance imaging (CT/RMI) in the follow-up: no urinary fistula, delayed bleeding or artery-venous fistula has been observed after a mean of 24 months of follow-up (8-48). 18/24 patients had pathological diagnosis of renal neoplasm; focal positive margin was observed in 3 (12.5%). One local recurrence (4.2%) with single lung metastasis was treated with nephrectomy and lung resection 16 months later after renal surgery for a mass with renal sinus extension (pT1bR0). **Discussion:** Tumor diameter itself and location are not contraindications to conservative surgery in cortical renal tumor; however, sinus tumor volume touching the renal sinus may have a higher risk of local recurrence linked to early endovascular microscopic tumour invasion. Risk of recurrence is linked to wide contact with renal sinus for 2 reasons. First, pathological evaluation of surgical margins in the adipose tissue is difficult to evaluate based on resection specimen and, second, tumour is enucleated from the adipose tissue of the renal sinus leaving intact as much as possible main vessels and collecting system, while cortical tumour is resected on normal looking parenchyma rim around the tumour pseudocapsule. Therefore, safety margin in sinus tumour is difficult to obtain without significant morbidity or wedge resection. **Conclusion:** Conservative NSS (enucleo-resection) for renal masses >4 cm, if technically feasible, can represent a valid approach in patients affected by CRF. In our experience, ischemia can be avoided in 58% of cases without significant bleeding. Although in cortical tumor the diameter or location is not a contraindication to NSS, the sinus tumor extension may be an oncological concern to NSS using enucleo-resection.


Introduction/Aim: Despite improvements in surgical techniques, anesthesia and perioperative care, radical cystectomy (RC) is still associated with significant morbidity and prolonged in-patient stay after surgery. Enhanced recovery after surgery (ERAS) protocols are multimodal perioperative care pathways designed to achieve early recovery after surgical procedures by maintaining pre-operative organ function and reducing the stress response following surgery. In the past, we have already demonstrated that ERAS protocols may improve perioperative results after RC when compared with standard protocols. The aim of this study was to present our 5-year experience with the use of ERAS protocols after RC and urinary diversion. Materials and Methods: We retrospectively reviewed our prospectively maintained database of RC and extracted the data of 120 patients (pts) treated with RC and urinary diversion (i.e. Bricker intervention [BrI] n=79; or Y neobladder[YNb] n=41), managed with the ERAS protocol between January 2011 and September 2015. Briefly, our protocol includes: no oral bowel preparation, combined anesthesia (general-epidural without opioids), removal of naso-gastric tube at the end of the surgery, oral clear fluids on day of surgery, parenteral and enteral nutrition in post-operative day (POD) 1, as well as mobilization in POD2. Peristalsis recovery, time to flatus and to pass stool, restored oral intake, mobilization, drain removal and complications (classified according to Clavien system) were recorded. For the purpose of this study, stable health status was defined as no drain, complete and free mobilization, standard oral intake and regular bowel function. Satisfaction of the patients in terms of ERAS protocol was investigated with a Likert type scale (1, very unsatisfied; 2, unsatisfied; 3, uncertain; 4, satisfied; 5, very satisfied). Results: Mean age, body mass index (BMI) and rate of male pts of the whole cohort were 69.5 years, 25.5 kg/cm² and 88%, respectively. Overall, time to peristalsis recovery, time to flatus and time to pass stool were 2, 2.3 and 4.1 days, respectively. Time to oral intake was 2.2 days, respectively. Time to oral intake was 2.2 days and mobilization was recorded after 1.6 days, respectively. Drain was removed after 3.9 days. Time to stable health status was 4.3 days. Ten patients (13.2%) dropped out due to complications, among these, high grade (>II) complications were recorded in 10 cases (100%). One-hundred (87.5%) patients were satisfied or very satisfied with ERAS program. When considering and comparing the results of the BrI and YNb, no differences were recorded for all the evaluated variables. Conclusion: The results of this study suggested that ERAS protocol allowed a fast return to bowel function and a short time to stable health status with acceptable complication rate. Not surprisingly, no differences between the two groups, in terms of the evaluated variables, were recorded. Finally, this program is well-accepted by the patients. Since ERAS protocols in urologic scenario is rather limited, the use of these protocols should be implemented in clinical practice.

106 RESULTS OF NEPHRON-SPARING SURGERY WITHOUT VASCULAR CLAMPING IN PATIENTS WITH CHRONIC RENAL FAILURE

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2Department of Urology, "Murri" Hospital, Fermo (AN), Italy;
3Department of Pathology, Università Politecnica Delle Marche, Ospedali Riuniti Di Ancona, Ancona (AN), Italy.

Aim: The aim of the study was to evaluate functional and oncological outcomes in nephron-sparing surgery (NSS) in patients (pts) with chronic renal failure (CRF) (stage II-V) without vascular clamping. Patients and Methods: We evaluated 73 consecutive pts who were scheduled for nephron-sparing surgery (NNS) in our center (1) and analyzed 35 with CRF as assessed by pre-operative estimated glomerular filtration rate (eGFR) less than 90. A single surgeon performed all procedures using main artery clamping as needed during enucleo-resection with open technique and retroperitoneal approach. Vascular clamping time was defined and warm ischemia (WI) time assessed in minutes. Baseline tumour stage in 73 pts was: 49 (67%) cT1a, 18 (25%) cT1b, 6 (8%) cT2. Median RENAL score was 7.05 (4-11): 28 (40%) 4-6, 35 (50%) 7-9 and 7 (10%) with 10-12 score. Two pts (3%) had multiple masses in the same kidney with 2 and 5 lesions, respectively. One patient had a single kidney unit. CRF was staged according to pre-operative eGFR measurement: normal or minimally reduced renal function (RF) stage I in 35/70 (50%) patients, stage II in 21/70 (30%) with eGFR 60-89, stage III in 11/70 (15.7%) with eGFR 30-69, stage IV in 2 (2.9%) with eGFR 15-29, stage V in 1 (1.4%) with eGFR <15. Results: We performed vascular clamping in 27/70 (38.6 %) cases and no clamping in 43 (61.4%). Median WI time was 15 s (5-26), including 2 cases of super-elective artery clamping. Mean blood loss was 290 ml (0-900 ml): 5/70 (7.1%) required blood transfusion (1 unit). To verify intraoperative urine leakage, we used saline flushing from the ureteral...
catheter in 29/70 (41.4%) cases. Different outcomes were found relating to eGFR between clamping vs. no clamping cases as reported in Tables I and II. NNS was technically feasible in 70 of 73 pts (96%): 1 was converted to total nephrectomy for incomplete tumor resection and 2 for bleeding and incomplete vascular control (1). RF worsened in 14 pts (20%) belonging to stage I, II and III, with 1 stage decline in 13 pts (18.6%) and 2 stages decline in 1 pt (1.4%). The 5-day post-operative eGFR was assessed as stage I in 30 (42.9%), stage II in 19 (27.1%), stage III in 16 (22.9%), stage IV in 4 (5.7%), stage V in 1 (1.4%). All patients underwent at least abdominal computed tomography/ magnetic resonance imaging (CT/RMI) in the follow-up: no rinary fistula, delayed bleeding or artery-venous fistula has been observed after a mean 24 months (8-48). 64/70 pts had pathological diagnosis of renal neoplasm; a focal positive margin was observed in 7/70 (10%). One local recurrence (1.4%), with single lung metastasis, was observed after 16 months (pT1bR0).

Discussion: Vascular clamping was delayed until significant bleeding obscured the surgical field to avoid inappropriate surgical resection. In order to have a well-defined dissection margin, only sharp dissection with scissors was used and no electrocautery or laser energy was applied during or enucleo-resection. Early vascular declamping was done as soon as medullary tissue stitching was completed.

Conclusion: Conservative enucleo-resection surgery in patients with renal masses with CRF is feasible in 96% of candidates. In order to maintain renal function, vascular clamping can be avoided in more than 60% cases and, if vascular clamping is needed (40%), WIT is limited to a mean of 15 min.

Table I. Pre-operative RF and tumor features in patients undergone NSS.

<table>
<thead>
<tr>
<th>Pre-operative RF</th>
<th>N’pts No clamping clamping</th>
<th>WIT&lt;10s</th>
<th>WIT≥10s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I (Normal)</td>
<td>35 20 (57%) 15 (43%) 4 (11%) 11 (32%)</td>
<td>11 (32%)</td>
<td></td>
</tr>
<tr>
<td>Stage II</td>
<td>21 11 (52%) 10 (48%) 0 (0%) 10 (48%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage III</td>
<td>11 9 (82%) 2 (18%) 1 (9%) 1 (9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IV-V</td>
<td>3 3 (100%) 0 (0%) 0 (0%) 0 (0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>70 43 27 5 22</td>
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<table>
<thead>
<tr>
<th>Renal score</th>
<th>N’pts No clamping clamping</th>
<th>WIT&lt;10s</th>
<th>WIT≥10s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low 4-6</td>
<td>28 22 (79%) 6 (21%) 2 (7%) 4 (14%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium 7-9</td>
<td>35 18 (51%) 17 (49%) 3 (9%) 14 (40%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High 10-12</td>
<td>7 3 (43%) 4 (57%) 0 (0%) 4 (57%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>70 43 27 5 22</td>
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</tbody>
</table>

Table II. Functional outcomes in patients undergone NSS.

<table>
<thead>
<tr>
<th>Post-operative RF</th>
<th>N’pts No clamping clamping</th>
<th>WIT&lt;10s</th>
<th>WIT≥10s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I (Normal)</td>
<td>30 20 (67%) 10 (33%) 2 (7%) 8 (26%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRF stable</td>
<td>56 39 (70%) 17 (30%) 3 (5%) 14 (25%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRF worse</td>
<td>15 5 (33%) 10 (67%) 2 (13%) 8 (54%)</td>
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107 PATHOLOGIC REPORTS’ CONCORDANCE IN REVIEWING BIOPSIES FROM PRIAS-ITA PROSTATE CANCER PATIENTS

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Introduction: Active surveillance (AS) is aimed to limit overtreatment and treatment-induced side effects in patients (pts) with low grade, localized, clinically indolent prostate cancer. Histopathologic features play a crucial role in the inclusion and follow-up of pts and may need to be confirmed through the revision of the biopsy samples carried out in other hospitals, since the literature shows a significant inter-observer discrepancy in the Gleason's score assessment. Methods and Results: Between January 2012 and March 2015, the Unit of Adult Uropathology and Histopathology at Milan National Cancer Institute reviewed prostate biopsies of 448 pts eligible for AS that had been performed in other centers. The following concordance standards, based on the original pathological reports and the second opinion, were evaluated: (i) concordance of the diagnosis of cancer or prostatic intraepithelial neoplasia
(PIN); (ii) identification of sample location of each biopsy core and the pathological report of each core; (iii) concordance between the grading of the diagnostic biopsies and the one confirmed by the review (Gleason score modified according to ISUP 2005). The review confirmed the histopathology characteristics of 372/448 pts (83%) eligible for AS. The pts, eventually, included in AS were 333 (74%). The remaining 39 pts (9%) decided to undergo treatment (surgery, external radiotherapy, brachytherapy) or be followed up elsewhere. The revision showed one or more changes of the histopathologic data in 76/448 pts (17%) who were, thus, not considered suitable for enrolling. The number of cores, which varied from 2 to 48, was adequate to the prostate volume (at least 8 cores for prostate volume up to 40 cc, 10 for prostate volume between 40 and 60 cc, 12 for prostate volume larger than 60 cc) except in 3 cases. In the revision, the number of positive biotomic cores varied from 0 to 6. Of the 76 cases showing changes of the histopathology characteristics, 20 were referred to the number of positive cores (sizing), 44 to grading variation and 12 to both sizing and grading modifications. Although the change of the grading for 3 pts permitted the inclusion in AS (Gleason confirmed as 3+3), they were not enrolled due to other reasons. Two pts who had a positive diagnostic biopsy showed no cancer at the revision. The number of biopsy cores that showed changes of the Gleason score after the review was: 1 core in 40 pts, 2 in 6 pts, 3 in 3 pts, 4 in 2 pts, 5 in 3 pts, 6 or 8 in the remaining 2 pts. In most cases, the variation consisted in the upgrading from Gleason 3 to 4. Out of the 76 cases with one or more changes of the histopathologic characteristics, 20 were selected, digitalized and examined by 3 uropathologists (EB, CP, MF) of the SIURO-PRIAS Italian AS working group. In 19/20 cases, a diagnostic concordance of at least 2 out of 3 pathologists of the grading proposed by the reviewer (MC, BP) was achieved. Conclusions: In 76/448 pts (17%), the centralized review permitted to show changes of the histopathology features of the diagnostic biopsies. Our analysis aimed at stressing the need for improved intra-observer reproducibility in the analysis of prostate biopsies. This result could be achieved with pathologists dedicated to uropathology and being aware of the compliance of shared guidelines as requested in AS protocols.

Introduction/Aim: Observational studies conducted in a ‘field-practice’ setting can provide valuable clinical information about the safety and effectiveness of cancer therapies and represent an additional, real-world source of clinical information. Vinflunine was approved by the European Medicines Agency in 2009 as a second-line treatment for patients with urothelial carcinoma resistant to first-line platinum-containing chemotherapy. A number of observational studies have recently been conducted to investigate vinflunine in the treatment of platinum-resistant, metastatic bladder cancer. Thus, a pooled analysis of efficacy and safety results of available trials is presented here. Materials and Methods: Endpoints of the analysis were objective response rate (ORR), progression-free survival (PFS), overall survival (OS) and the incidence of acute, grade 3-4 (according to CTC-AE), neutropenia, anemia and constipation. PFS was defined as the time from starting treatment until objective tumor progression or death; time to progression was used whenever it was reported instead of PFS since it was judged an acceptable estimator of PFS in the analyzed studies. Random-effects models, using inverse variance weighting, were used to pool trial-level data. For each study, the standard error (SE) of the median OS or PFS was derived from the respective 95% confidence interval (CI). The statistical analyses were carried out using R software. All tests and CIs were two-sided.

Results: Nine trials were eligible for the review and 8 (accounting for 615 patients) were included in the analysis. Time to event, efficacy results are presented in Table I and incidence rates concerning both activity and safety are presented in Table II. Discussion: On comparing our results with those from the Vinflunine-registrative, phase III study (Bellmunt et al., 2009), better activity, efficacy and safety results were observed. Confounding due to both patient selection according to daily practice and different accuracy in end-point assessment may account for that diversity. However, despite the limitations inherent in observational trials, this analysis demonstrates that the efficacy and safety of vinflunine therapy -as observed in the controlled, randomized study- is transferable in the daily routine of clinical practice.

Table I. Time-to-event efficacy results.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Median estimate</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>I-squared (p-Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PFS*</td>
<td>3.836</td>
<td>2.628</td>
<td>5.045</td>
<td>55.637 (0.061)</td>
</tr>
<tr>
<td>OS*</td>
<td>8.248</td>
<td>0.488</td>
<td>7.292</td>
<td>14.389 (0.317)</td>
</tr>
</tbody>
</table>

*According to Kaplan-Meier; †random effects model; ‡95%CI
QUALITY OF LIFE AT TIME OF DIAGNOSIS OF PROSTATE CANCER: PRELIMINARY RESULTS OF THE PROS-IT CNR STUDY

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Introduction/Aim: Physical and mental health, urinary symptoms and erectile function of men with a newly diagnosed prostate cancer (PCa) are determinants for the clinical outcomes after radical treatment. Aim of present study is to evaluate, in a large cohort of consecutive patients, the general health and the cancer-specific quality of life (QoL) at the time of the diagnosis of PCa.

Materials and Methods: QoL of the enrolled patients was assessed by SF-12 (Physical Component Summary (PCS) and Mental Component Summary (MCS)), as well as UCLA-PCI (Urinary Function/Bother (UF,UB), Sexual Function/Bother (SF, SB) and Bowel Function/Bother (BF, BB)). The differences between subjects enrolled in urologic centers (URO) and radiotherapy and oncology centers (RO) were evaluated through the Generalized Linear Model procedure on the ranked data, adjusting for age at diagnosis. Spearman’s rho non-parametric correlation coefficients between symptoms and bother were also calculated.

Results: A total of 1,684 men were enrolled: 996 patients (59.1%) in URO and 688 (40.9%) in RO centers. The average PCS was 51.8±7.5, while the average MCS was 49.3±9.6. The average UCLA-PCI scores at enrollment were: UF=93.1±15.9, UB=88.5±23.5, BF=93.8±17.8, SF=49.4±32.1 and SB=64±35.1. Age, was the main determinant of the general and prostate cancer-specific health (all items: <0.01). We reported remarkable differences between URO vs. RO populations in MCS (48.8±9.6 vs. 50.1±9.6, p=0.0446) but not in PCS (52.2±7.3 vs. 51.2±7.7, p=0.8858). Moreover, we identified significant differences between URO and RO patients regarding urinary symptoms (UF=93.1±15.9 vs. 91.6±17.5, p=0.0350; UB=88.5±23.5 vs. 85±25.7, p<0.0001), sexual activity (SF=56.8±30.6 vs. 38.6±31.2, p<0.0001, SB=68.2±33.2 vs. 57.8±36.8, p=0.0001) and bowel function (BF=94.9±11.6 vs. 92.2±14.7, p=0.0015). We reported a strong or moderate correlation between UF-UB (a) and BF-BB (b) in both URO and RO centers.
and RO populations (0.5 ≤ ρ ≤ 0.63), while we found remarkable differences between SF-SB (c) in the subgroup of RO men (ρ = 0.38, indicating a weak correlation, see Figure 1).

Conclusion: Pros-IT CNR is a multicenter, observational, prospective cohort study on PCa in Italy. The preliminary data, regarding the QoL at time of diagnosis, underline the remarkable differences between men enrolled in URO vs. RO centers, in particular, regarding mental health and sexual activity.

111
COMORBIDITIES AND CONCOMITANT MEDICATIONS AT TIME OF DIAGNOSIS OF PROSTATE CANCER: DATA FROM THE PROS-IT CNR STUDY

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Introduction/Aim: Prostate cancer (PCa) is a significant health concern and increases in prevalence as the population ages. Several comorbidities may coexist in elderly men affected by PCa, requiring several medications. Aim of the present analyses, based on Pros-IT CNR (a multicenter, observational, prospective cohort study), is to evaluate the comorbidities and the medications of men with PCa at the time of the diagnosis. Materials and Methods: A structured interview was used to record comorbidities and drugs’ assumptions. The severity of comorbidities was measured by the Cumulative Illness Rating Scale. Drugs used by patients were classified using the Anatomical Therapeutic Chemical classification. Quality of life (QoL) was assessed by the SF-12 (Physical Component Summary (PCS) and Mental Component Summary (MCS)) and UCLA-PCI (Urinary Function/Bother (UF,UB), Sexual Function/Bother (SF,SB) and Bowel Function/Bother (BF,BB)). The differences between the characteristics of the men enrolled in urologic (URO) and radiotherapy and oncology centers (RO) were assessed, adjusting for age at diagnosis, considering logistic regression or generalized linear models on the ranked data.

Results: A sum of 1,684 patients was consecutively enrolled: 996 patients (59.1%) in URO and 688 (40.0%) in RO centers: CIRS data were available from 1637 patients. Moderate, severe or very severe diseases (MSVS), according to CIRS, were recorded in: a) 445 subjects (27.2%) at vascular, lymphatic or hematopoietic level, b) 304 (18.6%) at cardiac apparatus, c) 231 (14.2%) at gastroenteric localization, d) 163 (10%) at neurologic site. The presence of ≥3 MSVS comorbidities had a significant negative impact on PCS, MCS, UB, BF and BB, SF as compared to 0-2 MSVS comorbidities (all: p<0.001). After age-adjustment, diabetes was more frequent in RO center vs. URO (18.4% vs. 11.4%, p=0.0082). Moreover, men enrolled in URO centers were more frequently affected by MSVS gastroenteric disease (18.8% vs. 7.5%), abdominal hernia (5.7% vs. 4.8%) and neurogenic disease (11.4% vs. 7.9%). 74.3% of the enrolled men took drugs for the circulatory system, 36.7% of men was under treatment with antithrombotic agents, 34.2% for the digestive system (21.8% for acidosis) and metabolism (14.4% hypoglycemic drugs). About a third of the patients enrolled in the study (31.6%) used urological drugs (for lower urinary tract symptoms (LUTS) or erectile dysfunction (ED). We found a significant difference between URO and RO populations regarding the use of antithrombotic agents: 32.5% URO vs. 44% RO (p=0.0377).

Conclusion: Our preliminary data demonstrate that number and severity of comorbidities had a remarkable negative impact on QoL of men at diagnosis of PCa. Moreover, men enrolled in urologic centers present a different pattern of associated diseases and medications as compared to those enrolled in radiotherapy/oncology centers that can determine the treatment choice and the clinical outcomes.

112 COMPLEMENTARY VALUE OF CONTRAST-ENHANCED ULTRASOUND (CEUS) IN THE DIAGNOSTIC ALGORITHM OF COMPLEX RENAL CYSTS

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Aim: To assess the role of contrast-enhanced ultrasound (CEUS) in the diagnostic algorithm of complex cysts, classified following the Bosniak system, compared with contrast-enhanced computed tomography (CECT). Materials and Methods: From March 2011 to September 2013, we selected 42 patients who underwent CECT after ultrasound (US) finding of complex renal cysts (Bosniak>II F). All patients were also evaluated with CEUS within a week. Two independent radiologists analyzed results of both techniques. Therapeutic approach was planned based on the highest grading CECT or CEUS. Results: CECT images found 14 B-II, 8 B-IIIF, 9 B-III and 11 B-IV, while CEUS images found 12 B-II, 13 B-IIIF, 6 B-III and 11 B-IV. CEUS upgraded CECT Bosniak grading from B-II to B-IIIF in 2 cases, from B-IIIF to B-III in 3 cases and downgraded from B-III to B-IIIF in 6 cases. Complete concordance between CEUS and CECT was observed in B-IV graded cysts. All B-III and B-IV cysts (23/42) underwent surgery and pathological findings documented 4 benign lesions and 19 malignant lesions. CET overestimated only 1 malignant lesion resulting minimal-fat angiomylipoma with no case of downstaging. All other patients were under imaging follow-up, showing morpho-dimensional stability at 2 years. Conclusion: CEUS showed promising results evaluating renal complicated cysts, especially differentiating B-IIIF from B-III with better results than CECT; therefore, CEUS should be considered in diagnostic algorithm of renal complex cysts as a second step imaging tool after B-mode US to better screen lesions that will require CECT planning before surgery.
113
LONG-TERM OUTCOMES AND PREDICTIVE FACTORS IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER SHOWING ABRIRATERONE WITHDRAWAL SYNDROME AFTER DOCETAXEL TREATMENT

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Introduction/Aim: Abiraterone acetate (AA) is able to improve overall survival (OS) of metastatic castration resistant prostate cancer (mCRPC) patients (pts) in both first- and second-line treatment. Abiraterone withdrawal syndrome (AWS) has been rarely described as a possible prostate-specific antigen (PSA) reduction parameter, with or without radiological responses, observed after AA suspension due to disease progression. According to this possibility, all pts who received AA after docetaxel (DOC) in our Institution, and discontinued AA due to progressive disease, were usually monitored for at least 4 weeks to evaluate if they developed AWS: if PSA decreased, the subsequent treatment was delayed until the occurrence of biochemical and/or radiological progression; imaging was repeated every 3 months. The aim of the present study was to assess long-term outcomes and predictive factors in DOC pre-treated mCRPC pts experiencing AWS.

Patients and Methods: We evaluated a consecutive series of 73 pre-treated mCRPC pts, who received AA in our Hospital after DOC failure. All pts were treated with AA 1,000 mg per os + prednisone 10 mg per os daily; the treatment continued until progression disease (PD), which required to be confirmed by imaging. After progression, we suspended the prednisone (PDN) administration as well. For each pt we have recorded the pre- and post-AA clinical history, treatment details and outcomes. All pts ended taking AA due to progressive disease and AWS was defined by PSA reduction ≥25%, compared to the AA-end values, observed in the first month after AA cessation. A logistic regression analysis was performed in order to predict AWS. Continuous variables were categorized by quartiles and chosen for the initial model after a univariate Chi-square analysis. Results: AWS was observed in 7 pts (9.5%) with a median duration of 17 wks (range=9-33). Two pts, undergoing the 3-month radiographic restaging, showed an objective response. A significant difference in terms of post-AA median OS was observed between AWS− and AWS+ pts (3.6 vs. 27.9 months; p=0.02); this differences was confirmed by 1-month landmark analysis (4.6 vs. 27.9 months; p=0.03). Among factors, only the absence of pain at AA therapy baseline was able to predict AWS: 100% of AWS− pts were asymptomatic, compared to 64.6% of AWS+ pts (p=0.04).

Conclusion: Despite the fact that AWS remains an unpredictable and rare phenomenon, it could represent a chance to delay the start of subsequent therapeutic line after AA failure. Moreover, our results seem to suggest that the occurrence of AWS may have a positive impact on the OS of mCRPC pts.

114
SEQUENTIAL ADMINISTRATION OF NEW AGENTS AFTER DOCETAXEL IN METASTATIC CASTRATION-RESISTANT PROSTATE CANCER PATIENTS: IMPACT OF DISEASE CONTROL DURATION IN SECOND-LINE ON THE SUBSEQUENT LINE OUTCOMES

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16Medical Oncology Department, General Hospital, Faenza, Italy;
Introduction/Aim: Abiraterone acetate (AA), cabazitaxel (CABA) and enzalutamide (ENZ) are new agents (NAs), which demonstrated their efficacy in metastatic castration-resistant prostate cancer (mCRPC) patients (pts) who have previously treated with docetaxel (DOC). Unfortunately, all pts develop a resistance to these drugs and, eventually, show a progression of disease. Since the androgen receptor machinery remains the ultimate target of NAs in mCRPC post-DOC, some mechanisms of resistance could be common to all NAs. To date, NAs are sequentially administered in the hope of obtaining a cumulative survival benefit. To date, it is unknown if the disease control (DC) duration influences the outcomes of subsequent treatments. The present study was aimed to retrospectively assess this issue in a large series of mCRPC pts. Patients and Methods: We collected data of pts who received sequentially two NAs after DOC in 38 Italian hospitals. For each pt we recorded the clinical outcomes of all treatments received after DOC. For the study’s purpose, we categorized the pts according to the duration of DC (absence of progression) during NA-based second-line treatment: DC ≤3 months (primary resistance (Pre)); DC from 3.1 to 11.9 months (intermediate sensitivity (IS)); DC ≥12 months (long-term disease control (LTDC)). Results: A consecutive series of 291 mCRPC pts of median age 71 years (46-91), with bone (88%), nodal (53%) or visceral (18%) metastases, was examined. All pts received a NA-based as second-line therapy after DOC: 160 (55%) received AA, 99 (33%) CABA and 32 (11%) ENZ. Pre was observed in 56 pts (23 AA; 25 CABA; 8 ENZ), IS in 178 (101 AA; 58 CABA; 19 ENZ) and LTDC in 57 (36 AA; 16 CABA; 5 ENZ). The third line clinical outcomes are detailed in the Table. Conclusion: From this data, it appears that DC duration may be a prognostic factor, as a probable result of pts/disease selection. In fact, pts progressing more than 12 months from the start of NA-based second-line therapy appear to have an increased probability to live longer, compared to pts progressing earlier, when they receive another NA-based third-line therapy.

Table 1. Clinical outcomes of the third line agents according to the second line disease control.

<table>
<thead>
<tr>
<th></th>
<th>PRe</th>
<th>IS</th>
<th>LTDC</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td># pts</td>
<td>56</td>
<td>178</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>Biochemical response rate</td>
<td>14.3%</td>
<td>29.5%</td>
<td>28.1%</td>
<td>0.07</td>
</tr>
<tr>
<td>Objective response rate</td>
<td>17.4%</td>
<td>27.8%</td>
<td>38.5%</td>
<td>0.3</td>
</tr>
<tr>
<td>Median progression-free survival*</td>
<td>3.5</td>
<td>4.5</td>
<td>5.4</td>
<td>0.1</td>
</tr>
<tr>
<td>Median overall survival*</td>
<td>9.1</td>
<td>11.2</td>
<td>20.4</td>
<td>0.002</td>
</tr>
</tbody>
</table>

*From the start of third-line (in months).
Authors Index*
(Figures indicate abstract number. *Missing abstracts were withdrawn.

Addesso M, 68
Alessio P, 76
Alongi F, 63
Alvisi MF, 45, 48
Andolina M, 33
Antonelli A, 72, 73, 74
Avuzzi B, 95
Badenchini F, 38, 44
Bartoncini S, 51
Beltramo G, 7, 8
Bollito E, 99, 100
Bonifazi M, 86
Bonome P, 88
Bruni A, 35
Cacciamani G, 29
Cagna E, 70
Campi R, 77, 78
Cerruto MA, 16, 18, 22
Cicchetti A, 30
Colecchia M, 107
Conti GN, 110, 111
D'agostino GR, 92
D'Angelo A, 15
De Luca S, 55, 66
Dell' Atti L, 1, 2, 3, 4, 6
Fersino S, 14
Festuccia C, 96
Fiori C, 53
Franzese C, 9
Galosi AB, 104, 106
Galuppini F, 36, 40
Garibaldi E, 58
Gravina GL, 102, 103
Guarneri A, 83
Loi M, 61
Maccagnano C, 25, 27, 28
Magli A, 47
Maines F, 114
Mangano MS, 79
Mangolini A, 5
Mari A, 87, 91
Marra G, 71, 75
Marvaso G, 69
Mazzotta M, 32
Meggiato L, 42
Menichetti J, 19
Minervini A, 81, 84, 85, 89, 90
Montebelli F, 43
Moschini M, 10, 11, 12
Olmetto E, 20
Pappagallo G, 108
Pavese F, 37
Piantelli M, 82
Porpiglia F, 54, 57, 59, 62, 64, 105
Rancati T, 94
Roberto M, 31
Rocca GC, 112
Rocchini L, 67
Ruatta F, 98
Russo F, 24
Sanseverino R, 39, 41
Siracusano S, 17, 80
Timon G, 97
Topulli J, 60
Tucci M, 101
Veccia A, 113
Ventura L, 93
Villa S, 34
Zerini D, 13