factors and to reserve salvage radiotherapy for low-risk patients, when biochemical recurrence occurs.

## 110
## PROGNOSTIC ASSESSMENT OF NEOPLASTIC INVOLVEMENT OF THE PROSTATIC APEX IN RADICAL PROSTATECTOMY

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*Aim:* To evaluate the prognostic role of prostatic apex tumor invasion in patients undergoing radical prostatectomy for prostate cancer (pca) clinically organ-confined, and to define its correlation with clinical and pathologic variables (age, clinical stage, preoperative psa,% frustules positive biopsy, Gleason score, surgical margin status). *Patients and Methods:* From our database of 1693 patients who underwent rp between 2000 and 2012 for clinically localized pca, data from 498 patients with pathological stage t2 were retrospectively evaluated. The entire prostate was examined with 2-4 mm intervals transections in a plane perpendicular to the urethra. The apical prostate was separately sectioned and examined in parallel slices and "apical involvement" was defined as the presence of neoplastic glands in the last 8 mm of the prostate. Patients with lymph nodes involvement were treated with early adjuvant hormonal therapy. Biochemical relapse was defined as the evidence of psa>0.2 ng/ml in two consecutive measurements. The probability of biochemical recurrence was estimated by the Kaplan-Meier method, with the log-rank test used to evaluate differences among levels of the analyzed variables (apical involvement, preoperative psa, gleason score, pathological stage, surgical margins status). The multivariate Cox proportional hazard model was used to estimate the relative importance of the variables in predicting survival. *Results:* Overall 280 patients (56.2%) had neoplastic involvement of the prostatic apex. The mean follow-up was 40 months (range 6-154). In 30 patients (6.02%) a biochemical relapse was observed, with a mean time of 30 months (range 3-149). Positive surgical margins were observed in 34 patients (6.8%), of whom, 26 (76.4%) presented involvement of the prostatic apex. The number and the percentage over the total of neoplastic biopsy cores were predictor factors of tumor apex involvement ($p$=0.018). The biochemical recurrence-free survival (brfs) for patients with positive apex was lower than in patients with negative apex (91.9% *vs*. 95.9% at 36 months, 88 % *vs*. 92.8 % at 60 months and 86% *vs*. 92.8% at 120 months, respectively) ($p$=0.05). Positive surgical margins, the apex involvement and pathological stage were significantly correlated with biochemical relapse at univariate analysis. Multivariate analysis confirmed the statistical independence of positive surgical margins ($p$=0.0004, rr=5.17) and apex involvement ($p$=0.0536, rr=2.47). *Conclusion:* The prostatic apex represents a crucial anatomical structure during radical prostatectomy for both oncological and functional outcomes. The absence of a well anatomically defined capsule at this level suppose the risk of understaging at final pathological analysis. Our data showed that tumor invasion into the prostatic apex is a significant prognostic factor regardless of the status of surgical margins.

## 111
## A PROPOSED SCORE FOR ASSESSING PROGRESSION IN PT1 HIGH-GRADE UROTHELIAL CARCINOMA OF THE BLADDER

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*Aim:* We tested a selected series of patients with single urothelial high-grade pT1 stage (pT1 HG) or urothelial carcinoma *in situ* (CIS) with a set of immunohistochemical markers to elaborate a risk score for progression. *Patients and Methods:* We retrospectively reviewed all first diagnoses of single, <3 cm, urothelial papillary carcinoma pT1 HG or isolated CIS between 2006 and 2009. Galectin-3, CD44, E-cadherin, CD138, p16, survivin, HYAL-1, and topoisomerase-II α were used. A grading score 0 or 1 for each immunohistochemical staining was assigned to obtain a total score for assessing progression. The median "progression score" was selected as cut-off value for statistical analysis. Overall, 23 patients (19 pT1 HG and 4 CIS) were included in the study. *Results:* After a median follow-up of 21 months (range, 12 to 34 mo), 9 patients (39.1%) showed disease recurrence whereas 4 patients (17.4%) showed tumor progression. Topoisomerase-II α, p16, survivin, galectin-3, and CD138 were significantly associated with progression. Progression score ranged from 0 (best prognosis) to 7 (worst prognosis). Using a score ≥5 as a threshold, specificity was 78.9%, sensitivity 100%, positive predictive value 50%, and

negative predictive value 100%. ROC area (a 95% confidence interval, 0.807-1.000; $p<0.001$). *Conclusion:* This immunohistochemistry-based progression score using a threshold ≥5, might help the clinician to focus on patients with HG pT1 or extended CIS at high risk for disease progression. These patients might benefit from a more intensive follow-up program or early cystectomy.

## 112
## CHARACTERISTICS OF LONG-TERM BIOCHEMICAL RELAPSE IN PATIENTS WHO UNDERWENT RADICAL PROSTATECTOMY FOR PATHOLOGIC STAGE T2

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*Aim:* To evaluate the characteristics of long term biochemical relapse in a cohort of patients undergoing radical prostatectomy for clinically localized prostatic disease with pathologic stage t2. *Patients and Methods:* From our database of 1628 patients who underwent radical prostatectomy from 2000 to 2012 we analyzed data from 727 patients, mean age 65.1 aa (range, 43-78 yr), with organ-confined disease at the definitive histopathological examination. Biochemical relapse of disease was defined as the relief of psa>0.2 ng/ml in two consecutive samples. Survival was assessed using the Kaplan-Meyer method with the log rank test for univariate analysis and the Cox method for multivariate analysis. We analyzed: the characteristics of biochemical relapse, the need and response to treatment and clinical and pathologic variables which correlate most with the relapse. *Results:* Surgical margins were positive in 64/727 patients (8.8%) and negative in 663/727 (91.2%). Nerve sparing technique (bilateral or unilateral) was performed in 480 of the 727 patients. The mean follow-up was 34.6 months (range 6-154). A biochemical relapse of disease was observed in 73/727 patients (10.04%). The mean time of relapse was 23.9 months (median 23.5, range 3-149). Of these 73 patients, 34 underwent delayed treatment (19 hormonal therapy, 15 radiotherapy). The opportunity of a treatment was evaluated according to patient age, comorbidities and time of relapse. Thirty-nine patients (53.4%) presented an elevation of psa >0.2 ng/ml, which remains stable in a range between 0.2 and 0.5 ng/ml over the years without any radio or hormonal therapy. The disease-free survival was significantly higher for patients with negative margins ($p<0.0001$). Pathological stage (pt2a, pt2b pt2c) and the presence of positive surgical margins (both $p<0.0001$) significantly correlate with the biochemical relapse, and were both confirmed as predictor factors at the multivariate analysis ($p=0.04$ and $<0.001$, respectively). *Conclusion:* An important rate of patients (>50%) presented a stable value of psa between 0.2 and 0.5 ng/ml over the years without any additional therapy. These data show that radical prostatectomy provides control of the disease in almost all patients with organ-confined disease, and, despite the occurrence of biochemical relapse, a treatment is not always necessary.

## 113
## NUCLEAR MATRIX PROTEIN NMP22 ANCILLARY TEST IN THE DETECTION OF UROTHELIAL CARCINOMA

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*Introduction:* Morphological CTM detection in voided urine samples is a cheap and universally adopted exam, though affected by a relatively low sensitivity, because of the usual challenge represented by the interpretation of the "atypical" category. Hence, new analytical methods of cancer detection like abnormal level of NMP22 matrix protein obtained a lot of attention in the last decade. NMP22 is an enzyme linked immunoassay performed in fresh collected urine, aimed to identify the NuMA matrix protein of the neoplastic urothelial cells. The exam is a time (30' to get the answer) and cost effective approach to the problem of splitting the wide "atypical" category of urine sediment. *Methods:* We analyzed 43 fresh voided urine samples both for cytology (one sediment as opposed to the conventional 3 days/3 sediment approach) and NMP22 of 43 patients submitted to TURB resection in the following hours (same day). *Results:* 36 out of 43 patients were positive for papillary urothelial carcinoma (18 low grade and 18 high grade), while 7 cases were affected by cystic cystitis. 19/36 (overall sensitivity: 52%) positive cases were CTM+ (4/18 low grade and 15/18 high grade); 8/36 cases were NMP22+ (overall sensitivity: 22%): 4/18 low grade and 4/18 high grade. None of the 7 negative cases showed morphological or NMP22 positivity. 15/19 cases of CTM+ cases were NMP 22 negative. 4/8 cases of NMP22+ cases were CTM negative (low grade papillary carcinoma). Comments: In the present experience, NMP22 is a test affected by a low sensitivity. Nevertheless, in combination with cytology it may increase the sensitivity of tumor detection, particularly in low grade tumors. Nevertheless, a limitation of our comparison between the two methods is due to the single sediment analysis of the CTM morphological investigation method, that might have further affected its sensitivity (52%).