INTRODUCTION AND OBJECTIVES: Frozen section analysis (FS) of the distal urethral margin is used to determine the feasibility of orthotopic reconstruction or the need for simultaneous urethrectomy in patients undergoing radical cystectomy for the treatment of bladder cancer. Despite the fact that this practice represents the contemporary standard of care, scant data exist upon which to base an evaluation of the accuracy and reliability of urethral FS at the time of surgery. We sought to determine the positive and negative predictive values of urethral FS by analyzing our clinical experience.

METHODS: The IRB-approved, institutional urothelial cancer database (2000-2012) was reviewed for patients undergoing radical cystectomy in which FS had been performed to assess distal urethral margins. We compared urethral FS status with that of the final urethral margin section in order to calculate the positive and negative predictive values of the FS. The cases of positive urethral FS were then specifically analyzed to assess rates of urethral recurrence and survival.

RESULTS: 750 patients with complete pathologic information underwent cystectomy for bladder cancer at our institution during this period (median follow-up, 36.9 months). Urethral FS were sent in 322 cases (43%). All patients with a negative FS were confirmed to have a negative margin on final pathology, resulting in a negative predictive value of 100%. Urethral FS were positive in 28 patients (8.7%), of which 13 (46%) ultimately had negative margins on final pathology, yielding a positive predictive value of 54%. Of the patients with positive urethral FS, 3 underwent urethrectomy (1 concurrent, 2 delayed). Four patients with positive final urethral margins had urethral recurrences (median follow up 29.1 months). These individuals were subsequently treated with adjuvant chemotherapy (2 patients) and urethrectomy (2 patients). No differences in freedom from urethral recurrence or overall survival were seen between those in whom positive FS remained positive (true positive) and those in whom positive FS became negative on final pathology (false positive).

CONCLUSIONS: A negative urethral FS reliably identifies individuals for whom urethrectomy is unnecessary and provides robust information for decision-making regarding the safety of orthotopic reconstruction. Nearly half of the patients with a positive FS were ultimately determined to have a negative final margin. Accordingly, we recommend that surgeons and pathologists discuss positive FS findings at the time of surgery and consider whether additional tissue should be analyzed in real time if practical.

Source of Funding: None

PD33-10
THE PRESENCE OF RESIDUAL CARCINOMA IN SITU ALONE (PTIS) IN PATIENTS TREATED WITH RADICAL CYSTECTOMY DOES NOT AFFECT LONG TERM RECURRENT AND SURVIVAL RATES
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INTRODUCTION AND OBJECTIVES: Local tumor invasion has been individuated as the most important prognostic factor in patients affected by bladder cancer (BCa). However, carcinoma in situ (CIS) is a recognized factor for recurrence and progression in BCa. In patients treated with radical cystectomy (RC), the absence of residual urothelial tumor (pT0) is associated to better survival as compared to other BCa stages. We sought to evaluate the impact of carcinoma in situ (pTis) as the only remaining BCa on recurrence, overall survival (OS) and cancer specific survival (CSS), as compared to patients who harbor pT0 at final pathology.

METHODS: The study focused on 1,280 consecutive non metastatic bladder cancer (BCa) patients treated with RC at a single tertiary care referral center between January 1994 and August 2013. No patients received neoadjuvant chemotherapy. Patients with pT0 or pTis at radical cystectomy specimen were included in the study. Kaplan-Meier analyses were used to assess long term recurrence, CSS and OS in pT0 vs. pTis patients. Cox regression analyses were used to test the role of pTis on the same outcomes, after adjusting for nodal status and age at surgery.

RESULTS: Overall, 128 (10.0%) patients were included in the study. Of these, 57 (45.5%) and 71 (55.5%) patients harbored either pT0 or pTis, respectively. In 8 (6.2%) patients, node metastases were recorded. Median years of follow up was 6 years. The 5-year recurrence free survival, CSS and OS were 80.4%, 85.2%, 82.1%, respectively. The 5-year recurrence free survival was recorded at follow-up (78.5% vs. 82.0%), CSS (85.8% vs. 84.4%), OS (79.2% vs. 84.4%) in patients pT0 vs. pTis, respectively.

Source of Funding: None
INTRODUCTION AND OBJECTIVES: Muscle-invasive bladder cancer (MIBC) can molecularly be grouped into intrinsic basal and luminal subtypes. Tumors within the luminal subtype and a ‘p53-like’ gene expression have been found to be resistant to neoadjuvant chemotherapy (NAC) with methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC). We investigated the response of these subtypes to gemcitabine plus cisplatin (GC), the other major frontline NAC regimen in this disease setting.

METHODS: Fifty-two MIBC patients received neoadjuvant GC followed by cystectomy. At cystectomy, 37 (71%) patients did not respond to NAC (ypT2 or any ypN1-3). With the RNeasy FFPE kit (Qiagen) RNA was isolated from pre-NAC transurethral resection (TUR) specimens and post-NAC cystectomy specimens. After cDNA amplification and labelling with the Ovation WTA FFPE system and Encore Biotin Module (NuGen) samples were hybridized to GeneChip Human Exon 1.0 ST oligonucleotide microarrays (Affymetrix). The tumors were assigned to the intrinsic subtypes using a one nearest neighbor prediction model.

RESULTS: Unsupervised hierarchical clustering separated the tumors into clusters characterized by non-overlapping expression of basal or luminal biomarkers. Assignment of pretreatment TUR tumors to subtypes yielded the expected ratios of basal, p53-like, and luminal tumors of which 5/14 (36%), 2/15 (17%) and 8/23 (35%) showed pathological down staging (<ypT2 any ypN neg), respectively. p53-like tumors had significantly the shortest recurrence free (p=0.006) and overall survival (p=0.003) compared to the other subtypes. Basal tumors with an enrichment of an immune signature responded to NAC, although this did not reach statistical significance. Matched analysis of tumors before and after NAC revealed an enrichment for p53-like tumors at cystectomy.

CONCLUSIONS: In line with the MVAC data, p53-like tumors displayed resistance to neoadjuvant GC. Moreover, p53-ness is associated with unfavorable outcome in MIBC treated with NAC. If these results are confirmed prospectively, patients with p53-like tumors should not be treated with cisplatin-based chemotherapy and should instead be steered to immediate cystectomy or clinical trials of novel therapies.

Source of Funding: GenomeDx Biosciences

PD33-11
NEOADJUVANT CHEMOTHERAPY IN BLADDER CANCER: P53-NESS IS ASSOCIATED WITH CHEMO-RESISTANCE AND UNFAVORABLE OUTCOME
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PD33-12
SINGLE LYMPH NODE MALIGNANT INVOLVEMENT POST RADICAL CYSTECTOMY FOR UROTHELIAL CARCINOMA OF THE BLADDER: CLINICAL OUTCOMES AND PROGNOSTIC IMPLICATIONS

INTRODUCTION AND OBJECTIVES: The number of positive lymph nodes is an important determinant of bladder cancer prognosis. It has been postulated that patients with single positive lymph nodes have good prognosis and can be cured with adequate lymphadenectomy. We aimed to characterize the clinical outcomes of patients with single positive lymph nodes in comparison to those with negative nodes and those with more than one positive node.

METHODS: We retrospectively reviewed our database for patients who underwent radical cystectomy and lymphadenectomy with curative intent for urothelial carcinoma of the bladder. Clinical and pathologic data were evaluated. Patients were analyzed in three groups according to node positivity: node negative, single positive lymph node, and more than one positive lymph node. Kaplan-Meier analysis with log rank test was performed to evaluate disease specific survival. Multivariable Cox regression modeling (including pathologic T stage, lymphovascular invasion, number of removed lymph nodes and adjuvant chemotherapy) was performed to evaluate associations between node positivity and survival.

RESULTS: In total, 1202 patients met the inclusion criteria. Of them, 862 (71.7%) patients had node negative disease, 123 (10.2%) had single positive lymph node and 217 (18%) had more than one positive lymph node. Five-year recurrence-free survival rates were 74.5% for node negative disease, 45.2% for those with single positive lymph node (p<0.001) and 35.6% for those with more than one positive lymph node (p=0.031). Subgroup analysis according to organ confinement revealed that single positive lymph node with organ-confined disease (pT2 or less) has the same survival as node negative disease with extravesical involvement (pT3 or more) 55.5% vs. 54.3% (p=0.064). (Figure 1) Multivariable analysis identified the number of positive lymph nodes and the presence of extravesical disease as predictors of lower recurrence-free survival (HR 2.43, p=0.031 and HR 2.25, p=0.015, respectively).

CONCLUSIONS: Single positive lymph node involvement reduces the survival by more than 20%. Single positive lymph node involvement with organ confined disease is associated with equivalent survival outcomes to node negative extravesical disease. Adjuvant therapy may be required in these patients.

Source of Funding: none